MODULATORS OF CELL SURFACE PROTEIN INTERACTIONS AND METHODS AND COMPOSITIONS RELATED TO SAME

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on March 27, 2020, is named 50474-182WO3_Sequence_Listing_3.27.20_ST25 and is 24,492 bytes in size.

FIELD OF THE INVENTION

Provided herein are methods for identifying modulators of cell surface protein interactions and activities, as well as modulators of cell surface protein interactions and activities.

BACKGROUND

Recent annotations predict that over 5,000 genes in the human genome encode plasma membrane-expressed or secreted proteins, i.e., proteins acting at the cell surface. Classes of proteins present at the cell surface include cell surface receptors (e.g., single transmembrane (STM) receptors) and Immunoglobulin Superfamily (IgSF) proteins. Many of these proteins have been linked to cancer and other diseases, and are thus prime targets for development of therapeutic agents; however, the binding partners of many plasma membrane proteins (e.g., STM and IgSF proteins) have remained uncharacterized. This discrepancy is due to the incompatibility of currently used proteomics technologies, e.g., yeast two-hybrid assays and affinity purification/mass spectrometry (AP/MS), for studying plasma membrane-expressed proteins. High-throughput screens for extracellular protein-protein interactions have recently been developed; however, therapeutic agents that modulate the majority of these interactions have not yet been identified.

Thus, there is an unmet need for methods and compositions for the identification of interactions between cell surface proteins, as well as novel modulators of such interactions and methods of using the same.

SUMMARY OF THE INVENTION

The present invention provides methods for identifying modulators of cell surface protein interactions and activities, as well as modulators of cell surface protein interactions and activities.

In one aspect, the disclosure features a method of identifying an individual having a cancer who may benefit from a treatment comprising a PD-L1 axis binding antagonist, the method comprising determining an expression level of a first member and a second member of at least one of the gene pairs of Table 15 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment comprising a PD-L1 axis binding antagonist.

In another aspect, the disclosure features a method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of a first member and a second member at least one of the gene pairs of Table 15 in a sample from the individual, wherein an expression level of

the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment comprising a PD-L1 axis binding antagonist.

In some aspects, the individual has an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level and the method further comprises administering to the individual an effective amount of a PD-L1 axis binding antagonist.

In another aspect, the disclosure features a method of treating an individual having a cancer, the method comprising (a) determining an expression level of a first member and a second member at least one of the gene pairs of Table 15 in a sample from the individual, wherein the expression level of the first member of the gene pair is above a first reference expression level and the expression level of the second member of the gene pair is above a second reference expression level; and (b) administering an effective amount of a PD-L1 axis binding antagonist to the individual.

In another aspect, the disclosure features a method of treating an individual having a cancer, the method comprising administering a PD-L1 axis binding antagonist to an individual who has been determined to have an expression level of a first member of a gene pair of Table 15 that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level.

In another aspect, the disclosure features a method of identifying an individual having a cancer who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist, the method comprising determining an expression level of a first member and a second member of at least one of the gene pairs of Table 16 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist.

In another aspect, the disclosure features a method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of a first member and a second member at least one of the gene pairs of Table 16 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist.

In some aspects, the individual has an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level and the method comprises administering to the individual an effective amount of a treatment other than or in addition to a PD-L1 axis binding antagonist.

In some aspects, the first reference expression level is a pre-assigned expression level and the second reference expression level is a pre-assigned reference expression level.

In some aspects, the sample from the individual is obtained from the individual prior to administration of an anti-cancer therapy. In some aspects, the sample from the individual is obtained from the individual after administration of an anti-cancer therapy.

In some aspects, the sample from the individual is a tumor tissue sample or a tumor fluid sample.

In some aspects, the sample is a formalin-fixed and paraffin-embedded (FFPE) sample, an archival sample, a fresh sample, or a frozen sample. In some aspects, the tumor tissue sample is a FFPE sample.

In some aspects, the expression level of the first member and the second member of the gene pair in the sample is a protein expression level; or the expression level of the first member and the second member of the gene pair in the sample is an mRNA expression level. In some aspects, the expression level of the first member and the second member of the gene pair in the sample is a mRNA expression level of the first member and the second member of the gene pair, respectively.

In some aspects, the mRNA expression level of the first member and the second member of the gene pair is determined by *in situ* hybridization (ISH), RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, FISH, or a combination thereof. In some aspects, the first reference expression level is between about 0.25 to about 0.5 counts per million (CPM) and the second reference expression level is between about 0.25 to about 0.5 CPM. In some aspects, the first reference expression level is 0.25 CPM and the second reference expression level is 0.25 CPM.

In some aspects, the first reference expression level and the second reference expression level are expression levels of the first member and the second member of the gene pair, respectively, in a reference population of individuals having a cancer. In some aspects, the cancer is a urinary tract cancer, e.g., a urinary tract carcinoma, e.g., a locally advanced urothelial carcinoma or a metastatic urothelial carcinoma (mUC).

In some aspects, the benefit comprises an extension in the individual's overall survival (OS) as compared to treatment without the PD-L1 axis binding antagonist.

In some aspects, the first member of the gene pair is SIGLEC6 and the second member of the gene pair is NCR1.

In some aspects, the first member of the gene pair is BTN3A1 and the second member of the gene pair is LRRC4B.

In some aspects, the first member of the gene pair is CD80 and the second member of the gene pair is CTLA4.

In some aspects, the first member of the gene pair is BTN3A3 and the second member of the gene pair is LRRC4B.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is TRHDE.

In some aspects, the first member of the gene pair is CTLA4 and the second member of the gene pair is PCDHGB4.

In some aspects, the first member of the gene pair is CTLA4 and the second member of the gene pair is FAM200A.

In some aspects, the first member of the gene pair is CA12 and the second member of the gene pair is SIGLEC6.

In some aspects, the first member of the gene pair is ILDR2 and the second member of the gene pair is CLEC12B.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is ITLN1.

In some aspects, the first member of the gene pair is CADM1 and the second member of the gene pair is CRTAM.

In some aspects, the first member of the gene pair is CD79B and the second member of the gene pair is CD244.

In some aspects, the first member of the gene pair is DAG1 and the second member of the gene pair is EFNB1.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is EVC2.

In some aspects, the first member of the gene pair is GPC4 and the second member of the gene pair is FGFRL1.

In some aspects, the first member of the gene pair is EFNB3 and the second member of the gene pair is EPHB4.

In some aspects, the first member of the gene pair is PTPRD and the second member of the gene pair is LRFN4.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is AQPEP.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is DSG4.

In some aspects, the first member of the gene pair is LDLR and the second member of the gene pair is LILRB5.

In some aspects, the first member of the gene pair is EFNB3 and the second member of the gene pair is EPHB3.

In some aspects, the first member of the gene pair is PLXNB3 and the second member of the gene pair is SEMA4G.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is EPHB6.

In some aspects, the first member of the gene pair is FLT4 and the second member of the gene pair is FLRT2.

In some aspects, the first member of the gene pair is AXL1 and the second member of the gene pair is IL1RL1.

In some aspects, the first member of the gene pair is CD320 and the second member of the gene pair is IGSF5.

In some aspects, the first member of the gene pair is CD59 and the second member of the gene pair is STAB1.

In some aspects, the first member of the gene pair is CNTN3 and the second member of the gene pair is PTPRG.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is EPHA3.

In some aspects, the first member of the gene pair is EFNB3 and the second member of the gene pair is EPHB2.

In some aspects, the first member of the gene pair is EGF and the second member of the gene pair is TNFRSF11B.

In some aspects, the first member of the gene pair is ENPEP and the second member of the gene pair is SLITRK1.

In some aspects, the first member of the gene pair is FCGR3B and the second member of the gene pair is EDA2R.

In some aspects, the first member of the gene pair is IL20RA and the second member of the gene pair is CLEC14A.

In some aspects, the first member of the gene pair is IL6R and the second member of the gene pair is BTNL9.

In some aspects, the first member of the gene pair is IZUMO1 and the second member of the gene pair is LILRA5.

In some aspects, the first member of the gene pair is NGFR and the second member of the gene pair is LRRTM3.

In some aspects, the first member of the gene pair is NTM and the second member of the gene pair is AMIGO2.

In some aspects, the first member of the gene pair is PCDHB3 and the second member of the gene pair is IGSF11.

In some aspects, the first member of the gene pair is PTGFRN and the second member of the gene pair is TMEM59L.

In some aspects, the first member of the gene pair is TREM1 and the second member of the gene pair is VSIG8.

In some aspects, the PD-L1 axis binding antagonist is selected from the group consisting of a PD-L1 binding antagonist, a PD-1 binding antagonist, and a PD-L2 binding antagonist.

In some aspects, the PD-L1 axis binding antagonist is a PD-L1 binding antagonist.

In some aspects, the PD-L1 binding antagonist inhibits the binding of PD-L1 to one or more of its ligand binding partners.

In some aspects, the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1.

In some aspects, the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1.

In some aspects, the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1.

In some aspects, the PD-L1 binding antagonist is an antibody or antigen-binding fragment thereof.

In some aspects, the antibody is selected from the group consisting of atezolizumab, MDX-1105, MEDI4736 (durvalumab), and MSB0010718C (avelumab).

In some aspects, the anti-PD-L1 antibody comprises the following hypervariable regions: (a) an HVR-H1 sequence of GFTFSDSWIH (SEQ ID NO: 19); (b) an HVR-H2 sequence of AWISPYGGSTYYADSVKG (SEQ ID NO: 20); (c) an HVR-H3 sequence of RHWPGGFDY (SEQ ID NO: 21); (d) an HVR-L1 sequence of RASQDVSTAVA (SEQ ID NO: 22); (e) an HVR-L2 sequence of SASFLYS (SEQ ID NO: 23); and (f) an HVR-L3 sequence of QQYLYHPAT (SEQ ID NO: 24).

In some aspects, the anti-PD-L1 antibody comprises: (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 3; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 4; or (c) a VH domain as in (a) and a VL domain as in (b).

In some aspects, the anti-PD-L1 antibody comprises (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 3; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 4; or (c) a VH domain as in (a) and a VL domain as in (b).

In some aspects, the anti-PD-L1 antibody comprises (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 96% sequence identity to the amino acid sequence of SEQ ID NO: 3; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 96% sequence identity to the amino acid sequence of SEQ ID NO: 4; or (c) a VH domain as in (a) and a VL domain as in (b).

In some aspects, the anti-PD-L1 antibody comprises (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 97% sequence identity to the amino acid sequence of SEQ ID NO: 3; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 97% sequence identity to the amino acid sequence of SEQ ID NO: 4; or (c) a VH domain as in (a) and a VL domain as in (b).

In some aspects, the anti-PD-L1 antibody comprises (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 98% sequence identity to the amino acid sequence of SEQ ID NO: 3; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 98% sequence identity to the amino acid sequence of SEQ ID NO: 4; or (c) a VH domain as in (a) and a VL domain as in (b).

In some aspects, the anti-PD-L1 antibody comprises (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 3; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 4; or (c) a VH domain as in (a) and a VL domain as in (b).

In some aspects, the anti-PD-L1 antibody comprises (a) a VH domain comprising the amino acid sequence of SEQ ID NO: 3; and (b) a VL domain comprising the amino acid sequence of SEQ ID NO: 4.

In some aspects, the anti-PD-L1 antibody is atezolizumab (MPDL3280A).

In some aspects, the PD-L1 axis binding antagonist is a PD-1 binding antagonist. In some aspects, the PD-1 binding antagonist inhibits the binding of PD-1 to one or more of its ligand binding partners.

In some aspects, the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1.

In some aspects, the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L2.

In some aspects, the PD-1 binding antagonist inhibits the binding of PD-1 to both PD-L1 and PD-L2.

In some aspects, the PD-1 binding antagonist is an antibody or antigen-binding fragment thereof.

In some aspects, the antibody is selected from the group consisting of: MDX-1106 (nivolumab), MK-3475 (pembrolizumab), MEDI-0680 (AMP-514), PDR001, REGN2810, and BGB-108.

In some aspects, the PD-1 binding antagonist is an Fc-fusion protein.

In another aspect, the disclosure features a method of treating an individual having a cancer comprising administering to the individual an effective amount of an agonist of CD177 activity.

In another aspect, the disclosure features a method of identifying an individual having a cancer who may benefit from a treatment comprising an agonist of CD177 activity, the method comprising determining an expression level of podoplanin (PDPN) in a sample from the individual, wherein an expression level of PDPN in the sample that is above a reference PDPN expression level identifies the individual as one who may benefit from a treatment comprising an agonist of CD177 activity.

In another aspect, the disclosure features a method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of PDPN in a sample from the individual, wherein an expression level of PDPN in the sample that is above a reference PDPN expression level identifies the individual as one who may benefit from a treatment comprising an agonist of CD177 activity.

In some aspects, the individual has an expression level of PDPN in the sample that is above a reference PDPN expression level and the method further comprises administering to the individual an effective amount of an agonist of CD177 activity.

In another aspect, the disclosure features a method of treating an individual having a cancer, the method comprising (a) determining an expression level of PDPN in a sample from the individual, wherein the expression level of PDPN in the sample is above a reference PDPN expression level; and (b) administering to the individual an effective amount of an agonist of CD177 activity.

In another aspect, the disclosure features a method of treating an individual having a cancer, the method comprising administering to the individual an effective amount of an agonist of CD177 activity, wherein the expression level of PDPN in a sample from the individual has been determined to be above a reference PDPN expression level.

In some aspects, the CD177 activity is inhibition of PDPN.

In some aspects, the sample from the individual is a tumor tissue sample or a tumor fluid sample. In some aspects, the tumor tissue sample is a formalin-fixed and paraffin-embedded (FFPE) sample, an archival sample, a fresh sample, or a frozen sample.

In some aspects, the expression level of PDPN in the sample is a protein expression level of PDPN or an RNA expression level of PDPN. In some aspects, the expression level of PDPN in the sample

is an RNA expression level of PDPN. In some aspects, the RNA expression level of PDPN is determined by *in situ* hybridization (ISH), RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, FISH, or a combination thereof.

In some aspects, the reference PDPN expression level is an expression level of PDPN in a population of individuals having a cancer. In some aspects, the cancer is a colorectal cancer (CRC), a squamous cell carcinoma of the head and neck, or a glioma.

In some aspects, the reference PDPN expression level is the 50th percentile of expression levels in the population.

In some aspects, the reference PDPN expression level is the 66th percentile of expression levels in the population.

In some aspects, the reference PDPN expression level is a pre-assigned PDPN expression level.

In some aspects, the cancer is a CRC, a squamous cell carcinoma of the head and neck, or a glioma. In some aspects, the cancer is a CRC, e.g., a stage II CRC or a stage IV CRC.

In some aspects, the benefit comprises an extension in the individual's recurrence-free survival (RFS) as compared to treatment without the agonist of CD177 activity.

In some aspects, the agonist of CD177 activity results in an increase in the binding of PDPN and CD177 relative to binding of the two proteins in the absence of the agonist.

In some aspects, the agonist of CD177 activity results in a change in a downstream activity of PDPN relative to the downstream activity in the absence of the agonist of CD177 activity.

In some aspects, the change in the downstream activity is a decrease in tumor growth.

In some aspects, the change in the downstream activity is a decrease in cancer-associated fibroblast (CAF) contractility.

In some aspects, the agonist of CD177 activity is a small molecule, an antibody or antigen-binding fragment thereof, a peptide, or a mimic.

In some aspects, the agonist of CD177 activity is a peptide. In some aspects, the peptide is a CD177 peptide. In some aspects, the CD177 peptide is an extracellular domain of CD177. In some aspects, the peptide is multimerized, e.g., tetramerized, e.g., tetramerized using streptavidin.

In some aspects, the agonist of CD177 activity is an antibody or antigen-binding fragment thereof.

In some aspects, the antibody or antigen-binding fragment thereof binds PDPN. In some aspects, the antibody or antigen-binding fragment thereof is an antagonist antibody or antigen-binding fragment thereof.

In some aspects, the antibody or antigen-binding fragment thereof binds CD177. In some aspects, the antibody or antigen-binding fragment thereof is an agonist antibody or antigen-binding fragment thereof.

In some aspects, the antigen-binding fragment is a bis-Fab, an Fv, a Fab, a Fab'-SH, a F(ab')$_2$, a diabody, a linear antibody, an scFv, an ScFab, a VH domain, or a VHH domain.

In some aspects, the individual is a human.

In another aspect, the disclosure features a collection of polypeptides, wherein each polypeptide comprises an extracellular domain, a tag, and an anchor, and wherein the collection of polypeptides comprises the extracellular domains of at least 81% of the proteins of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domains of at least 85% of the proteins of Table 7. In some aspects, the collection of polypeptides comprises at least 90% of the proteins of Table 7. In some aspects, the collection of polypeptides comprises the extracellular domains of at least 95% of the proteins of Table 7. In some aspects, the collection of polypeptides comprises the extracellular domains of all of the proteins of Table 7.

In some aspects, the anchor is capable of tethering the extracellular domain to the surface of a plasma membrane of a cell. In some aspects, the anchor is a glycosylphosphatidyl-inositol (GPI) polypeptide.

In some aspects, the tag can be directly or indirectly visualized. In some aspects, the tag comprises a moiety that can be detected using an antibody or an antibody fragment. In some aspects, the tag is a glycoprotein D (gD) polypeptide. In some aspects, the tag comprises a fluorescent protein.

In some aspects, the extracellular domain has a native conformation. In some aspects, the extracellular domain comprises a native post-translational modification.

In some aspects, the cell is a mammalian cell. In some aspects, the cell is a COS7 cell.

In some aspects, the cell has been transiently transfected with a plasmid encoding the polypeptide.

In another aspect, the disclosure features a collection of vectors encoding the collection of polypeptides of any one of the above aspects.

In another aspect, the disclosure features a collection of cells comprising the collection of vectors vectors of the above aspect. In some aspects, a plurality of the cells are capable of expressing at least one polypeptide of any one of the above aspects, optionally wherein different cells express different polypeptides.

In some aspects, each of the one or more of said polypeptides is immobilized to a distinct location on one or more solid surfaces.

In another aspect, the disclosure features a method for identifying a protein-protein interaction, the method comprising providing the collection of polypeptides of any one of the above aspects, optionally wherein said polypeptides are immobilized on one or more solid surfaces; contacting the collection of step (a) with a multimerized query protein under conditions permitting the binding of the multimerized query protein and at least one of the extracellular domains of the polypeptides; and detecting an interaction between the multimerized query protein and the at least one extracellular domain, thereby identifying a protein-protein interaction. In some aspects, one or more of said polypeptides each is immobilized to a distinct location on said one or more solid surfaces. In some aspects, the distinct location comprises a cell that displays the polypeptide.

In some aspects, the cells are mammalian cells.

In some aspects, the contacting step is semi-automated.

In some aspects, detecting an interaction comprises detecting a signal, optionally a fluorescent signal, at a location on the solid surface that is above a threshold level. In some aspects, the detecting is automated.

In some aspects, the interaction is a transient interaction.

In some aspects, the interaction is a low-affinity interaction. In some aspects, the low-affinity interaction is a micromolar-affinity interaction.

In some aspects, the multimerized query protein is a dimerized, trimerized, tetramerized, or pentamerized query protein. In some aspects, the multimerized query protein is a tetramerized query protein. In some aspects, the multimerized query protein comprises an isolated extracellular domain of the query protein. In some aspects, the isolated extracellular domain of the query protein has been biotinylated and conjugated to a fluorescent streptavidin to tetramerize the query protein.

In another aspect, the disclosure features a method of identifying a modulator of the interaction between a protein of Table 1 and a protein of Table 2, the method comprising (a) providing a candidate modulator; (b) contacting a protein of Table 1 with a protein of Table 2 in the presence or absence of the candidate modulator under conditions permitting the binding of the protein of Table 1 to the protein of Table 2, wherein the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (c) measuring the binding of the protein of Table 1 to the protein of Table 2, wherein an increase or decrease in binding in the presence of the candidate modulator relative to binding in the absence of the candidate modulator identifies the candidate modulator as a modulator of the interaction between the protein of Table 1 and the protein of Table 2.

In another aspect, the disclosure features a method of identifying a modulator of a downstream activity of a protein of Table 1, the method comprising (a) providing a candidate modulator; (b) contacting the protein of Table 1 with a protein of Table 2 in the presence or absence of the candidate modulator under conditions permitting the binding of the protein of Table 1 to the protein of Table 2, wherein the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (c) measuring a downstream activity of the protein of Table 1, wherein a change in the downstream activity in the presence of the candidate modulator relative to the downstream activity in the absence of the candidate modulator identifies the candidate modulator as a modulator of the downstream activity of the protein of Table 1.

In another aspect, the disclosure features a method of identifying a modulator of a downstream activity of a protein of Table 2, the method comprising (a) providing a candidate modulator; (b) contacting the protein of Table 2 with a protein of Table 1 in the presence or absence of the candidate modulator under conditions permitting the binding of the protein of Table 2 to the protein of Table 1, wherein the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (c) measuring a downstream activity of the protein of Table 2, wherein a change in the downstream activity in the presence of the candidate modulator relative to the downstream activity in the absence of the candidate modulator identifies the candidate modulator as a modulator of the downstream activity of the protein of Table 2.

In some aspects, the increase or decrease in binding is at least 70%, as measured by surface plasmon resonance, biolayer interferometry, or an enzyme-linked immunosorbent assay (ELISA).

In some aspects, the modulator is an inhibitor of the downstream activity of the protein of Table 1 or Table 2. In some aspects, the modulator is an activator of the downstream activity of the protein of Table 1 or Table 2.

In some aspects, the change in the downstream activity is a decrease in the amount, strength, or duration of the downstream activity. In some aspects, the change in the downstream activity is an increase in the amount, strength, or duration of the downstream activity.

In some aspects, the modulator is a small molecule, an antibody or antigen-binding fragment thereof, a peptide, a mimic, an antisense oligonucleotide, or a small interfering RNA (siRNA). In some aspects, the antigen-binding fragment is a bis-Fab, an Fv, a Fab, a Fab'-SH, a $F(ab')_2$, a diabody, a linear antibody, an scFv, an ScFab, a VH domain, or a VHH domain. In some aspects, the antibody or antigen-binding fragment thereof binds the protein of Table 1. In some aspects, the antibody or antigen-binding fragment thereof binds the protein of Table 2.

In some aspects, the protein of Table 1 is podoplanin (PDPN). In some aspects, the protein of Table 2 is CD177.

In some aspects, the downstream activity is cancer-associated fibroblast (CAF) contractility. In some aspects, CAF contractility is decreased in the presence of the modulator. In some aspects, CAF contractility is decreased by at least 20%, as measured in a gel contraction assay. In some aspects, CAF contractility is decreased by at least 20%, as measured in a 3D gel elongation assay.

In some aspects, the downstream activity is tumor growth. In some aspects, tumor growth is decreased in the presence of the modulator. In some aspects, tumor growth is decreased by at least 20%, as measured in a tumor growth assay.

In some aspects, the modulator is an antibody or antigen-binding fragment thereof targeting PDPN. In some aspects, the modulator is an antibody or antigen-binding fragment thereof targeting CD177.

In some aspects, the protein of Table 1 is PD-L1 (CD274). In some aspects, the protein of Table 2 is EPHA3.

In some aspects, the protein of Table 1 is PD-L2 (PDCD1LG2). In some aspects, the protein of Table 2 is CEACAM4, ICAM5, NECTIN3, PSG9, or TNFRSF11A. In some aspects, the protein of Table 2 is CEACAM4.

In some aspects, the downstream activity is immune checkpoint inhibition. In some aspects, immune checkpoint inhibition is decreased in the presence of the modulator. In some aspects, immune checkpoint inhibition is decreased by at least 30%, as measured in a cell-based assay.

In some aspects, the protein of Table 1 is PTPRD. In some aspects, the PTPRD comprises a G203E and K204E; R232C and R233C; P249L; G285E; E406K; S431L; R561Q; P666S; E755K; V892I; S912F; R995C; or R1088C amino acid substitution mutation or a ΔG61 ΔE106 amino acid deletion mutation. In some aspects, the protein of Table 2 is BMP5, CEACAM3, IL1RAP, IL1RAPL2, LECT1, LRFN5, SIRPG, SLITRK3, SLITRK4, SLITRK6, or TGFA.

In some aspects, the downstream activity is suppression of cell proliferation. In some aspects, suppression of cell proliferation is increased in the presence of the modulator. In some aspects, suppression of cell proliferation is increased by at least 30%, as measured in a colony formation assay. In some aspects, the downstream activity is suppression of STAT3 phosphorylation. In some aspects, suppression of STAT3 phosphorylation is increased in the presence of the modulator. In some aspects,

suppression of STAT3 phosphorylation is increased by at least 30%, as measured in a Western blot for phosphorylated STAT3.

In some aspects, the protein of Table 1 is PTPRS. In some aspects, the protein of Table 2 is C6orf25, IL1RAP, IL1RAPL1, IL1RAPL2, LRFN1, LRFN5, LRRC4B, NCAM1, SLITRK1, SLITRK2, SLITRK3, SLITRK4, or SLITRK6.

In some aspects, the protein of Table 1 is PTPRF. In some aspects, the protein of Table 2 is CD177, IL1RAP, or LRFN5.

In some aspects, the downstream activity is inhibition of cell migration. In some aspects, inhibition of cell migration is increased in the presence of the modulator. In some aspects, inhibition of cell migration is increased by at least 20%.

In some aspects, the downstream activity is phosphorylation of EGFR. In some aspects, phosphorylation of EGFR is decreased in the presence of the modulator. In some aspects, phosphorylation of EGFR is decreased by at least 30%, as measured in an assay for phosphorylation of EGFR.

In some aspects, the protein of Table 1 is CHL1. In some aspects, the protein of Table 2 is CNTN1, CNTN5, SIRPA, L1CAM, or TMEM132A.

In some aspects, the downstream activity is suppression of tumor formation. In some aspects, suppression of tumor formation is increased in the presence of the modulator. In some aspects, suppression of tumor formation is increased by at least 20%.

In some aspects, the protein of Table 1 is CNTN1. In some aspects, the protein of Table 2 is CDH6, CHL1, FCGRT, PCDHB7, or SGCG.

In some aspects, the downstream activity is cell proliferation or cell invasion. In some aspects, cell proliferation or cell invasion is decreased in the presence of the modulator. In some aspects, cell proliferation is decreased by at least 20%, as measured in a colony formation assay. In some aspects, cell invasion is decreased by at least 20%, as measured in a gel invasion assay.

In some aspects, the protein of Table 1 is LILRB1. In some aspects, the protein of Table 2 is CLEC6A, CXADR, EDAR, FLT4, IL6R, ILDR1, or LILRA5.

In some aspects, the downstream activity is suppression of phagocytosis. In some aspects, suppression of phagocytosis is decreased in the presence of the modulator. In some aspects, suppression of phagocytosis is decreased by at least 20%.

In some aspects, the protein of Table 1 is LILRB2. In some aspects, the protein of Table 2 is IGSF8 or MOG.

In some aspects, the protein of Table 1 is LILRB3. In some aspects, the protein of Table 2 is LRRC15 or LY6G6F.

In some aspects, the protein of Table 1 is LILRB4. In some aspects, the protein of Table 2 is CNTFR.

In some aspects, the protein of Table 1 is LILRB5. In some aspects, the protein of Table 2 is APLP2, CD177, CLEC10A, CLECSF13, LDLR, PILRA, or UNC5C. In some aspects, the protein of Table 2 is LDLR.

In some aspects, the downstream activity is osteoclast differentiation. In some aspects, osteoclast differentiation is decreased by at least 20% in the presence of the modulator. In some aspects, osteoclast differentiation is measured in an assay for TRAP+ multinucleated cells.

In some aspects, the protein of Table 1 is AXL. In some aspects, the protein of Table 2 is IL1RL1 or VSIG10L.

In some aspects, the downstream activity is activation of the RAS/RAF/MAPK/ERK1/2 pathway, activation of the JAK/STAT pathway, activation of the PI3K signaling pathway, cell migration, formation of filopodia, or phosphorylation of AXL. In some aspects, cell migration is decreased by at least 20% as measured in a gel invasion assay.

In some aspects, the protein of Table 1 is LRRC4B. In some aspects, the protein of Table 2 is BTN3A1 or BTN3A3

In some aspects, expression of the protein of Table 1 or the protein of Table 2 is upregulated or downregulated in tumor tissue relative to healthy tissue.

In another aspect, the disclosure features an isolated modulator of the interaction between a protein of Table 1 and a protein of Table 2, wherein (a) the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (b) the modulator causes an increase or decrease in the binding of the protein of Table 1 to the protein of Table 2 relative to binding in the absence of the modulator.

In another aspect, the disclosure features an isolated modulator of the downstream activity of a protein of Table 1 or a protein of Table 2, wherein (a) the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (b) the modulator causes a change in the downstream activity of the protein of Table 1 or the protein of Table 2 relative to downstream activity in the absence of the modulator.

In some aspects, the increase or decrease in binding is at least 70%, as measured by surface plasmon resonance, biolayer interferometry, or an enzyme-linked immunosorbent assay (ELISA).

In some aspects, the modulator is an inhibitor of the downstream activity of the protein of Table 1 or Table 2. In some aspects, the modulator is an activator of the downstream activity of the protein of Table 1 or Table 2.

In some aspects, the change in the downstream activity is a decrease in the amount, strength, or duration of the downstream activity. In some aspects, the change in the downstream activity is an increase in the amount, strength, or duration of the downstream activity.

In some aspects, the modulator is a small molecule, an antibody or antigen-binding fragment thereof, a peptide, or a mimic. In some aspects, the antigen-binding fragment is a bis-Fab, an Fv, a Fab, a Fab'-SH, a $F(ab')_2$, a diabody, a linear antibody, an scFv, an ScFab, a VH domain, or a VHH domain. In some aspects, the antibody or antigen-binding fragment thereof binds the protein of Table 1. In some aspects, the antibody or antigen-binding fragment thereof binds the protein of Table 2.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1A is a pair of graphs showing the occurrence of main protein domains and motifs according to UniProt annotations in the set of immunoglobulin superfamily (IgSF) members and other non-IgSF

proteins that were tested for pairwise interaction in the study. EGF = epidermal growth factor, TNF = tumor necrosis factor.

Fig. 1B is a schematic diagram depicting the automated high-throughput technology for extracellular interactome discovery (extracellular interaction screen). (I) depicts a library of STM receptors (prey proteins) consisting of 1,364 human proteins expressed as receptor extracellular domain (ECD)-Fc fusion proteins for expression in the conditioned media of transfected cells. (II) depicts a library of IgSF priority members (query proteins) to be tested for binding against the collection of STM receptors. IgSF proteins were expressed as pentameric constructs fused to a beta lactamase enzyme for increased binding avidity and sensitive detection of binding partners. (III) depicts the automated extracellular interaction screen. Each IgSF query protein was screened for binding to all STM receptors and processed through a computational pipeline to minimize false positive, incorporate gene expression data, and enable further analyses. (IV) depicts the IgSF interactome, which comprises more than 800 high confidence protein-protein interactions. (V) depicts a method for validation of selected interactions. Validation methods include surface plasmon resonance and immunofluorescence for detection of binding partners on the cell surface.

Fig. 1C is a scatter plot showing two independent replicates of the extracellular interaction screen for each of PD-1 (PDCD1) and PD-L2 (PDCD1LG2). Binding partners known from the literature are depicted in blue; these binding partners are PDCD1LG2 and CD274 for PD-1 and PDCD1 for PD-L2.

Fig. 2A is a network representation of all predicted receptor interaction pairs identified by the extracellular interaction screen (the "IgSF interactome"). Nodes represent the IGSF query and STM prey proteins, and edges represent the interactions between them. The node size corresponds to the number of network neighbors (node degree) to indicate network hubs. Edges representing known interactions (e.g., interactions previously predicted in the Bioplex, Biogrid, or STRING databases) are depicted in red. Recapitulated sub-networks mapping to well-studied immunoglobulin (Ig) families are marked as follows: (1) the Semaphorin-Plexin sub-network; (2) The ephrin receptor tyrosine kinase sub-network; (3) the PD-1/PD-L1 immune regulatory axis; and (4) the PVR/TIGIT sub-network.

Fig. 2B is a ridge plot showing the separation in Specificity Score distributions between the Non-specific, Positive, and Negative classes in the training set.

Fig. 2C is a regression plot depicting that the topological coefficients within the IgSF interactome network follow a power law, a hallmark of scale-free networks.

Fig. 2D is a Venn diagram showing the overlap between the interactions identified in the extracellular interaction screen and known interactions in the Bioplex, Biogrid, and STRING databases.

Fig. 2E is a bar plot showing that the percentage of interactions identified between two extracellular proteins (Bioplex; 1%), according the Human Protein Atlas cellular localization associations, is substantially under-represented relative to the estimated percentage (18%) of extra-cellular proteins in the human proteome.

Fig. 2F is a bar plot showing the number of reported unique interaction pairs (577) broken down by directionality subsets: 114 pairs for which the prey in the STM library was included in the query set and the reported interaction was reciprocally confirmed (red); 124 pairs for which the prey in the STM library

was included in the query set and the reported interaction was not reciprocally confirmed (orange); and 463 pairs for which the prey in the STM library was not included in the query set.

Fig. 3A is a network representation showing the IgSF interactome dissected by Markov clustering (MCL) clusters based on network connectivity and healthy tissue gene expression profiles from Genotype-Tissue Expression (GTEx). Edges connecting nodes in a single cluster are annotated in black; edges connecting nodes in different clusters are colored in light grey. All clusters are annotated with their most common statistically significant enriched Biological Process gene ontology (GO) term, corresponding to the numbered legend below. Network nodes with prior annotation of the enriched GO term are colored differentially corresponding to their term. Nodes with an unknown annotation, or different annotation to the cluster assigned term, are shown as diamonds.

Fig. 3B is a set of violin plots showing that the average correlation (Pearson's r) of mRNA expression measured across all GTEx tissues is significantly higher ($p < 1.2x10^{-20}$) for all pairs of reported interacting proteins (left plot, yellow) compared to the complement set of all possible non-interacting pairs of network nodes (right plot, blue). The dotted line indicates the 95th percentile of the correlation distribution, above which selected novel interactions, validated in this study, are indicated.

Fig. 3C is a scatter plot showing a comparison of normalized mRNA expression (log_2 nRPKM) of the reported binding partners NECTIN1 and NECTIN4 in the esophagus GTEx Tissue subset. The expression pattern was significantly correlated ($q < 0.05$) with the regression model overlaid (red).

Fig. 3D is a scatter plot showing a comparison of normalized mRNA expression (log_2 nRPKM) of the reported binding partners CEACAM5 and CEACAM7 in the colon GTEx Tissue subset. The expression pattern was significantly correlated ($q < 0.05$) with the regression model overlaid (red).

Fig. 3E is a scatter plot showing a comparison of normalized mRNA expression (log_2 nRPKM) of the reported binding partners LILRA5 and LILRB1 in the blood GTEx Tissue subset. The expression pattern was significantly correlated ($q < 0.05$) with the regression model overlaid (red).

Fig. 3F is a scatter plot showing a comparison of normalized mRNA expression (log_2 nRPKM) of the reported binding partners PTPRZ1 and CNTN1 in the brain GTEx Tissue subset.

Fig. 3G is a set of scatter plots showing a comparison of normalized mRNA expression (log_2 nRPKM) of the reported binding partners L1CAM and CHL1 in specific GTEx Tissue subsets (left to right: colon, small intestine, nerve, and stomach) where the expression pattern was significantly correlated ($q < 0.05$) with the regression model overlaid (red).

Fig. 3H is a schematic showing the design of the cell surface interaction assay. Binding partners (BP) were expressed on cells, and binding of the protein of interest, expressed as recombinant purified ECD, to the cell surface of untransfected (UT) and receptor-expressing cells was analyzed using immunofluorescence. The recombinant proteins were biotinylated and multimerized using fluorescent streptavidin for increased binding avidity and detection of transient interactions.

Fig. 3I is a set of micrographs showing results of the cell surface interaction assay for the soluble query NCR1 and the binding partners SIGLEC6, SIGLEC7, and SIGLEC8 relative to control UT cells. "Binding" shows only the query protein in gray. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 μm.

Fig. 3J is a set of micrographs showing results of the cell surface interaction assay for the soluble query CHL1 and the binding partner L1CAM relative to control UT cells. "Binding" shows only the query protein in gray. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 µm.

Fig. 3K is a set of micrographs showing results of the cell surface interaction assay for the soluble query CNTN1 and the binding partner PTPRZ1 relative to control UT cells. "Binding" shows only the query protein in gray. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 µm.

Fig. 3L is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for NCR1-FLAG in cells co-expressing SIGLEC7-HA or a vector control.

Fig. 3M is a set of immunoblots showing the results of a co-IP assay for NCR1-FLAG in cells co-expressing SIGLEC8-HA or a vector control.

Fig. 3N is a set of immunoblots showing the results of a co-IP assay for NCR1-FLAG in cells co-expressing CD4-HA or a vector control.

Fig. 4A is an IgSF interactome network representation showing the PD-L1 (CD274) and PD-L2 (PDCD1LG2) immune regulatory cluster (shaded in light red). Edges corresponding to the CD274-EPHA3 and CEACAM4-PDCD1LG2 interactions are depicted with thick lines and highlighted in red. Nodes are colored according their primary assigned GO category, as provided in Figure 3.

Fig. 4B is a sensorgram showing binding of PD-1, PD-L1, and PD-L2 (expressed as ECD-Fc fusion proteins) to CEACAM4 as analyzed by SPR. Recombinant CEACAM4 (expressed as an ECD-Fc fusion protein) was immobilized on a sensor chip and the indicated proteins were injected at 250 nM concentration. An irrelevant Fc-tagged protein was used as a control. Sensorgram shown is representative of at least 3 independent runs.

Fig. 4C is a sensorgram showing binding of PD-L1, EPHA3, and EPHA5 (expressed as ECD-Fc fusion proteins) to LILRA3 as analyzed by SPR. Recombinant LILRA3 (expressed as an ECD-Fc fusion protein) was immobilized on a sensor chip and the indicated proteins were injected at 250 nM concentration. An irrelevant Fc-tagged protein was used as a control. Sensorgram shown is representative of at least 3 independent runs.

Fig. 4D is a graph showing binding of PD-L1 to its partners PD-1 and EPHA3 in the presence of increasing concentrations of the anti-PD-1/PD-L1 antibody atezolizumab. Response units were measured at the end of the injection. Bar plots shows mean ± standard deviation. Experiments are representative of 2 independent assays.

Fig. 4E is a sensorgram showing binding of PD-1, PD-L1, and PD-L2 (expressed as ECD-Fc fusion proteins) to EPHA3 as analyzed by SPR. Recombinant EPHA3 (expressed as an ECD-Fc fusion protein) was immobilized on a sensor chip and the indicated proteins were injected at 250 nM concentration. An irrelevant Fc-tagged protein was used as a control. Sensorgram shown is representative of at least 3 independent runs.

Fig. 4F is a set of micrographs showing results of the cell surface interaction assay for the soluble queries PD-L1 and PD-L2 and the binding partners PD-1, CD80, EPHA3, EPHB1, PD-L2, PD-L1,

CEACAM4, and CEACAM5. The query protein is shown in red, and nuclei stained with DAPI are shown in blue. Scale bar = 50 µm.

Fig. 4G is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for LILRB1-FLAG in cells co-expressing EDAR-HA or a vector control.

Fig. 4H is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for LILRB1-FLAG in cells co-expressing IL6R-HA or a vector control.

Fig. 4I is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for LILRB4-FLAG in cells co-expressing CNTFR-HA or a vector control.

Fig. 5A is a simplified network representation of interactions in the neural system related community centered around the PTPR family (Fig. 3A, cluster 1) individual binding partners within the SLITRK, NTRK, LFRN, IL1RAP, and LRRC families. Red edges represent interactions that were validated using the cell surface interaction assay, as shown in Figs. 5B-5E. Dotted edges represent interactions having weak binding.

Fig. 5B is a set of micrographs showing results of the cell surface interaction assay for the soluble queries SLITRK2 (top) and SLITRK3 (bottom) and the binding partners PTPRD and PTPRS relative to control untransfected (UT) cells. "Binding" shows only the query protein in gray. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 µm.

Fig. 5C is a set of micrographs showing results of the cell surface interaction assay for the soluble query LFRN5 and the binding partners PTPRD, PTPRS, and PTPRF relative to control UT cells. "Binding" shows only the query protein in gray. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 µm.

Fig. 5D is a set of micrographs showing results of the cell surface interaction assay for the soluble query IL1RAP and the binding partners PTPRD, PTPRS, and PTPRF relative to control UT cells. "Binding" shows only the query protein in gray. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 µm.

Fig. 5E is a set of micrographs showing results of the cell surface interaction assay for the soluble queries BTN3A1, BTN3A3, and BTN2A2 and the binding partner LRRC4B relative to control UT cells. "Binding" shows only the query protein in gray. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 µm.

Fig. 5F is a set of sensorgrams showing binding of ILRAP, ILRAPL1, SLITRK1, SLITRK4, LRFN1, and LRFN4 to PTPRD as analyzed by SPR. The indicated protein (expressed as an ECD-Fc fusion protein) was immobilized on a sensor chip and PTPRD (expressed as an ectodomain fused to an Fc tag) was injected at the indicated concentrations.

Fig. 5G is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for FAM-FLAG in cells co-expressing BTN2A1-HA or a vector control.

Fig. 5H is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for LRRC4B-FLAG in cells co-expressing BTN3A2-HA or a vector control.

Fig. 5I is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for LRRC4B-FLAG in cells co-expressing BTN3A3-HA or a vector control.

Fig. 5J is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for LRRC4B-FLAG in cells co-expressing EDAR-HA or a vector control.

Fig. 5K is a schematic showing cancer-relevant amino acid substitution mutations in PTPRD.

Fig. 5L is a heat map showing the row-clustered log2 ratio of normalized absorbance per binding partner, color-coded from white (loss of binding) to red (conserved binding).

Fig. 5M is a network representation showing interactions between LILR family members and their previously uncharacterized binding partners showing concerted up-regulation of LILR proteins in kidney renal clear cell carcinoma (KIRC).

Fig. 5N is a set of micrographs showing results of the cell surface interaction assay for the soluble queries EDAR, LDLR, LILRA5, and CNTFR and the binding partners LILRB1, LILRB2, LILRB3, LILRB4, and LILRB5 relative to control UT cells. The query protein is shown in red, and nuclei stained with DAPI are shown in blue.

Fig.6A is a network diagram showing the IgSF interactome represented as network communities, augmented with the results of a differential expression analysis between tumor and adjacent normal tissue per TCGA indication. Node color and size are indicative for the number of TCGA indications where the gene was found to be significantly dysregulated ($|\log2 \text{ fold-change}| > 1$ and $p < 0.05$).

Fig. 6B is a bar plot showing the number of edges connecting significantly deregulated nodes per TCGA indication, in descending order. LUSC = lung squamous cell carcinoma, KIRC = kidney renal clear cell carcinoma, COAD = colon adenocarcinoma, KICH = kidney chromophobe, LUAD = lung adenocarcinoma, UCEC = uterine corpus endometrial carcinoma, KIRP = kidney renal papillary cell carcinoma, BLCA = bladder urothelial carcinoma, LIHC = liver hepatocellular carcinoma, BRCA = breast invasive carcinoma, THCA = thyroid carcinoma, ESCA = esophageal carcinoma, STAD = stomach adenocarcinoma, HNSC = head and neck squamous cell carcinoma, PRAD = prostate adenocarcinoma. Red bars represent the IgSF interactome. Light red bars represent a reference set of unrelated gene pairs reported in TCGA.

Fig. 6C is a network diagram showing up- or down-regulated genes in the immune regulatory community (as defined in Fig. 3B) in kidney renal clear cell carcinoma (KIRC).

Fig. 6D is a network diagram showing up- or down-regulated genes in the immune regulatory community (as defined in Fig. 3B) in head and neck squamous cell carcinoma (HNSC).

Fig. 6E is a set of violin plots showing that the average correlation (Pearson's r) of mRNA expression measured across all Cancer Cell Line Encyclopedia (CCLE) cell lines is significantly higher ($p < 4x10^{-2}$) for all pairs of reported interacting proteins (left plot, yellow) compared to the complement set of all possible non-interacting pairs of network nodes (right plot, blue). The dotted line indicates the 95th percentile of the correlation distribution, above which selected novel interactions, validated in this study, are indicated.

Fig. 6F is a scatter plot showing a comparison of relative protein expression of the reported binding partners CEACAM5 and CEACAM6 in the large intestine CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 6G is a scatter plot showing a comparison of relative protein expression of the reported binding partners CNTN1 and NRCAM in the lung CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 6H is a scatter plot showing a comparison of relative protein expression of the reported binding partners BTN3A1 and LRRC4B in the large intestine CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 6I is a scatter plot showing a comparison of relative protein expression of the reported binding partners FLRT3 and UNC5C in the breast CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 6J is a scatter plot showing a comparison of relative protein expression of the reported binding partners CNTN1 and PTPRZ1 in the hematopoietic and lymphoid tissue CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 6K is a scatter plot showing a comparison of relative protein expression of the reported binding partners IGSF3 and PTGFRN in the large intestine CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 6L is a scatter plot showing a comparison of relative protein expression of the reported binding partners IGSF3 and PTGFRN in the breast CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 6M is a scatter plot showing a comparison of relative protein expression of the reported binding partners AXL and VSIG10L in the hematopoietic and lymphoid tissue CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 6N is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for IL1RL1-FLAG and VSIG10L-FLAG in cells co-expressing AXL-HA or a vector control.

Fig. 6O is a set of sensorgrams showing binding of AXL and TYRO3 to IL1RL1 or GAS6 as analyzed using biolayer interferometry.

Fig. 6P is a set of sensorgrams showing binding of AXL and MER to IL1RL1 or GAS6 as analyzed using biolayer interferometry.

Fig. 6Q is a set of micrographs showing results of the cell surface interaction assay for the soluble query AXL and the binding partner IL1RI1 relative to control UT cells. "Binding" shows only the query protein in gray. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 μm.

Fig. 7A is a graph showing the distribution of relevant protein domains and motifs according to UniProt annotations for the set of 1,129 unique single-pass transmembrane proteins ("prey constructs") in the receptor library. ITIM/ITAM = immunoreceptor tyrosine-based inhibition motif/immunoreceptor tyrosine-based activation motif, TNFR = tumor necrosis factor receptor, TLR/ILR = Toll-like receptor/interleukin receptor, Ig-like = immunoglobulin-like, EGF = epidermal growth factor.

Fig. 7B is a Venn diagram showing the overlap between the unique protein entries present in the Biogrid, Bioplex, and STRING databases (three comprehensive protein-protein interaction resources) and the present study.

Fig. 7C is a schematic representation of a set of 384-well plates showing two independent replicates of an automated cell surface interaction assay for PD-1 (PDCD1) tested against the single-pass transmembrane protein (STM) receptor library.

Fig. 7D is a schematic representation of a set of 384-well plates showing two independent replicates of an automated cell surface interaction assay for PD-L2 (PDCD1LG2) tested against the STM receptor library.

Fig. 7E is a box plot showing, from top to bottom: the distribution of the raw enzymatic absorbance background estimate per plate; the maximal enzymatic absorbance controls per plate; the unscaled enzymatic absorbance values across wells; the enzymatic absorbance values corrected by the background estimate per plate; and the subsequent 'normalized' absorbance values to the estimated maximal absorbance per plate.

Fig. 8A is a heatmap of clustered Normalized Absorbance values for the 1,364 prey proteins (STM ECDs) by the 445 screened IgSF query proteins.

Fig. 8B is a set of ridge plots depicting the discriminating potential of predictive features between Non-specific, True Positive, and True Negative interactions in the training set. From top to bottom: Normalized Absorbance; Query Z-score for one query screened against the entire STM library; Prey Z-score for a single prey in the STM library across all query proteins that were screened; and custom Specificity Score.

Fig. 8C is a plot showing a principal component analysis (PCA) for the training set negative, training set non-specific, training set positive, predicted non-specific/negative, and predicted positive interactions. Mapping the four-dimensional feature matrix to the first and second principal components shows that predicted true positive interactions (dark blue) align well with the true positive interactions from our training set (light blue) and are well separated from the known non-specific interactions (orange) and sampled true negative interactions (red).

Fig. 8D is a dot plot showing normalized intensity colored by predicted class (red: negative; green: positive/specific: blue: non-specific) for all reciprocally observed interactions of CD274, PDCD1, and PDCD1LG2 showing excellent reciprocal reproducibility and specificity across multiple query clones.

Fig. 8E is a dot plot showing normalized intensity colored by predicted class (red: negative; green: positive/specific: blue: non-specific) for all reciprocally observed interactions of CD274, PDCD1, and PDCD1LG2 showing excellent reciprocal reproducibility and specificity across multiple query clones.

Fig. 8F is a bar plot showing the total number of extracellular interactions in Bioplex ("Bioplex interactions extra-cellular proteins (Human Protein Atlas)"; 627), the number of Bioplex interactions between two proteins we screened for interaction ("Bioplex interactions proteins in this study"; 350), and the total number of reported extracellular interactions in this study ("all interactions in this study"; 577).

Fig. 8G is a histogram showing that the shortest-path distribution in the IgSF interactome network is centered around 6.

Fig. 9A is a clustered heatmap of the row-scaled (Z-transformed), $\log_2$ rpkm counts for all IgSF interactome genes across GTEx Tissue detail categories.

Fig. 9B is a violin plot showing that the tissue expression correlation (Pearson's r in GTEx) distribution mean for all pairs of reported interacting proteins is significantly higher ($p < 1.2\ e^{-20}$) compared

to the distribution of all possible non-interacting pairs (screening library complement). In the clustered network, the intra-cluster correlation is also significantly higher ($p < 0.05$) compared to the distribution of all inter-cluster interactions.

Fig. 9C is a scatter plot of the binding pair CEACAM5 and CEACAM7, for which mRNA expression across all GTEx tissues was highly correlated.

Fig. 9D is a scatter plot of the binding pair LILRB1 and LILRA5, for which mRNA expression across all GTEx tissues was highly correlated.

Fig. 9E is a scatter plot of the binding pair SIGLEC7 and NCR1, for which mRNA expression across all GTEx tissues was highly correlated.

Fig. 9F is a set of faceted scatter plots showing L1CAM and CHL1 mRNA expression across different brain regions, showing constitutively high expression of CHL1 in the cerebellar regions and strongly correlated expression patterns for all other regions.

Fig. 9G is a set of micrographs showing results of a cell surface interaction assay for the soluble query CHL1 and the cell-surface-expressed binding partners BTLA and CNTN5 relative to control untransfected (UT) cells. Query protein binding to the cell surface is shown in red in the merged image, and nuclei stained with DAPI are shown in blue. Scale bar = 50 μm.

Fig. 9H is a network diagram showing the new interactions identified using independent assays for the CNTN1 and CHL1 cluster.

Fig. 9I is a set of graphs showing analysis of the binding of NRCAM, NFASC, MCAM, CHL1, and a control protein to CNTN1 using SPR. Recombinant NRCAM, NFASC, MCAM, CHL1, and a control protein were immobilized on a sensor chip and CNTN1 (expressed as a recombinant ECD-Fc) was injected at 250 nM concentration.

Fig. 9J is a clustered heatmap of the row-scaled expression values for a representative network cluster (cluster 1). Network clusters often comprise distinct tissue expression sub-groups, exemplified by the Brain versus Whole Blood, Spleen, Lung and Small Intestine sub-groups.

Fig. 9K is a clustered heatmap showing the representation of simplified GO categories (rows) for all network clusters with > 2 members (columns). Cell values are colored according each category's OddsRatio (capped at OddsRatio > 50). Network clusters recurrently comprise genes with multiple biological annotations.

Fig. 10A is a clustered tissue expression heatmap for members of the PD-L1/CD274 and PDCD1LG2/PD-L2 immune regulatory cluster (green) along with the Ephrin (purple) and CEACAM (olive) family members, highlighting evidence for co-expression of CEACAM4 with PD-L2 and divergence in co-expression between EPHA3 and the Ephrin cluster.

Fig. 10B is a set of box plots showing expression of PD-L1 (CD274) and EPHA3 in normal tissues based on GTEx data.

Fig. 10C is a set of box plots showing expression of CEACAM4 and PD-L2 in normal tissues based on GTEx data.

Fig. 10D is a sensorgram showing a representative SPR experiment showing EPHA3 binding to PD-L1. PD-L1 was immobilized on sensor chips, and EPHA3, expressed as a recombinant His-tagged

ECD, was injected at 0, 50, 10, 20, 50, and 100 nM concentrations. Binding kinetics were calculated in equilibrium.

Fig. 10E is a sensorgram showing a representative SPR experiment showing CEACAM4 binding to PD-L2. PD-L2 was immobilized on sensor chips, and CEACAM4, expressed as a recombinant His-tagged ECD, was injected at 0, 10, 20, 50, 100, and 200 nM concentrations. Binding kinetics were calculated in equilibrium.

Fig. 10F is a set of micrographs showing results of a cell surface interaction assay for the soluble query MDGA1 and the cell-surface-expressed binding partners NLGN3 and NLGN4X relative to control untransfected (UT) cells. Query protein binding to the cell surface is shown in red in the merged image, and nuclei stained with DAPI are shown in blue. Scale bar = 50 μm.

Fig. 10G is a set of micrographs showing results of a cell surface interaction assay for the soluble query TREML2 and the cell-surface-expressed binding partner ANTRX1 relative to control untransfected (UT) cells. Query protein binding to the cell surface is shown in red in the merged image, and nuclei stained with DAPI are shown in blue. Scale bar = 50 μm.

Fig. 10H is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for IGSF5-FLAG in cells co-expressing CD300A-HA or a vector control.

Fig. 10I is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for IGSF5-FLAG in cells co-expressing CD300LF-HA or a vector control.

Fig. 10J is a set of micrographs showing results of a cell surface interaction assay for the soluble queries FLRT1, FLRT2, and FLRT3 and the cell-surface-expressed binding partners UNC5A, UNC5C, and UNC5D relative to control untransfected (UT) cells. Query protein binding to the cell surface is shown in red in the merged image, and nuclei stained with DAPI are shown in blue. Scale bar = 50 μm.

Fig. 11A is a clustered heatmap of network nodes by TCGA indications. Cell values represent the $\log_2$ mean change between Tumor and adjacent Normal gene expression levels.

Fig. 11B is a set of micrographs showing results of a cell surface interaction assay for the soluble query CHL1 and the cell-surface-expressed binding partners L1CAM, BTLA, and CNTN5 relative to control untransfected (UT) cells. Query protein binding to the cell surface is shown in red in the merged image, and nuclei stained with DAPI are shown in blue. Scale bar = 50 μm.

Fig. 11C is a subnetwork diagram of the IgSF interactome showing putative interactions identified for the CNTN1 and CHL1 IgSF proteins. Edges represented in yellow indicate interactions that were validated by independent technologies.

Fig. 12A is a set of micrographs showing results of a cell surface interaction assay for the soluble query LFRN5 and the binding partners PTPRZ1, PTPRG, PTPRT, PTPRS, PTPRO, PTPRM, PTPRF, and PTPRD relative to control untransfected (UT) cells. "Binding" shows only the query protein in gray. Experiments shown are representative of two independent assays. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 μm.

Fig. 12B is a set of micrographs showing results of a cell surface interaction assay for the soluble query SLITKR2 and the binding partners PTPRZ1, PTPRG, PTPRT, PTPRS, PTPRO, PTPRM, PTPRF, and PTPRD relative to control untransfected (UT) cells. "Binding" shows only the query protein in gray.

Experiments shown are representative of two independent assays. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 μm.

Fig. 12C is a set of micrographs showing results of a cell surface interaction assay for the soluble query IL1RAP and the binding partners PTPRZ1, PTPRG, PTPRT, PTPRS, PTPRO, PTPRM, PTPRF, and PTPRD relative to control untransfected (UT) cells. "Binding" shows only the query protein in gray. Experiments shown are representative of two independent assays. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 μm.

Fig. 12D is a set of micrographs showing results of a cell surface interaction assay for the soluble query CNTN1 and the binding partners PTPRZ1, PTPRG, PTPRT, PTPRS, PTPRO, PTPRM, PTPRF, and PTPRD relative to control untransfected (UT) cells. "Binding" shows only the query protein in gray. Experiments shown are representative of two independent assays. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 μm.

Fig. 12E is a set of micrographs showing results of a cell surface interaction assay for the soluble query BTN2A2 and the binding partner LRRC4B relative to control untransfected (UT) cells. "Binding" shows only the query protein in gray. Experiments shown are representative of two independent assays. "Merge" shows the query protein in red and nuclei stained with DAPI in blue. Scale bar = 50 μm.

Fig. 12F is a set of immunoblots showing the results of a co-immunoprecipitation (co-IP) assay for LRRC4B-FLAG, LRRC4C-FLAG, TGOLN2-FLAG, VSIG8-FLAG, CDH9-FLAG, and ST14-FLAG in cells co-expressing BTN3A1-HA or a vector control.

Fig. 12G is a bar plot showing the binding specificities of the indicated PTPRD variants to the indicated binding partners, relative to wild-type PTPRD.

Fig. 13A is a set of Kaplan-Meier curves and a table showing the survival probability of patients with stage II disease split into tertiles by levels of podoplanin (PDPN) expression (T1, T2, and T3) in the publicly available CRC (stage II) microarray gene expression dataset GSE33113. Logrank p-values (Logrank p) are associated with Kaplan-Meier curves. Cox proportional hazard (CoxPH) p-values are associated with the univariate models detailed in Table 10.

Fig. 13B is a set of Kaplan-Meier curves and a table showing the survival probability of patients with any stage of disease split into tertiles by levels of PDPN expression in the publicly available CRC (all stages) microarray gene expression dataset GSE39582. Logrank p-values are associated with Kaplan-Meier curves. Cox proportional hazard p-values are associated with the univariate models detailed in Table 10.

Fig. 13C is a plot showing the correlation between PDPN expression and tumor content (percentage of cancer cells) in The Cancer Genome Atlas (TCGA).

Fig. 13D is a plot showing the correlation between PDPN and an activated fibroblast signature (fibroblast score) in TCGA.

Fig. 13E is a set of Kaplan-Meier curves and a table showing the survival probability of patients with stage II CRC split into tertiles by expression levels of the activated fibroblast signature (Act. Fib tertiles) in the GSE33113 and GSE39582 datasets. Logrank p-values are associated with Kaplan-Meier curves. Cox proportional hazard p-values are associated with the univariate models detailed in Table 10.

Fig. 13F is a set of Kaplan-Meier curves and a table showing the survival probability of patients with any stage of CRC split into tertiles by expression levels of the activated fibroblast signature (Act. Fib tertiles) in the GSE33113 and GSE39582 datasets. Logrank p-values are associated with Kaplan-Meier curves. Cox proportional hazard p-values are associated with the univariate models detailed in Table 10.

Fig. 14A is a diagram and a set of photomicrographs showing binding of monomeric or tetrameric PD-L1 to PD-1 or PD-L2. The diagram (top) shows normalized fluorescence intensity detected for cells expressing PD-1 or PD-L2 on the cell surface that have been contacted with 5 nM, 10 nM, 50 nM, 200 nM, or 500 nM monomeric or tetrameric PD-L1. The photomicrographs (bottom) are representative images of fluorescence for cells expressing PD-1 or PD-L2 on the cell surface that have been contacted with 500 nM monomeric or tetrameric PD-L1.

Fig. 14B is a diagram and a set of photomicrographs showing binding of monomeric or tetrameric poliovirus receptor (PVR) to CD96, CD226, or TIGIT. The diagram (top) shows normalized fluorescence intensity of fluorescent streptavidin detected for cells expressing CD96, CD226, or TIGIT on the cell surface that have been contacted with 5 nM, 10 nM, 50 nM, 200 nM, or 500 nM monomeric or tetrameric PVR. The photomicrographs (bottom) are representative images of fluorescence for cells expressing CD96, CD226, or TIGIT on the cell surface that have been contacted with 500 nM monomeric or tetrameric PVR.

Fig. 14C is a schematic diagram showing the design of members of the ectodomain-gD-GPI library. Left: an untagged, full-length single-pass transmembrane (STM) protein. Right: an ectodomain-gD-GPI protein comprising the ectodomain of the STM protein, a glycoprotein D (gD) tag, and a glycosylphosphatidyl-inositol (GPI) linker.

Fig. 14D is a graph showing a quantification of surface expression (as fluorescence intensity per cell) of members of the ectodomain-gD-GPI library, as measured using an anti-gD antibody. Representative images of surface staining for not detectable (no), low, medium, and high expressers are shown. Dotted lines indicate arbitrary cut-offs for the different expression levels. Expression is representative of two independent assays.

Fig. 14E is a schematic representation of an automated cell-based platform for receptor discovery (cell surface interaction screen). (1) depicts a library consisting of about 1200 unique single transmembrane (STM) receptors expressed as the STM extracellular domain (ECD) fused to a gD-GPI tag. (2) depicts tetramerization of the query protein podoplanin (PDPN). PDPN was expressed as the PDPN extracellular domain (ECD) fused to an Avidity AVITAG™ (Avi tag) for site-directed biotinylation, was biotinylated, and was conjugated to fluorescent streptavidin (SA) to form a high avidity tetramer. (3) depicts automated receptor-ligand interaction screens (cell surface interaction screens). Individual single transmembrane (STM) receptors were transfected into mammalian cells and were cultured in individual wells on a plate. The high avidity PDPN tetramer was incubated with the cells at 4°C. When PDPN interacted with the STM receptor, the fluorescent SA tag was retained at the cell surface. (4) depicts high content fluorescent imaging of individual wells of the assays of (3). (5) depicts a representation of fluorescent signal intensity. Background is calculated by averaging signal intensity for interaction with all receptors within the library. (6) depicts a representative surface plasmon resonance (SPR) plot. SPR is used as an orthogonal technique to further validate interactions.

Fig. 14F is an intersection plot showing the results of an automated cell surface interaction screen in which the immune receptor B7-H3 (CD276) was tested for interaction with a library of ectodomain-gD-GPI STM proteins. Each circle represents a binding interaction between B7-H3 and an STM receptor. Unique high-scoring hits are shown in red circles. Hits shown in gray circles are empirically determined non-specific binders. The interleukin-20 receptor subunit alpha (IL20-RA) was identified as an interacting partner.

Fig. 14G is an intersection plot showing the results of an automated cell surface interaction screen in which the immune receptor B7-H3 (CD276) was tested for interaction with a library of full-length STM proteins not comprising tags. Each circle represents a binding interaction between B7-H3 and an STM receptor. Unique high-scoring hits are shown in red circles. Hits shown in gray circles are empirically determined non-specific binders. The interleukin-20 receptor subunit alpha (IL20-RA) was identified as an interacting partner.

Fig. 14H is an intersection plot showing the results of an automated cell surface interaction screen in which podoplanin (PDPN) was tested for interaction with a library of STM proteins. Hits shown in gray circles are empirically determined non-specific binders. Each interaction was tested in duplicate. Each circle represents a binding interaction between PDPN and an STM receptor. CD177 was identified as a novel interacting partner.

Fig. 14I is a sensorgram showing binding of PDPN and CD177 as analyzed by surface plasmon resonance (SPR). Recombinant CD177 (expressed as an ECD) was immobilized on a sensor chip and recombinant PDPN (expressed as an Fc-tagged ECD) and a control protein were injected at the concentrations indicated. Dissociation constant (K_D) values for each interaction, measured using recombinant PDPN expressed as a monomeric ectodomain, are indicated.

Fig. 14J is a sensorgram showing the absence of binding between a control ECD and PDPN as analyzed by SPR. The control ECD was immobilized on a sensor chip and recombinant PDPN (expressed as an Fc-tagged ECD) and a control protein were injected at the concentrations indicated. Dissociation constant (K_D) values for each interaction, measured using recombinant PDPN expressed as a monomeric ectodomain, are indicated.

Fig. 15A is a pair of graphs showing CD177 expression on neutrophils. The left panel is a representative histogram showing CD177 expression on neutrophils in healthy blood from three different donors and an isotype control. The right panel is a graph depicting the percentage of neutrophils that were CD177+ in donor blood samples (n= 31).

Fig. 15B is a set of plots showing the gating strategy for identification of neutrophils in healthy volunteer blood, CRC patient blood, adjacent normal colon tissue (adjacent colon), and cancerous colon tissue (CRC colon) using flow cytometry. Blood plots represent data from blood samples in which red blood cells (RBCs) were lysed. Colon tissue plots represent data from single-cell suspensions of colon tissue samples in which red blood cells were lysed and the suspension was strained with a 70-micron mesh. All samples were stained with 7-aminoactinomycin D (7-AAD) to gate out dead cells and incubated with the indicated antibodies. Shaded regions represent the data selected for analysis ("gate"). Gates were chosen to include events that were live (as indicated by absence of 7-AAD staining), were singlets, and were $CD45^+$. Data are representative of 4-7 independent donors.

Fig. 15C is a graph showing the percentage of cells that were neutrophils in samples from 4-7 independent donors for healthy volunteer blood (norm blood), CRC patient blood (pt blood), adjacent normal colon tissue (adj colon), and cancerous colon tissue (CRC colon). ***$p < 0.001$, Kruskal-Wallis with Dunn's multiple comparisons test.

Fig. 15D is a graph showing the percentage of neutrophils that were $CD177^+$ in samples from 4-7 independent donors for healthy volunteer blood, CRC patient blood, adjacent normal colon tissue, and cancerous colon tissue.

Fig. 15E is a representative histogram showing CD177 expression levels in neutrophils in healthy blood, patient blood, adjacent normal (adj) colon tissue, and cancerous (CRC) colon tissue compared to isotype controls. Data are representative of 4-7 independent donors.

Fig. 15F is a set of plots showing the gating strategy for identification of stromal cells in adjacent normal colon tissue, cancerous (CRC) colon tissue, and diverticulitis (Div) colon tissue using flow cytometry. Plots represent data from single cell suspensions of tissue samples. Samples were stained as indicated. Gates were chosen to include events that were live (as indicated by absence of 7-AAD staining), were singlets, were $CD45^-$ (i.e., were not immune cells), and were $EpCAM^-$ (i.e., were not tumor cells) for examination of stromal cells. DN= double negative T cell; BEC= blood endothelial cells. Data are representative of 3-7 independent samples.

Fig. 15G is a graph showing the percentage of cells that are $PDPN^+$ in CRC colon cells that are cancer-associated fibroblast (CAF) cells ($EpCAM^-$, $CD45^-$, $CD31^-$); endothelial cells (EC) ($EpCAM^-$, $CD45^-$, $CD31^+$); tumor cells (TC) ($EpCAM^+$), myeloid cells ($CD45^+$, $CD11B^+$), CD4 T cells ($CD45^+$, $CD3^+$, $CD4^+$); or CD8 T cells ($CD45^+$, $CD3^+$,$CD8^+$). Data are representative of 3-7 independent samples. **$p < 0.01$, ***$p < 0.001$, Kruskal-Wallis with Dunn's multiple comparisons test.

Fig. 15H is a graph showing the mean fluorescent intensity (MFI) of PDPN in CRC colon cells that are cancer-associated fibroblast (CAF) cells ($EpCAM^-$, $CD45^-$, $CD31^-$); endothelial cells (EC) ($EpCAM^-$, $CD45^-$, $CD31^+$); tumor cells (TC) ($EpCAM^+$), myeloid cells ($CD45^+$, $CD11B^+$), CD4 T cells ($CD45^+$, $CD3^+$, $CD4^+$); or CD8 T cells ($CD45^+$, $CD3^+$,$CD8^+$). Data are representative of 3-7 independent samples. **$p < 0.01$, ****$p < 0.0001$, Kruskal-Wallis with Dunn's multiple comparisons test.

Fig. 15I is a graph showing the percentage of fibroblasts that are $PDPN^+$ in adjacent normal (adj) colon tissue, cancerous (CRC) colon tissue, and diverticulitis (div) colon tissue. Data are representative of 3-7 independent samples.

Fig. 15J is a graph showing the MFI of PDPN fibroblasts in adjacent normal (adj) colon tissue, cancerous (CRC) colon tissue, and diverticulitis (div) colon tissue. Data are representative of 3-7 independent samples.

Fig. 16A is a pair of micrographs from a tissue microarray showing adjacent normal colon tissue stained for CD177 (blue) and PDPN (pink). PDPN staining was largely absent on fibroblasts and marked the lymphatics. CD177 staining was rarely observed. Lower panels show magnified images.

Fig. 16B is a pair of micrographs from a tissue microarray showing cancerous (CRC) colon tissue stained for CD177 (blue) and PDPN (pink). PDPN staining was largely absent on fibroblasts and marked the lymphatics. CD177 staining was rarely observed. This tumor showed strong PDPN staining in the

stroma surrounding the tumor beds, but not in the epithelial cells themselves. Lower panels show magnified images.

Fig. 16C is a set of micrographs showing representative images of dual immunofluorescence staining for PDPN and CD177 in cancerous (CRC) colon cells. The first panel shows an overview of the tissue with PDPN (green) and CD177 (red) staining. The second, third, and fourth panels show an inset of the micrograph of the first panel, as indicated by the box in the first panel. The second panel shows PDPN and CD77 staining. The third panel shows only CD177 staining. The fourth panel shows only PDPN staining. Scale bars 50 µm.

Fig. 16D is a set of micrographs showing representative images of dual immunofluorescence staining for myeloperoxidase (MPO; a marker of neutrophils) and CD177 in CRC cells. The first panel shows an overview of the tissue with MPO (green) and CD177 (red) staining. The second, third, and fourth panels show an inset of the micrograph of the first panel, as indicated by the box in the first panel. The second panel shows MPO and CD77 staining. The third panel shows only CD177 staining. The fourth panel shows only MPO staining. Scale bars 50 µm.

Fig. 16E is a bar graph showing the percentage of normal adjacent colon (normal) and CRC cancer (tumor) cells that were negative (-) or positive (+) for staining for PDPN or CD177.

Fig. 17A is a bar graph showing the morphology index of wild-type cancer-associated fibroblasts (CAFs) seeded into 3D gels and treated with an isotype control, recombinant human CLEC-2 (rCLEC-2), or recombinant human CD177 (r-CD177). Dots represent single wells containing >50 cells and 6 independent experiments. Data are plotted relative to the isotype control for each experiment. **p < 0.01, Kruskal-Wallis with Dunn's multiple comparisons test.

Fig. 17B is a set of micrographs showing representative images of cancer-associated fibroblasts in 3D gels stained for actin and DAPI. The left panel shows a cell treated with the isotype control. The center panel shows a cell treated with recombinant human CLEC-2 (rCLEC-2). The right panel shows a cell treated with recombinant human CD177 (rCD177). Scale bar: 20 µm.

Fig. 17C is a bar graph showing the morphology index of wild-type cancer-associated fibroblasts (CAFs) seeded into 3D gels either alone (-) or with a 5:1 ratio of primary neutrophils (neut) or T cells isolated from blood. Dots represent single wells containing >50 cells and 2-3 independent experiments representing 5 donors each. **p < 0.01, Kruskal-Wallis with Dunn's multiple comparisons test.

Fig. 17D is a bar graph showing the morphology index of primary human fibroblasts from healthy human bladder, colon, or ovary (HOF) tissues seeded into 3D gels and treated with an isotype control, recombinant human CLEC-2 (r-CLEC2), or recombinant human CD177 (r-CD177). Dots represent single wells containing >50 cells and 3 independent experiments. *p < 0.05, Kruskal-Wallis with Dunn's multiple comparisons test.

Fig. 17E is a representative histogram showing staining for PDPN expression on fibroblasts from healthy human bladder, colon, and ovary (HOF) tissues and an isotype control.

Fig. 17F is a bar graph showing contraction (in µm) of wild-type cancer-associated fibroblasts (CAFs) treated with an isotype control, recombinant human CLEC-2 (rCLEC-2), or recombinant human CD177 (r-CD177) relative to unstimulated cells (un). Dots represent the average of 2-3 wells per

condition. Graph comprises data from 4 independent experiments. *p < 0.05, Kruskal-Wallis with Dunn's multiple comparisons test.

Fig. 18A is a schematic representation depicting the workflow of a multiplexed global proteomic and phospho-proteomic experiment in parallel with tandem mass tagging and fractionation for deep coverage. Cancer-associated fibroblasts (CAFs) were treated in duplicate with a DMSO control, CLEC-2, or CD177 for 2 minutes or 30 minutes and then lysed. The protein lysate was reduced and digested with LysC and trypsin, then peptides were normalized. Peptides were labeled with tandem mass tags (TMT). A proportion of peptides (~0.5 mg) were used for protein profiling. These peptides were fractionated by high pH reversed-phase fractionation (Hi pH RP). Samples were run on an HPLC, and peptides were identified by liquid chromatography-mass spectrometry (LC MS/MS) analysis. The remainder of the peptides (~6.5 mg) was used for global phosphorylation analysis. Peptides were fractionated by strong cation-exchange chromatography (SCX) and analyzed by liquid chromatography-mass spectrometry (LC MS/MS).

Fig. 18B is a heatmap showing the fold change in protein phosphorylation (compared to an untreated control) for all phosphosites that changed significantly ($|Log_2FC| > 1$ and $p<0.05$) in CAFs treated with CLEC-2 or CD177 for 2 minutes (2') or 30 minutes (30').

Fig. 18C is a volcano plot showing significant changes in protein phosphorylation in CAFs stimulated with CD177 (circles) or CLEC-2 (triangles) relative to untreated cells after 2 minutes.

Fig. 18D is a volcano plot showing significant changes in protein phosphorylation in CAFs stimulated with CD177 (circles) or CLEC-2 (triangles) relative to untreated cells after 30 minutes.

Fig. 18E is a bar graph showing enriched ($q<0.05$) gene ontology (GO) pathways represented by the proteins for which phosphosites were significantly altered in the CLEC-2 or CD177 treatment group compared to untreated CAFs. Numbers indicate the phospho-site groups associated with each curated GO term.

Fig. 18F is a table depicting the relative abundance change across treatment conditions (relative to an unstimulated control) for selected phosphorylation sites on proteins with enriched biological process pathways. Grouped phosphorylation sites are indicated with a separating "/".

Fig. 18G is a Venn diagram indicating the ~70% overlap (2,912 proteins) between the unique proteins identified in the global proteome (6,309 proteins) and the phospho-proteome (4,122 proteins). Overall, 18,558 unique phosphopeptides with high quality reporter ion intensities were identified, which mapped to 4,122 unique proteins with at least one phosphorylated residue.

Fig. 18H is a Venn diagram summarizing the number of phosphosites that were altered significantly ($p <0.05$ and $|Log2 Fold Change| > 1$) by CLEC-2 (190 phosphosites), CD177 (54 phosphosites) or both (32 phosphosites) at 30 min.

Fig. 18I is a ternary plot depicting all phosphopeptides detected in the phosphoproteomic assay. Significantly altered phosphosites are depicted as upward triangles (de-phosphorylated compared to unstimulated) or downward triangles (hyper-phosphorylated compared to unstimulated) and are colored according to the fold change measured between CLEC-2 at 30 min (purple) or CD177 at 30 min (green).

Fig. 19A is a set of Kaplan-Meier curves and a table showing the survival probability of patients with stage II disease split into tertiles by levels of podoplanin (PDPN) expression (T1, T2, and T3) in the

publicly available CRC microarray gene expression dataset GSE39582. Logrank p-values (Logrank p) are associated with Kaplan-Meier curves. Cox proportional hazard (CoxPH) p-values are associated with the univariate models detailed in Table 10.

Fig. 19B is a set of Kaplan-Meier curves and a table showing the survival probability of patients with stage IV disease split into tertiles by levels of podoplanin (PDPN) expression (T1, T2, and T3) in the publicly available CRC microarray gene expression dataset GSE39582. Logrank p-values (Logrank p) are associated with Kaplan-Meier curves. Cox proportional hazard (CoxPH) p-values are associated with the univariate models detailed in Table 10.

Fig. 19C is a set of Kaplan-Meier curves and a table showing the survival probability of patients with stage II disease split into tertiles by levels of FAP^+ fibroblast (FAP^+ fib) signature expression (T1, T2, and T3) in the publicly available CRC microarray gene expression dataset GSE33113. Logrank p-values (Logrank p) are associated with Kaplan-Meier curves. Cox proportional hazard (CoxPH) p-values are associated with the univariate models detailed in Table 10.

Fig. 19D is a set of Kaplan-Meier curves and a table showing the survival probability of patients with all stages of disease split into tertiles by levels of FAP^+ fibroblast signature expression (T1, T2, and T3) in the publicly available CRC microarray gene expression dataset GSE39582. Logrank p-values (Logrank p) are associated with Kaplan-Meier curves. Cox proportional hazard (CoxPH) p-values are associated with the univariate models detailed in Table 10.

Fig. 19E is a set of Kaplan-Meier curves and a table showing the survival probability of patients with stage II disease split into tertiles by levels of active (Act.) fibroblast signature expression (T1, T2, and T3) in the publicly available CRC microarray gene expression dataset GSE39582. Logrank p-values (Logrank p) are associated with Kaplan-Meier curves. Cox proportional hazard (CoxPH) p-values are associated with the univariate models detailed in Table 10.

Fig. 19F is a set of Kaplan-Meier curves and a table showing the survival probability of patients with stage II disease split into tertiles by levels of FAP^+ fibroblast signature expression (T1, T2, and T3) in the publicly available CRC microarray gene expression dataset GSE39582. Logrank p-values (Logrank p) are associated with Kaplan-Meier curves. Cox proportional hazard (CoxPH) p-values are associated with the univariate models detailed in Table 10.

Fig. 20 is an intersection plot showing the results of an automated cell surface interaction screen in which podoplanin (PDPN), expressed as a tetramer using fluorescent streptavidin, was tested in duplicate for interaction with a library of full-length, untagged STM proteins. The newly identified binding partner CD177 was not present in this receptor library. Images from individual wells were acquired using a high content microscope, images were processed using the InCell Developer software, and the amount of PDPN binding to the cell surface was represented as signal over background (S/N ratio). Each circle represents a binding interaction between PDPN and an STM receptor. Green dots represent non-specific binders observed as hits in unrelated screens. CLEC-2 was identified as a novel interacting partner.

Fig. 21 is a sensorgram showing binding of PDPN and CLEC-2 as analyzed by SPR. Recombinant CLEC-2 was immobilized on a sensor chip and purified PDPN (expressed as an Fc-tagged ECD) and an irrelevant FC-tagged ECD control protein were injected at the concentrations indicated.

Dissociation constant (K_D) values for each interaction, measured using recombinant PDPN expressed as a monomeric ectodomain, are indicated.

Fig. 22A is a box plot showing the level of CD177 RNA expression (log_2 nRPKM) in normal colon tissue and CRC tumors in a The Cancer Genome Atlas (TCGA) dataset.

Fig. 22B is a box plot showing the level of PDPN RNA expression (log_2 nRPKM) in normal colon tissue and CRC tumors in a The Cancer Genome Atlas (TCGA) dataset.

Fig. 22C is a box plot showing the level of PDPN and CD177 RNA expression in CRC tumors in the GSE39582 dataset.

Fig. 22D is a box plot showing the level of PDPN and CD177 RNA expression in CRC tumors in the GSE33113 dataset.

Fig. 23A is a set of micrographs showing serial sections of normal adjacent (adj) colon tissue stained for PDPN (left panel) and CD177 (right panel). PDPN staining was largely absent on fibroblasts and marked the lymphatics. CD177 staining was rarely observed.

Fig. 23B is a set of micrographs showing serial sections of cancerous (CRC) colon tissue stained for PDPN (left panel) and CD177 (right panel). Insets show magnified images. This tumor showed strong PDPN staining in the stroma surrounding the tumor beds, but not in the epithelial cells themselves.

Fig. 23C is a set of micrographs showing representative images of dual immunofluorescence staining for PDPN and CD177 in adjacent normal colon tissue. The first panel shows an overview of the tissue with PDPN and CD177 staining. The second, third, and fourth panels show an inset of the micrograph of the first panel, as indicated by the box in the first panel. The second panel shows PDPN and CD77 staining. The third panel shows only CD177 staining. The fourth panel shows only PDPN staining.

Fig. 23D is a set of micrographs showing representative images of dual immunofluorescence staining for myeloperoxidase (MPO; a marker of neutrophils) and CD177 in adjacent normal colon tissue. The first panel shows an overview of the tissue with MPO and CD177 staining. The second, third, and fourth panels show an inset of the micrograph of the first panel, as indicated by the box in the first panel. The second panel shows PDPN and CD77 staining. The third panel shows only CD177 staining. The fourth panel shows only MPO staining.

Fig. 24A is a set of density plots depicting the changes observed in phosphorylated residues (x-axis) versus total protein abundance changes (y-axis) for proteins that were identified both in the proteomic assay and the phospho-proteomic assay in CAFs that were stimulated with CD177 or CLEC-2 for 2 minutes or 30 minutes.

Fig. 24B is a heat map showing the fold change in protein phosphorylation (compared to an untreated control) for all phosphosites that changed significantly ($|Log_2FC| > 1$ and $p<0.05$) in CAFs treated with CLEC-2 or CD177 for 2 minutes (2') or 30 minutes (30'), as shown in Fig. 18B, including the identity of phosphoproteins for which significant changes were observed.

Fig. 25 is a pair of illustrations showing a model for CD177 and PDPN interactions in the tumor microenvironment. The left panel shows an overview of a tissue. Dense bands of CAFs form between islands of tumor beds. These fibers generally run parallel to tumor beds and contain many immune cells. Specifically, neutrophils and regulatory T cells (Tregs) can be found in these stroma-rich regions. While

there are still numerous PDPN+ CAFs not in contact with these CD177+ immune cells, some CAFs will interact with these cells and receive inhibitory signals downstream of PDPN. The right panel shows a model of the molecular interaction between CD177 and PDPN and downstream outcomes in the CAF. CD177 engagement alters contraction, motility, extracellular matrix (ECM) remodeling, and metabolism in the CAFs.

Fig. 26A is a histogram showing the expression of podoplanin (PDPN) on wild-type (WT) cancer-associated fibroblasts (CAFs) and on *Pdpn* -/- CAFs compared to an isotype control sample.

Fig. 26B is a graph showing the morphology index (perimeter^2/4*π*area) of WT and *Pdpn* -/- CAFs seeded into 3D gels. Each dot represents an average of one well containing >50 cells, and the plot is representative of 3 independent experiments. *$p < 0.05$, Mann-Whitney U test.

Fig. 26C is a pair of micrographs showing WT (left) and *Pdpn* -/- (right) CAFs in 3D gels with staining for actin (red) and nuclei (DAPI; blue).

Fig. 26D is a graph showing the relative contraction of *Pdpn*-/- cells compared with WT cells. Each dot represents the average of 3-4 wells each from 4 independent experiments. *$p < 0.05$, Mann-Whitney U test.

Fig. 26E is a graph showing the percent confluency of WT and *Pdpn*-/- CAFs over time. Each point represents the mean of 16 different fields of view from 4 wells per condition and the plot is representative of 4-6 independent experiments. ****$p < 0.0001$, ANOVA.

Fig. 27A is a set of photomicrographs showing representative images from single wells of SW480 tumor organoids expressing red fluorescent protein (RFP) in 3D culture at 8 days of growth with no CAFs (tumor only), *Pdpn* $^{-/-}$ CAFs, or wild-type (WT) CAFs. Wells without tumor cells (WT CAFs only and *Pdpn* $^{-/-}$ CAFs only) are shown as controls.

Fig. 27B is a graph showing the total area (in μm^2) of spheroids from maximum intensity projections of the wells of Fig. 27A at time points between 1 and 8 days in culture. Data are representative of two independent experiments (n=4 wells per condition in each experiment). Dunn's multiple comparison test was performed on all conditions against the tumor only control. *$p < 0.05$, ****$p < 0.0001$.

Fig. 27C is a set of photomicrographs showing representative images from single wells of SW480 tumor organoids expressing RFP in 3D culture at 17 days of growth with no CAFs (tumor only), WT CAFs, or WT CAFs treated with a control, tetrameric CD177, or tetrameric CLEC-2. A well without tumor cells (WT CAFs only) is shown as a control.

Fig. 27D is a graph showing the total area (in μm^2) of spheroids from maximum intensity projections of the wells of Fig. 27C at time points between 1 and 17 days in culture. Data are representative of two independent experiments (n=4 wells per condition in each experiment). Dunn's multiple comparison test showed a significant difference of ****$p < 0.0001$ between the tumor WT CAFs group to all other conditions except to the tumor + WT CAFs + control group.

Fig. 28A is a heat map showing all genes in the IgSF Interactome and their association with a CD8+ Teff cell signature, a pan-fibroblast TFGb signature, and gene sets based on the Lund subtyping scheme for immune desert (UroA: urothelial-like A), immune excluded (Inf: infiltrated) or immune inflamed tumors (UroB: urothelial-like B, SCCL: basal/SCC-like).

Fig. 28B is a volcano plot showing protein interactions significantly associated with positive (blue) or negative (red) clinical outcome. Select interactions are highlighted.

Fig. 28C is a scatter plot showing interactions with a high synergistic effect visualized by comparing the hazard ratio computed from joint expression of interacting pairs to the compound hazard ratio of the individual genes. Select interactions with improved predictive power for clinical outcome over single genes are highlighted. Red represents interactions predictive for lack of response; blue shows interactions associated with response.

Fig. 28D is a forest plot showing increased significance for association with lack of response and patient survival for each of the EFNB1 interactions, relative to the individual genes. Improved prediction of poor overall survival of EFNB1/EVC2 interactions (HR: 1.61; 95% CI: 1.24; 2.09, P=3.78e-4) than individual genes of EFNB1 (HR: 1.25; 95% CI: 0.97; 1.62, P=0.087) and EVC2 (HR: 1.32; 95% CI: 1.02; 1.71, P=0.035, n=348 patients).

Fig. 28E is a survival plot showing the probability of survival for individuals having an expression level of EFNB1 that is greater than or less than or equal to a median expression level, an expression level of EVC2 that is greater than or less than or equal to a median expression level, or an expression level of EFNB1 and EVC2 that is greater than or less than or equal to a median expression level.

Fig. 28F is a box-and-whisker plot for the EFNB1/ECV2 interaction and each gene separately. Whisker plots represent minimum and maximum, and black circles are outliers. Y axis: Z score expression. Responder group: complete response (CR) and partial response (PR); non-responder group: progressive disease (PD) and stable disease (SD). (p-values: EFBN1: 0.0008901; EVC2: 0.009046; EFBN1/EVC2: $9.19x10^{-5}$, n=298 patients).

Fig. 29A is a heat map showing the clustered, differential expression between tumor and adjacent normal samples for all IgSF interactome genes (rows) by TCGA tumor indications (columns). Cell values represent the mean change between Tumor and adjacent Normal log_2 rsem values.

Fig. 29B is a network diagram showing jointly up- (red) and down-regulated (blue) genes within the LILR family of proteins in the TCGA tumor indication HNSC (head neck squamous cell carcinoma).

Fig. 29C is a network diagram showing jointly up- (red) and down-regulated (blue) genes within the LILR family of proteins in the TCGA tumor indication KIRC (kidney renal clear cell carcinoma).

Fig. 29D is a clustered heat map showing normalized protein expression values for network genes in the CCLE, partitioned by Tissue.

Fig. 29E is a scatter plot showing a comparison of relative protein expression of the reported binding partners IGSF3 and PTGFRN in the lung CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 29F is a scatter plot showing a comparison of relative protein expression of the reported binding partners IGSF3 and PTGFRN in the upper aerodigestive tract CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 29G is a scatter plot showing a comparison of relative protein expression of the reported binding partners IGSF3 and PTGFRN in the esophagus CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 29H is a scatter plot showing a comparison of relative protein expression of the reported binding partners CEACAM5 and CEACAM6 in the lung CCLE Tissue subset. The expression pattern was significantly correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 29I is a scatter plot showing a comparison of relative protein expression of the reported binding partners CEACAM5 and CEACAM6 in the lung CCLE Tissue subset. The expression pattern was significantly negatively correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 29J is a scatter plot showing a comparison of relative protein expression of the reported binding partners ICOSLG and NTM in the lung CCLE Tissue subset. The expression pattern was significantly negatively correlated ($q < 0.2$) with the regression model overlaid (red).

Fig. 30A is a volcano plot showing protein interactions significantly correlated with CD8+ Teff cells. Select interactions are highlighted.

Fig. 30B is a network diagram showing the PD-1/PD-L1 community of immune-related interactions colored by hazard ratio, with a visual indication of the inhibited interaction by atezolizumab.

Fig. 30C is a network diagram showing select binding partners for LRRC4B, colored by hazard ratio.

Fig. 30D is a network diagram showing select interaction within the ephrin family, colored by hazard ratio.

Fig. 30E is a forest plot showing increased significance for association with lack of response and patient survival for each of the CD274 (PD-L1) interactions, relative to the individual genes.

Fig. 30F is a forest plot showing increased significance for association with lack of response and patient survival for each of the LRRC4B interactions, relative to the individual genes

DETAILED DESCRIPTION OF THE INVENTION

I. DEFINITIONS

The term "about" as used herein refers to the usual error range for the respective value readily known to the skilled person in this technical field. Reference to "about" a value or parameter herein includes (and describes) aspects that are directed to that value or parameter *per se*.

The term "single transmembrane receptor," "single-pass transmembrane receptor," or "STM receptor," as used herein, refers to a protein having a single transmembrane domain. In some aspects, the STM receptor is expressed on the cell surface. Exemplary STM receptors are provided in Table 5, Table 7, and Table 8 and in Martinez-Martin et al., *Cell*, 174(5): 1158-1171, 2018 and Clark et al., *Genome Res*, 13: 2265-2270, 2003. In some aspects, the STM protein has the UniProt annotation "leucine-rich,," "cysteine-rich," "ITIM/ITAM" (immunoreceptor tyrosine-based inhibition motif/immunoreceptor tyrosine-based activation motif), "TNFR" (tumor necrosis factor receptor), "TLR/ILR" (Toll-like receptor/interleukin receptor), "semaphorin," "Kinase-like," "Ig-like" (immunoglobulin-like), "fibronectin," "ephrin," "EGF," "cytokineR," or "cadherin". STM receptors may be identified based on, e.g., the presence of a signal peptide or a predicted transmembrane region in the amino acid sequence. In some aspects, the STM receptor is expressed as an extracellular domain.

The term "immunoglobulin superfamily protein" or "IgSF protein," as used herein, refers to a protein containing at least one immunoglobulin (Ig) domain or immunoglobulin fold, having the annotation

"immunoglobin-like superfamily," e.g., in the UniProt database, or otherwise indicated to have structural or functional similarity to such a protein. In some aspects, the IgSF protein has the annotation "immunoglobulin-like domain superfamily" in the UniProt database. In some aspects, the IgSF protein is included based on its participation in key biological activities, e.g., leukocyte activation, cell-cell adhesion, cell communication, or signal transduction. In some aspects, the IgSF protein has the UniProt annotation "TFNR" (transcription factor-like nuclear regulator), "TLR/ILR (Toll-like receptor/interleukin receptor), "semaphorin," "Kinase-like," "IgSF/Ig-like fold," "Ig-like fold," "fibronectin," "ephrin," "EGF," "CytokineR," or "cadherin". In some aspects, the IgSF protein is expressed on the cell surface. In other aspects, the IgSF protein is secreted. Exemplary IgSF proteins are provided in Table 4 and in Ozkan et al., *Cell*, 154(1): 228-239, 2013 and Yap et al., *J Mol Biol,* 426(4), 945-961. In some aspects, the IgSF superfamily protein is Programmed cell death 1 ligand 1 (PD-L1; CD274), Programmed cell death 1 ligand 2 (PD-L2; CD274; PDCD1LG2), Receptor-type tyrosine-protein phosphatase delta (PTPRD), Receptor-type tyrosine-protein phosphatase S (PTPRS), Receptor-type tyrosine-protein phosphatase S (PTPRF), Neural cell adhesion molecule L1-like protein ("Close homolog of L1"; CHL1), Contactin 1 (CNTN1), Leukocyte immunoglobulin-like receptor subfamily B member 1 (LILRB1), Leukocyte immunoglobulin-like receptor subfamily B member 3 (LILRB3), Leukocyte immunoglobulin-like receptor subfamily B member 4 (LILRB4), Leukocyte immunoglobulin-like receptor subfamily B member 5 (LILRB5), MAM domain-containing glycosylphosphatidylinositol anchor protein 1 (MDGA1), or Tyrosine-protein kinase receptor AXL (UFO). In some aspects, the IgSF protein is expressed as an extracellular domain. In some aspects, the IgSF protein is a secreted protein.

As used herein, the term "immunoglobulin domain" or "Ig domain" refers to a domain of an IgSF protein that is characterized by about 7-9 antiparallel β-strands comprising a two-layer β-sheet sandwich, spanning about 70–125 amino acid residues. In some aspects, the immunoglobulin domain contains a conserved disulfide bond connecting its *B* and *F* strands. Exemplary immunoglobulin domains are described in Bork et al., JMB, 242(4): 309-320, 1194 and Yap et al., *J Mol Biol,* 426(4), 945-961.

As used herein, the term "extracellular domain" or "ECD" refers to a protein domain that is predicted to be localized outside of the outer plasma membrane of the cell. In some instances, the ECD is an ECD of a receptor, e.g., a STM receptor. In some aspects, the ECD is an ECD of an IgSF protein. In some aspects, the ECD is the ECD of PDPN. In some aspects, the boundaries of the extracellular domain may be identified by prediction of domains that indicate that the protein crosses the plasma membrane, e.g., a transmembrane domain (e.g., a transmembrane helix). In some aspects, the presence of an extracellular domain may be predicted by the presence of a domain, sequence, or motif that indicates that the protein is trafficked to the plasma membrane, e.g., a signal sequence or a glycosylphosphatidylinositol (GPI) linkage site. In some aspects, the boundaries of the ECD are determined according to UniProt annotations. In some aspects, the ECD is soluble. In some aspects, the extracellular domain is expressed in the context of a full-length protein. In other aspects, the extracellular domain is expressed as an isolated extracellular domain, e.g., a sequence of amino acid residues comprising only the amino acid residues of a protein that are predicted to be extracellular.

In some aspects, the isolated ECD is included in a fusion protein. In some aspects, inclusion in a fusion protein increases solubility, ease of expression, ease of capture (e.g., on a protein A-coated plate),

multimerization, or some other desirable property of the ECD. In some aspects, the ECD or ECD fusion protein is a monomer. In other aspects, the ECD or ECD fusion protein is a multimer, e.g., a tetramer or a pentamer. In some aspects, the ECD is fused to a human IgG. In some aspects, the ECD is fused to a human Fc tag. In some aspects, the ECD is fused to an Avidity AVITAG™ (Avi tag). In some aspects, the ECD is fused to a polyhistidine (His) tag. In some aspects, the ECD is fused to a glycoprotein D (gD) tag and a glycosylphosphatidylinositol (GPI) linker, e.g., a gD-GPI tag. In other aspects, the ECD is fused to the pentamerization domain of rat cartilaginous oligomeric matrix protein (COMP) and the β-lactamase protein, e.g., as described in Bushell et al., *Genome Res*, 18: 622-630, 2008. In some aspects, the ECD fusion protein further includes a cleavage sequence, e.g., a TEV cleavage sequence, to allow removal of one or more domains. In some instances, an ECD fusion protein having an Avi tag and an Fc tag cleavable at a cleavage sequence is further processed to remove the Fc tag, to biotinylate the Avi tag, and to fuse the biotinylated ECD fusion protein to a fluorescent streptavidin (SA), e.g., to form a tetramerized ECD fusion protein. In some instances, the isolated ECD or ECD fusion protein is purified.

As used herein, a "modulator" is an agent that modulates (e.g., increases, decreases, activates, or inhibits) a given biological activity, e.g., an interaction or a downstream activity resulting from an interaction. A modulator or candidate modulator may be, e.g., a small molecule, an antibody, an antigen-binding fragment (e.g., a bis-Fab, an Fv, a Fab, a Fab'-SH, a $F(ab')_2$, a diabody, a linear antibody, an scFv, an ScFab, a VH domain, or a VHH domain), a peptide, a mimic, an antisense oligonucleotide, or a small interfering RNA (siRNA).

By "increase" or "activate" is meant the ability to cause an overall increase, for example, of 20% or greater, of 50% or greater, or of 75%, 85%, 90%, or 95% or greater. In certain aspects, increase or activate can refer to a downstream activity of a protein-protein interaction.

By "reduce" or "inhibit" is meant the ability to cause an overall decrease, for example, of 20% or greater, of 50% or greater, or of 75%, 85%, 90%, or 95% or greater. In certain aspects, reduce or inhibit can refer to a downstream activity of a protein-protein interaction.

"Affinity" refers to the strength of the sum total of noncovalent interactions between a single binding site of a molecule (e.g., a receptor) and its binding partner (e.g., a ligand). Unless indicated otherwise, as used herein, "binding affinity" refers to intrinsic binding affinity, which reflects a 1:1 interaction between members of a binding pair (e.g., receptor and ligand). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (K_D). Affinity can be measured by common methods known in the art, including those described herein.

"Complex" or "complexed" as used herein refers to the association of two or more molecules that interact with each other through bonds and/or forces (*e.g.,* Van der Waals, hydrophobic, hydrophilic forces) that are not peptide bonds. In one aspect, a complex is heteromultimeric. It should be understood that the term "protein complex" or "polypeptide complex" as used herein includes complexes that have a non-protein entity conjugated to a protein in the protein complex (e.g., including, but not limited to, chemical molecules such as a toxin or a detection agent).

A "disorder" is any condition that would benefit from treatment including, but not limited to, chronic and acute disorders or diseases including those pathological conditions which predispose the mammal to the disorder in question. In one aspect, the disorder is a cancer.

The terms "cancer" and "cancerous" refer to or describe the physiological condition in mammals that is typically characterized by unregulated cell growth/proliferation. Aspects of cancer include solid tumor cancers and non-solid tumor cancers. Solid cancer tumors include, but are not limited to a colorectal cancer, a head and neck cancer (e.g., a squamous cell carcinoma of the head and neck), a glioma, a melanoma, a breast cancer, a lung cancer, a bladder cancer, a kidney cancer, an ovarian cancer, a pancreatic cancer, or a prostate cancer, or metastatic forms thereof. In some aspects, the cancer is a colorectal cancer (CRC). In some aspects, the cancer is a head and neck cancer. Further aspects of head and neck cancer include a squamous cell carcinoma of the head & neck (SCCHN). In some aspects, the cancer is a breast cancer. Further aspects of breast cancer include a hormone receptor-positive (HR+) breast cancer, e.g., an estrogen receptor-positive (ER+) breast cancer, a progesterone receptor-positive (PR+) breast cancer, or an ER+/PR+ breast cancer. Other aspects of breast cancer include a HER2-positive (HER2+) breast cancer. Yet other aspects of breast cancer include a triple-negative breast cancer (TNBC). In some aspects, the breast cancer is an early breast cancer. In some aspects, the cancer is a lung cancer. Further aspects of lung cancer include an epidermal growth factor receptor-positive (EGFR+) lung cancer. Other aspects of lung cancer include an epidermal growth factor receptor-negative (EGFR-) lung cancer. Yet other aspects of lung cancer include a non-small cell lung cancer, e.g., a squamous lung cancer or a non-squamous lung cancer. Other aspects of lung cancer include a small cell lung cancer. In some aspects, the cancer is a urinary tract cancer. Urinary tract cancers include urothelial carcinomas (UC), non-urothelial carcinomas of the urinary tract, and carcinomas of the urinary tract having mixed histology. Non-urothelial carcinomas of the urinary tract include all subtypes listed in the World Health Organization classification, e.g., a squamous cell carcinoma, a verrucous carcinoma, an adenocarcinoma, a glandular carcinoma, a carcinoma of the Bellini collecting duct, a neuroendocrine carcinoma, or a small cell carcinoma. The adenocarcinoma may be an enteric adenocarcinoma, a mucinous adenocarcinoma, a signet-ring cell adenocarcinoma, or a clear cell adenocarcinoma. Urinary tract cancers may be located in the bladder, the renal pelvis, the ureter, or the urethra. In some aspects, the urinary tract cancer (e.g., urothelial carcinoma, non-urothelial carcinoma, or carcinoma of the urinary tract having mixed histology) is locally advanced, e.g., stage T4b N_{any} or T_{any} N2–3, according to the TNM classification, at the onset of treatment. In some aspects, the urinary tract cancer is a metastatic urothelial carcinoma (mUC), a metastatic form of a non-urothelial carcinoma of the urinary tract, or a metastatic form of a carcinoma of the urinary tract having mixed histology. In some aspects, the urinary tract cancer is TNM stage M1, according to the TNM classification, at the onset of treatment. In some aspects, the cancer is a bladder cancer. Further aspects of bladder cancer include a urothelial bladder cancer (UBC), a muscle invasive bladder cancer (MIBC), or a non-muscle invasive bladder cancer (NMIBC). In some aspects, the cancer is a kidney cancer. Further aspects of kidney cancer include a renal cell carcinoma (RCC). In some aspects, the cancer is a liver cancer. Further aspects of liver cancer include a hepatocellular carcinoma. In some aspects, the cancer is a prostate cancer. Further aspects of prostate cancer include a castration-resistant prostate cancer (CRPC). In some aspects, the cancer is a metastatic form of a solid tumor. In some aspects, the metastatic form of a solid tumor is a metastatic form of a melanoma, a breast cancer, a colorectal cancer, a lung cancer, a head and neck cancer, a bladder cancer, a kidney cancer, an ovarian cancer, a pancreatic cancer, or a prostate

cancer. In some aspects, the cancer is a non-solid tumor cancer. Non-solid tumor cancers include, but are not limited to, a B-cell lymphoma. Further aspects of B-cell lymphoma include, e.g., a chronic lymphocytic leukemia (CLL), a diffuse large B-cell lymphoma (DLBCL), a follicular lymphoma, myelodysplastic syndrome (MDS), a non-Hodgkin lymphoma (NHL), an acute lymphoblastic leukemia (ALL), a multiple myeloma, an acute myeloid leukemia (AML), or a mycosis fungoides (MF).

The terms "host cell," "host cell line," and "host cell culture" are used interchangeably and refer to cells into which exogenous nucleic acid has been introduced, including the progeny of such cells. Host cells include "transfected cells," "transformed cells," and "transformants," which include the primary transformed cell and progeny derived therefrom without regard to the number of passages. Progeny may not be completely identical in nucleic acid content to a parent cell, but may contain mutations. Mutant progeny that have the same function or biological activity as screened or selected for in the originally transformed cell are included herein. In some aspects, the host cell is stably transformed with the exogenous nucleic acid. In other aspects, the host cell is transiently transformed with the exogenous nucleic acid.

The term "cancer-associated fibroblast" ("CAF") or "tumor-associated fibroblast," as used herein, refers to a fibroblast cell (e.g., a mammalian stromal cell) present in or associated with the tumor microenvironment (TME), e.g., the stroma. In some aspects, the CAFs are active fibroblasts. CAFs may regulate the structure and/or function of the TME, e.g., via extracellular matrix (ECM) remodeling and/or secretion of soluble factors, e.g., growth factors and/or inflammatory factors. CAFs may contribute to tumorigenesis, tumor growth, tumor invasion, angiogenesis or metastasis. CAFs may impair anti-tumor immunity. In some aspects, CAFs express podoplanin (PDPN). In some aspects, CAFs are characterized by actomyosin contractility, a property that affects tissue stiffness. In some aspects, CAFs are associated with an activated fibroblast signature and/or an FAP^+ fibroblast signature, e.g., express genes provided in Table 11 and/or Table 12.

The term "podoplanin" or "PDPN," as used herein, broadly refers to any native PDPN from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. PDPN is also called gp38, Aggrus, and T1α. The term encompasses full-length PDPN and isolated regions or domains of PDPN, e.g., the PDPN extracellular domain (ECD). The term also encompasses naturally occurring variants of PDPN, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human PDPN is shown under UniProt Accession No. Q86YL7. Minor sequence variations, especially conservative amino acid substitutions of PDPN that do not affect PDPN function and/or activity, are also contemplated by the invention.

The term "cluster of differentiation 177" or "CD177," as used herein, broadly refers to any native CD177 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length CD177 and isolated regions or domains of CD177, e.g., the CD177 ECD. The term also encompasses naturally occurring variants of CD177, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human CD177 is shown under UniProt Accession No. Q8N6Q3. Minor sequence variations, especially conservative amino acid substitutions of CD177 that do not affect CD177 function and/or activity, are also contemplated by the invention.

The term "agonist of CD177 activity" or "CD177 agonist" refers to a molecule that increases signal transduction resulting from the interaction of CD177 with one or more of its binding partners, e.g., PDPN. The agonist of CD177 activity may result in an increase in the binding of CD177 to one or more of its binding partners (e.g., PDPN) relative to binding of the two proteins in the absence of the agonist. Agonists of CD177 activity may include antibodies, antigen binding fragments thereof, immunoadhesins, fusion proteins, peptides (e.g., multimerized peptides, e.g., multimerized CD177 polypeptides), oligopeptides, and other molecules that increase signal transduction resulting from the interaction of CD177 with one or more of its binding partners, e.g., PDPN.

The term "Programmed cell death 1 ligand 1" or "PD-L1," as used herein, broadly refers to any native PD-L1 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. PD-L1 is also called CD274. The term encompasses full-length PD-L1 and isolated regions or domains of PD-L1, e.g., the PD-L1 ECD. The term also encompasses naturally occurring variants of PD-L1, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human PD-L1 is shown under UniProt Accession No. Q9NZQ7. Minor sequence variations, especially conservative amino acid substitutions of PD-L1 that do not affect PD-L1 function and/or activity, are also contemplated by the invention.

The term "ephrin type-A receptor 3" or "EPHA3," as used herein, broadly refers to any native EPHA3 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length EPHA3 and isolated regions or domains of EPHA3, e.g., the EPHA3 ECD. The term also encompasses naturally occurring variants of EPHA3, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human EPHA3 is shown under UniProt Accession No. P29320. Minor sequence variations, especially conservative amino acid substitutions of EPHA3 that do not affect EPHA3 function and/or activity, are also contemplated by the invention.

The term "Programmed cell death 1 ligand 2" or "PD-L2," as used herein, broadly refers to any native PD-L2 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. PD-L2 is also called PDCD1LG2. The term encompasses full-length PD-L2 and isolated regions or domains of PD-L2, e.g., the PD-L2 ECD. The term also encompasses naturally occurring variants of PD-L2, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human PD-L2 is shown under UniProt Accession No. Q9BQ51. Minor sequence variations, especially conservative amino acid substitutions of PD-L2 that do not affect PD-L2 function and/or activity, are also contemplated by the invention.

The term "CEACAM4," as used herein, broadly refers to any native CEACAM4 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length CEACAM4 and isolated regions or domains of CEACAM4, e.g., the CEACAM4 ECD. The term also encompasses naturally occurring variants of CEACAM4, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human CEACAM4 is shown under UniProt Accession No. O75871. Minor sequence variations, especially conservative amino acid substitutions of CEACAM4 that do not affect CEACAM4 function and/or activity, are also contemplated by the invention.

The term "Receptor-type tyrosine-protein phosphatase delta" or "PTPRD," as used herein, broadly refers to any native PTPRD from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length PTPRD and isolated regions or domains of PTPRD, e.g., the PTPRD ECD. The term also encompasses naturally occurring variants of PTPRD, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human PTPRD is shown under UniProt Accession No. P23468. Minor sequence variations, especially conservative amino acid substitutions of PTPRD that do not affect PTPRD function and/or activity, are also contemplated by the invention.

The term "Receptor-type tyrosine-protein phosphatase F" or "PTPRF," as used herein, broadly refers to any native PTPRF from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length PTPRF and isolated regions or domains of PTPRF, e.g., the PTPRF ECD. The term also encompasses naturally occurring variants of PTPRF, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human PTPRF is shown under UniProt Accession No. P10586. Minor sequence variations, especially conservative amino acid substitutions of PTPRF that do not affect PTPRF function and/or activity, are also contemplated by the invention.

The term "Receptor-type tyrosine-protein phosphatase S" or "PTPRS," as used herein, broadly refers to any native PTPRS from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length PTPRS and isolated regions or domains of PTPRS, e.g., the PTPRS ECD. The term also encompasses naturally occurring variants of PTPRS, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human PTPRS is shown under UniProt Accession No. Q13332. Minor sequence variations, especially conservative amino acid substitutions of PTPRS that do not affect PTPRS function and/or activity, are also contemplated by the invention.

The term "CHL1," as used herein, broadly refers to any native CHL1 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length CHL1 and isolated regions or domains of CHL1, e.g., the CHL1 ECD. The term also encompasses naturally occurring variants of CHL1, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human CHL1 is shown under UniProt Accession No. O00533. Minor sequence variations, especially conservative amino acid substitutions of CHL1 that do not affect CHL1 function and/or activity, are also contemplated by the invention.

The term "Contactin 1" or "CNTN1," as used herein, broadly refers to any native CNTN1 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length CNTN1 and isolated regions or domains of CNTN1, e.g., the CNTN1 ECD. The term also encompasses naturally occurring variants of CNTN1, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human CNTN1 is shown under UniProt Accession No. Q12860. Minor sequence variations, especially conservative amino acid substitutions of CNTN1 that do not affect CNTN1 function and/or activity, are also contemplated by the invention.

The term "Leukocyte immunoglobulin-like receptor subfamily B member 1" or "LILRB1," as used herein, broadly refers to any native LILRB1 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length LILRB1 and isolated regions or domains of LILRB1, e.g., the LILRB1 ECD. The term also encompasses naturally occurring variants of LILRB1, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human LILRB1 is shown under UniProt Accession No. Q8NHL6. Minor sequence variations, especially conservative amino acid substitutions of LILRB1 that do not affect LILRB1 function and/or activity, are also contemplated by the invention.

The term "Leukocyte immunoglobulin-like receptor subfamily B member 2" or "LILRB2," as used herein, broadly refers to any native LILRB2 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length LILRB2 and isolated regions or domains of LILRB2, e.g., the LILRB2 ECD. The term also encompasses naturally occurring variants of LILRB2, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human LILRB2 is shown under UniProt Accession No. Q8N423. Minor sequence variations, especially conservative amino acid substitutions of LILRB2 that do not affect LILRB2 function and/or activity, are also contemplated by the invention.

The term "Leukocyte immunoglobulin-like receptor subfamily B member 3" or "LILRB3," as used herein, broadly refers to any native LILRB3 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length LILRB3 and isolated regions or domains of LILRB3, e.g., the LILRB3 ECD. The term also encompasses naturally occurring variants of LILRB3, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human LILRB3 is shown under UniProt Accession No. O75022. Minor sequence variations, especially conservative amino acid substitutions of LILRB3 that do not affect LILRB3 function and/or activity, are also contemplated by the invention.

The term "Leukocyte immunoglobulin-like receptor subfamily B member 4" or "LILRB4," as used herein, broadly refers to any native LILRB4 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length LILRB4 and isolated regions or domains of LILRB4, e.g., the LILRB4 ECD. The term also encompasses naturally occurring variants of LILRB4, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human LILRB4 is shown under UniProt Accession No. Q8NHJ6. Minor sequence variations, especially conservative amino acid substitutions of LILRB4 that do not affect LILRB4 function and/or activity, are also contemplated by the invention.

The term "Leukocyte immunoglobulin-like receptor subfamily B member 5" or "LILRB5," as used herein, broadly refers to any native LILRB5 from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length LILRB5 and isolated regions or domains of LILRB5, e.g., the LILRB5 ECD. The term also encompasses naturally occurring variants of LILRB5, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human LILRB5 is shown under UniProt Accession No. O75023. Minor sequence variations, especially conservative amino acid substitutions of LILRB5 that do not affect LILRB5 function and/or activity, are also contemplated by the invention.

The term "AXL," as used herein, broadly refers to any native AXL from any mammalian source, including primates (e.g. humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses full-length AXL and isolated regions or domains of AXL, e.g., the AXL ECD. AXL is also known as UFO. The term also encompasses naturally occurring variants of AXL, e.g., splice variants or allelic variants. The amino acid sequence of an exemplary human AXL is shown under UniProt Accession No. P30530. Minor sequence variations, especially conservative amino acid substitutions of AXL that do not affect AXL function and/or activity, are also contemplated by the invention.

The term "protein," as used herein, refers to any native protein from any vertebrate source, including mammals such as primates (e.g., humans) and rodents (e.g., mice and rats), unless otherwise indicated. The term encompasses "full-length," unprocessed protein any form of the protein that results from processing in the cell. The term also encompasses naturally occurring variants of the protein, e.g., splice variants or allelic variants, e.g., amino acid substitution mutations or amino acid deletion mutations. The term also includes isolated regions or domains of the protein, e.g., the extracellular domain (ECD).

An "isolated" protein or peptide is one which has been separated from a component of its natural environment. In some aspects, a protein or peptide is purified to greater than 95% or 99% purity as determined by, for example, electrophoresis (e.g., SDS-PAGE, isoelectric focusing (IEF), capillary electrophoresis) or chromatography (e.g., ion exchange or reverse phase HPLC).

An "isolated" nucleic acid refers to a nucleic acid molecule that has been separated from a component of its natural environment. An isolated nucleic acid includes a nucleic acid molecule contained in cells that ordinarily contain the nucleic acid molecule, but the nucleic acid molecule is present extrachromosomally or at a chromosomal location that is different from its natural chromosomal location.

The term "interactome," as used herein, refers to the set of molecular interactions, e.g., protein-protein interactions, occurring within a set of molecules. In some aspects, the interactome is represented as a network, e.g., a network in which nodes represent a specific molecule and edges connect nodes for which an assay (e.g., a cell surface interaction assay or an extracellular interaction assay) detects interaction between the two nodes.

The term "vector," as used herein, refers to a nucleic acid molecule capable of propagating another nucleic acid to which it is linked. The term includes the vector as a self-replicating nucleic acid structure as well as the vector incorporated into the genome of a host cell into which it has been introduced. Certain vectors are capable of directing the expression of nucleic acids to which they are operatively linked. Such vectors are referred to herein as "expression vectors."

As used herein, the term "immune checkpoint inhibitor" refers to a therapeutic agent that targets at least one immune checkpoint protein to alter the regulation of an immune response, e.g., down-modulating, inhibiting, up-modulating, or activating an immune response. The term "immune checkpoint blockade" may be used to refer to a therapy comprising an immune checkpoint inhibitor. Immune checkpoint proteins are known in the art and include, without limitation, cytotoxic T-lymphocyte antigen 4 (CTLA-4), programmed cell death 1 (PD-1), programmed cell death ligand 1 (PD-L1), programmed cell death ligand 2 (PD-L2), V-domain Ig suppressor of T cell activation (VISTA), B7-H2, B7-H3, B7-H4, B7-H6, 2B4, ICOS, HVEM, CD160, gp49B, PIR-B, KIR family receptors, TIM-1, TIM-3, TIM-4, LAG-3, BTLA,

SIRPalpha (CD47), CD48, 2B4 (CD244), B7.1, B7.2, ILT-2, ILT-4, TIGIT, LAG-3, BTLA, IDO, OX40, and A2aR. In some aspects, an immune checkpoint protein may be expressed on the surface of an activated T cell. Therapeutic agents that can act as immune checkpoint inhibitors useful in the methods of the present invention, include, but are not limited to, therapeutic agents that target one or more of CTLA-4, PD-1, PD-L1, PD-L2, VISTA, B7-H2, B7-H3, B7-H4, B7-H6, 2B4, ICOS, HVEM, CD160, gp49B, PIR-B, KIR family receptors, TIM-1, TIM-3, TIM-4, LAG- 3, BTLA, SIRPalpha (CD47), CD48, 2B4 (CD244), B7.1, B7.2, ILT-2, ILT-4, TIGIT, LAG-3, BTLA, IDO, OX40, and A2aR. In some aspects, an immune checkpoint inhibitor enhances or suppresses the function of one or more targeted immune checkpoint proteins. In some aspects, the immune checkpoint inhibitor is a PD-L1 axis binding antagonist, such as atezolizumab.

The term "PD-L1 axis binding antagonist" refers to a molecule that inhibits the interaction of a PD-1 axis binding partner with either one or more of its binding partner, so as to remove T cell dysfunction resulting from signaling on the PD-1 signaling axis – with a result being to restore or enhance T cell function (e.g., proliferation, cytokine production, target cell killing). As used herein, a PD-L1 axis binding antagonist includes a PD-L1 binding antagonist, a PD-1 binding antagonist, and a PD-L2 binding antagonist.

The term "PD-1 binding antagonist" refers to a molecule that decreases, blocks, inhibits, abrogates or interferes with signal transduction resulting from the interaction of PD-1 with one or more of its binding partners, such as PD-L1, or PD-L2. In some aspects, the PD-1 binding antagonist is a molecule that inhibits the binding of PD-1 to one or more of its binding partners. In a specific aspect, the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1 and/or PD-L2. For example, PD-1 binding antagonists include anti-PD-1 antibodies, antigen binding fragments thereof, immunoadhesins, fusion proteins, oligopeptides and other molecules that decrease, block, inhibit, abrogate or interfere with signal transduction resulting from the interaction of PD-1 with PD-L1 and/or PD-L2. In one aspect, a PD-1 binding antagonist reduces the negative co-stimulatory signal mediated by or through cell surface proteins expressed on T lymphocytes mediated signaling through PD-1 so as render a dysfunctional T cell less dysfunctional (e.g., enhancing effector responses to antigen recognition). In some aspects, the PD-1 binding antagonist is an anti-PD-1 antibody. In a specific aspect, a PD-1 binding antagonist is MDX-1106 (nivolumab). In another specific aspect, a PD-1 binding antagonist is MK-3475 (pembrolizumab). In another specific aspect, a PD-1 binding antagonist is AMP-224. In another specific aspect, a PD-1 binding antagonist is MED1-0680. In another specific aspect, a PD-1 binding antagonist is PDR001 (spartalizumab). In another specific aspect, a PD-1 binding antagonist is REGN2810 (cemiplimab). In another specific aspect, a PD-1 binding antagonist is BGB-108.

The term "PD-L1 binding antagonist" refers to a molecule that decreases, blocks, inhibits, abrogates or interferes with signal transduction resulting from the interaction of PD-L1 with either one or more of its binding partners, such as PD-1 and B7-1. In some aspects, a PD-L1 binding antagonist is a molecule that inhibits the binding of PD-L1 to its binding partners. In a specific aspect, the PD-L1 binding antagonist inhibits binding of PD-L1 to PD-1 and/or B7-1. In some aspects, the PD-L1 binding antagonists include anti-PD-L1 antibodies, antigen binding fragments thereof, immunoadhesins, fusion proteins, oligopeptides and other molecules that decrease, block, inhibit, abrogate or interfere with signal transduction resulting from the interaction of PD-L1 with one or more of its binding partners, such as PD-1

and B7-1. In one aspect, a PD-L1 binding antagonist reduces the negative co-stimulatory signal mediated by or through cell surface proteins expressed on T lymphocytes mediated signaling through PD-L1 so as to render a dysfunctional T cell less dysfunctional (e.g., enhancing effector responses to antigen recognition). In some aspects, a PD-L1 binding antagonist is an anti-PD-L1 antibody. In still another specific aspect, an anti-PD-L1 antibody is MPDL3280A (atezolizumab, marketed as TECENTRIQ™ with a WHO Drug Information (International Nonproprietary Names for Pharmaceutical Substances), Recommended INN: List 74, Vol. 29, No. 3, 2015 (see page 387)). In a specific aspect, an anti-PD-L1 antibody is YW243.55.S70. In another specific aspect, an anti-PD-L1 antibody is MDX-1105. In another specific aspect, an anti PD-L1 antibody is MSB0015718C. In still another specific aspect, an anti-PD-L1 antibody is MEDI4736.

The term "PD-L2 binding antagonist" refers to a molecule that decreases, blocks, inhibits, abrogates or interferes with signal transduction resulting from the interaction of PD-L2 with either one or more of its binding partners, such as PD-1. In some aspects, a PD-L2 binding antagonist is a molecule that inhibits the binding of PD-L2 to one or more of its binding partners. In a specific aspect, the PD-L2 binding antagonist inhibits binding of PD-L2 to PD-1. In some aspects, the PD-L2 antagonists include anti-PD-L2 antibodies, antigen binding fragments thereof, immunoadhesins, fusion proteins, oligopeptides and other molecules that decrease, block, inhibit, abrogate or interfere with signal transduction resulting from the interaction of PD-L2 with either one or more of its binding partners, such as PD-1. In one aspect, a PD-L2 binding antagonist reduces the negative co-stimulatory signal mediated by or through cell surface proteins expressed on T lymphocytes mediated signaling through PD-L2 so as render a dysfunctional T cell less dysfunctional (e.g., enhancing effector responses to antigen recognition). In some aspects, a PD-L2 binding antagonist is an immunoadhesin.

The term "antibody" herein is used in the broadest sense and encompasses various antibody structures, including but not limited to monoclonal antibodies, polyclonal antibodies, multispecific antibodies (e.g., bispecific antibodies), and antibody fragments (e.g., bis-Fabs) so long as they exhibit the desired antigen-binding activity.

An "antigen-binding fragment" or "antibody fragment" refers to a molecule other than an intact antibody that comprises a portion of an intact antibody that binds the antigen to which the intact antibody binds. Examples of antigen-binding fragments include but are not limited to bis-Fabs; Fv; Fab; Fab, Fab'-SH; $F(ab')_2$; diabodies; linear antibodies; single-chain antibody molecules (e.g., scFv, ScFab); and multispecific antibodies formed from antibody fragments.

A "single-domain antibody" refers to an antibody fragment comprising all or a portion of the heavy chain variable domain or all or a portion of the light chain variable domain of an antibody. In certain aspects, a single-domain antibody is a human single-domain antibody (see, e.g., U.S. Patent No. 6,248,516 B1). Examples of single-domain antibodies include but are not limited to a VHH.

A "Fab" fragment is an antigen-binding fragment generated by papain digestion of antibodies and consists of an entire L chain along with the variable region domain of the H chain (VH), and the first constant domain of one heavy chain (CH1). Papain digestion of antibodies produces two identical Fab fragments. Pepsin treatment of an antibody yields a single large $F(ab')_2$ fragment which roughly corresponds to two disulfide linked Fab fragments having divalent antigen-binding activity and is still

capable of cross-linking antigen. Fab' fragments differ from Fab fragments by having an additional few residues at the carboxy terminus of the CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. $F(ab')_2$ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

The term "Fc region" herein is used to define a C-terminal region of an immunoglobulin heavy chain, including native sequence Fc regions and variant Fc regions. Although the boundaries of the Fc region of an immunoglobulin heavy chain might vary, the human IgG heavy chain Fc region is usually defined to stretch from an amino acid residue at position Cys226, or from Pro230, to the carboxyl-terminus thereof. The C-terminal lysine (residue 447 according to the EU numbering system) of the Fc region may be removed, for example, during production or purification of the antibody, or by recombinantly engineering the nucleic acid encoding a heavy chain of the antibody. Accordingly, a composition of intact antibodies may comprise antibody populations with all Lys447 residues removed, antibody populations with no Lys447 residues removed, and antibody populations having a mixture of antibodies with and without the Lys447 residue.

"Fv" consists of a dimer of one heavy- and one light-chain variable region domain in tight, non-covalent association. From the folding of these two domains emanate six hypervariable loops (3 loops each from the H and L chain) that contribute the amino acid residues for antigen binding and confer antigen binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although often at a lower affinity than the entire binding site.

The terms "full-length antibody," "intact antibody," and "whole antibody" are used herein interchangeably to refer to an antibody having a structure substantially similar to a native antibody structure or having heavy chains that contain an Fc region as defined herein.

"Single-chain Fv" also abbreviated as "sFv" or "scFv" are antibody fragments that comprise the VH and VL antibody domains connected into a single polypeptide chain. Preferably, the scFv polypeptide further comprises a polypeptide linker between the VH and VL domains, which enables the scFv to form the desired structure for antigen binding. For a review of scFv, see Pluckthun, The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994); Malmborg *et al.*, J. Immunol. Methods 183:7-13, 1995.

The term "small molecule" refers to any molecule with a molecular weight of about 2000 daltons or less, e.g., about 1000 daltons or less. In some aspects, the small molecule is a small organic molecule.

The term "mimic" or "molecular mimic," as used herein, refers to a polypeptide having sufficient similarity in conformation and/or binding ability (e.g., secondary structure, tertiary structure) to a given polypeptide or to a portion of said polypeptide to bind to a binding partner of said polypeptide. The mimic may bind the binding partner with equal, less, or greater affinity than the polypeptide it mimics. A molecular mimic may or may not have obvious amino acid sequence similarity to the polypeptide it mimics. A mimic may be naturally occurring or may be engineered. In some aspects, the mimic is a mimic of the protein of Table 1. In other aspects, the mimic is a mimic of the protein of Table 2. In yet

other aspects, the mimic is a mimic of another protein that binds to the protein of Table 1 or the protein of Table 2. In some aspects, the mimic may perform all functions of the mimicked polypeptide. In other aspects, the mimic does not perform all functions of the mimicked polypeptide.

As used herein, the term "conditions permitting the binding" of two or more proteins to each other (e.g., a protein of Table 1 and a protein of Table 2) refers to conditions (e.g., protein concentration, temperature, pH, salt concentration) under which the two or more proteins would interact in the absence of a modulator or a candidate modulator. Conditions permitting binding may differ for individual proteins and may differ between protein-protein interaction assays (e.g., surface plasmon resonance assays, biolayer interferometry assays, enzyme-linked immunosorbent assays (ELISA), extracellular interaction assays, and cell surface interaction assays.

The term "survival" refers to the patient remaining alive, and includes overall survival as well as progression-free survival.

As used herein, "recurrence-free survival" or "RFS" refers to the length of time after primary treatment for a cancer ends that the patient survives without any signs or symptoms of that cancer. RFS may also be referred to as "disease-free survival" or "DFS". In some aspects, Disease-free survival (RFS) is defined as the time between randomization (e.g., assignment to an adjuvant treatment group) and recurrence of a disease (e.g., a cancer), new occurrence of a disease (e.g., a cancer), or death from any cause.

As used herein, "progression-free survival" or "PFS" refers to the length of time during and after treatment during which the disease being treated (e.g., cancer) does not get worse. Progression-free survival may include the amount of time patients have experienced a complete response or a partial response, as well as the amount of time patients have experienced stable disease.

As used herein, "overall survival" or "OS" refers to the percentage of individuals in a group who are likely to be alive after a particular duration of time.

"Percent (%) amino acid sequence identity" with respect to a reference polypeptide sequence is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the reference polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for aligning sequences, including any algorithms needed to achieve maximal alignment over the full-length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the sequence comparison computer program ALIGN-2. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc., and the source code has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available from Genentech, Inc., South San Francisco, California, or may be compiled from the source code. The

ALIGN-2 program should be compiled for use on a UNIX operating system, including digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program.

As used herein, "treatment" (and grammatical variations thereof such as "treat" or "treating") refers to clinical intervention in an attempt to alter the natural course of the individual being treated, and can be performed either for prophylaxis or during the course of clinical pathology. Desirable effects of treatment include, but are not limited to, preventing occurrence or recurrence of disease, alleviation of symptoms, diminishment of any direct or indirect pathological consequences of the disease, preventing metastasis, decreasing the rate of disease progression, amelioration or palliation of the disease state, and remission or improved prognosis. In some aspects, an agent (e.g., a modulator, a PD-L1 axis binding antagonist, or an agonist of CD177 activity) is used to delay development of a disease or to slow the progression of a disease.

A "subject" or an "individual" is a mammal. Mammals include, but are not limited to, domesticated animals (e.g., cows, sheep, cats, dogs, and horses), primates (e.g., humans and non-human primates such as monkeys), rabbits, and rodents (e.g., mice and rats). In certain aspects, the subject or individual is a human.

As used herein, "administering" is meant a method of giving a dosage of a compound to a subject. In some aspects, the compositions utilized in the methods herein are administered intravenously. The compositions utilized in the methods described herein can be administered, for example, intramuscularly, intravenously, intradermally, percutaneously, intraarterially, intraperitoneally, intralesionally, intracranially, intraarticularly, intraprostatically, intrapleurally, intratracheally, intranasally, intravitreally, intravaginally, intrarectally, topically, intratumorally, peritoneally, subcutaneously, subconjunctivally, intravesicularlly, mucosally, intrapericardially, intraumbilically, intraocularly, orally, topically, locally, by inhalation, by injection, by infusion, by continuous infusion, by localized perfusion bathing target cells directly, by catheter, by lavage, in cremes, or in lipid compositions. The method of administration can vary depending on various factors (e.g., the compound or composition being administered and the severity of the condition, disease, or disorder being treated).

The term "sample," as used herein, refers to a composition that is obtained or derived from a subject and/or individual of interest that contains a cellular and/or other molecular entity that is to be characterized and/or identified, for example, based on physical, biochemical, chemical, and/or physiological characteristics. For example, the phrase "disease sample" and variations thereof refers to any sample obtained from a subject of interest that would be expected or is known to contain the cellular and/or molecular entity that is to be characterized. Samples include, but are not limited to, tissue samples, primary or cultured cells or cell lines, cell supernatants, cell lysates, platelets, serum, plasma, vitreous fluid, lymph fluid, synovial fluid, follicular fluid, seminal fluid, amniotic fluid, milk, whole blood, plasma, serum, blood-derived cells, urine, cerebro-spinal fluid, saliva, buccal swab, sputum, tears, perspiration, mucus, tumor lysates, and tissue culture medium, tissue extracts such as homogenized tissue, tumor tissue, cellular extracts, and combinations thereof. The sample may be an archival sample, a fresh sample, or a frozen sample. In some aspects, the sample is a formalin-fixed and paraffin-embedded (FFPE) tumor tissue sample.

II. METHODS OF IDENTIFYING PROTEIN-PROTEIN INTERACTIONS

A. Assays for protein-protein interaction

Interactions between two proteins are commonly tested using yeast two-hybrid (Y2H) assays and/or biochemical purification assays (e.g., affinity purification-mass spectrometry (AP/MS)); however, these methods are not well-suited to testing interactions between cell surface proteins. Cell surface proteins are often not soluble in the cytoplasm and/or nucleoplasm (e.g., due to hydrophobic transmembrane regions) and are thus inappropriate for Y2H assays. Further, interactions between cell surface proteins are often low-affinity and/or highly transient, e.g., having a half-life of less than one second, and are thus not compatible with assays involving lengthy purification protocols (e.g., AP/MS) (Bushell et al., *Genome Res*, 18: 622-630, 2008). The protein-protein interaction assays described herein, e.g., extracellular interaction assays and cell surface interaction assays, are compatible with cell surface proteins and are thus able to identify novel interactions among these proteins.

i. Extracellular interaction assays

In some aspects of the invention, the protein-protein interaction assay is an extracellular interaction assay, e.g., an avidity-based extracellular interaction screen (AVEXIS) (Bushell et al., *Genome Res*, 18: 622-630, 2008; Martinez-Martin et al., *J Immunol Res*, 2197615, 2017). In this type of assay, one or more prey proteins (e.g., one or more STM receptors) and one or more bait proteins (e.g., one or more IgSF proteins) are expressed as soluble extracellular domain (ECD) fusion proteins, as described below, and are assayed for interaction (e.g., using a colorimetric assay) in conditioned media.

ia. Extracellular interaction assay prey proteins

In some aspects, the prey protein or prey proteins comprise one or more fusion proteins (e.g., a library of prey fusion proteins) in which the extracellular domain (ECD) of a prey protein of interest (e.g., an STM protein) is conjugated (e.g., fused) to one or more additional moieties (e.g., an IgG or an Fc tag,

e.g., a human Fc tag) such that the prey fusion protein is soluble. ECDs may be identified as described in Section 2B*(i)*.

ib. Extracellular interaction assay bait proteins

In some aspects, the bait protein (query protein) or bait proteins comprise one or more fusion proteins (e.g., a library of bait fusion proteins) in which the ECD of a bait protein of interest is conjugated (e.g., fused) to one or more additional moieties such that the bait fusion protein is soluble. The additional moiety may also increase the avidity of the bait fusion protein for the prey protein, e.g., by multimerizing the bait protein ECD. Increasing avidity may increase the detection of low-affinity interactions. In some aspects, the additional moiety or moieties cause pentamerization of the bait protein ECD. In some aspects, the additional moiety is the pentamerization domain of rat cartilaginous oligomeric maintenance protein (COMP). ECDs may be identified as described in Section 2B*(i)*.

The bait protein may also be conjugated to a moiety that allows detection of the bait protein, e.g., the beta-lactamase (β-lactamase) protein. β-lactamase hydrolyzes the substrate nitrocefin, producing a yellow to red color change, which may be detected in a colorimetric assay (e.g., measurement of absorbance at 485 nm).

In some aspects, the bait fusion protein comprises both a COMP pentamerization domain and a β-lactamase protein.

ic. Expression

The bait fusion protein and/or prey fusion protein may be expressed (e.g., transfected, e.g., transiently transfected) in a cell. The cell may be a human cell, e.g., a HEK293 cell (e.g., an Expi293F cell). In some aspects, the bait fusion protein and/or prey fusion protein is expressed in conditioned media, e.g., the conditioned media of transfected cells, e.g., the conditioned media of transfected human cells. Expression in human cells may increase the likelihood that posttranslational modifications (e.g., disulfide bonds, addition of one or more glycans) occur, thus increasing the likelihood that functionally relevant interactions may be detected.

Cells may be removed from the conditioned media (e.g., by centrifugation) after a period of growth (e.g., 7 days); bait fusion proteins and/or prey fusion proteins are present in the conditioned media from which cells have been removed (e.g. the supernatant of a centrifugation step).

id. Assay for interaction

The prey fusion protein may be captured from conditioned media, e.g., captured on a protein A-coated substrate based on the affinity between protein A and an Fc tag of the prey fusion protein. The substrate may be a well, e.g., a well in a 384-well plate.

The bait fusion protein may be assayed directly in the conditioned media. The concentration of the bait protein may be normalized before the assay for interaction is performed, e.g., by dilution.

To perform the protein-protein interaction assay, a solution comprising the bait protein may be added to one or more substrates comprising a prey protein (e.g., to one or more wells of a 384-well plate). The assay may then be incubated and washed one or more times to remove non-bound bait

protein. In aspects in which the bait fusion protein comprises β-lactamase, interaction between the bait fusion protein and the prey fusion protein may be detected by the addition of the substrate nitrocefin and measurement of nitrocefin hydrolysis, e.g., by measuring absorbance at 485 nm. A relatively high absorbance indicates that the bait fusion protein is retained, i.e., that the bait fusion protein and the prey fusion protein interact.

In some aspects, the assay is quantitative and the level of absorbance may be used to measure the relative strength of the interaction (e.g., as in Fig. 6G).

ie. Automated extracellular interaction screen

The extracellular interaction assay may be a high-throughput assay, e.g., a screen. A screen may include between 1 and more than 1500 prey fusion proteins (e.g., 1, more than 1, more than 10, more than 100, more than 250, more than 500, more than 750, more than 1000, more than 1250, or more than 1500 prey fusion proteins) and between 1 and more than 1500 bait fusion proteins (e.g., 1, more than 1, more than 10, more than 100, more than 250, more than 500, more than 750, more than 1000, more than 1250, or more than 1500 bait fusion proteins). In some aspects, the assay uses an integrated robotic system. In some aspects, the assay is performed in one or more 384-well plates. In some aspects, assays are assessed by a computational pipeline, e.g., a supervised classification algorithm, to determine whether interaction has occurred.

ii. Cell surface interaction assay

In some aspects of the invention, the protein-protein interaction assay is a cell surface interaction assay. In this type of assay, one or more prey proteins (e.g., one or more STM receptors) are expressed as extracellular domain (ECD) fusion proteins on the cell surface and are tested for interaction with one or more bait proteins (e.g., an IgSF protein or PDPN) expressed as a soluble extracellular domain using, e.g., a fluorescent assay wherein the bait protein comprises a fluorescent tag.

In some aspects, the invention comprises a method for identifying a protein-protein interaction, the method comprising (a) providing the collection of polypeptides, wherein each polypeptide comprises an extracellular domain, a tag, and an anchor, and wherein the collection of polypeptides comprises the extracellular domains of all or a subset of the proteins of Table 7, optionally wherein said polypeptides are immobilized on (e.g., attached to or fixed to) on one or more solid surfaces, e.g., wells of a plate or a set of plates; (b) contacting the collection of step (a) with a multimerized query protein under conditions permitting the binding of the multimerized query protein and at least one of the extracellular domains of the polypeptides; and (c) detecting an interaction between the multimerized query protein and the at least one extracellular domain, thereby identifying a protein-protein interaction. Each of the polypeptides may be localized to (e.g., immobilized to) a distinct location (e.g., a distinctly interrogatable location, e.g., a location that can be interrogated distinctly by the methods described herein) on the one or more solid surfaces. For example, each distinct location may comprise one or more cells that display the polypeptide. Exemplary collections of polypeptides that may be used in the method are described in Section II*B*.

In some aspects, the invention comprises a method for identifying a protein-protein interaction, the method comprising: (a) providing a solid surface or a set of solid surfaces comprising a number of

locations, each of the locations comprising a unique polypeptide from a collection of polypeptides, wherein each polypeptide comprises an extracellular domain, a tag, and an anchor, and wherein the collection of polypeptides comprises the extracellular domains of all or a subset of of the proteins of Table 7; (b) contacting the solid surface of step (a) with a multimerized query protein under conditions permitting the binding of the multimerized query protein and the extracellular domains of the polypeptides; and (c) detecting an interaction between the multimerized query protein and at least one polypeptide from the collection of polypeptides, thereby identifying a protein-protein interaction.

In some aspects, the solid surface or set of solid surfaces together comprise at least 965 locations, each of the locations comprising a unique polypeptide from a collection of polypeptides, wherein each polypeptide comprises an extracellular domain, a tag, and an anchor, and wherein the collection of polypeptides comprises the extracellular domains of at least 81% of the proteins of Table 7.

In some aspects, each of the locations comprises a cell, e.g., a mammalian cell, that displays the unique polypeptide. In some aspects, the cell has been transfected, e.g., transiently transfected, with a vector encoding the unique polypeptide. In some aspects, the transient transfection is semi-automated.

In some aspects, the multimerized query protein is a query protein as described in described in Section IIA(*iib).* The multimerized query protein may be, e.g., a dimerized, trimerized, tetramerized, or pentamerized query protein. In some aspects, the multimerized query protein is a tetramerized query protein. The multimerized query protein may comprise an isolated extracellular domain of the query protein. For example, the isolated extracellular domain may be biotinylated and conjugated to a fluorescent streptavidin to tetramerize the query protein.

In some aspects, protein-protein interactions are identified as described in Section IIA(*iid).*

iia. Cell surface interaction assay prey proteins

In some aspects, the prey protein or prey proteins comprise one or more fusion proteins (e.g., a library of prey fusion proteins) in which the extracellular domain (ECD) of a prey protein of interest (e.g., an STM protein) is conjugated (e.g., fused) to one or more additional moieties (e.g., a glycosylphosphatidylinositol (GPI)-gD (gDGPI) tag) such that the prey fusion protein is expressed on the cell surface. ECDs may be identified as described in Section 2B*(i)*.

In some aspects in which the polypeptide comprises an extracellular domain, a tag, and an anchor, the anchor is capable of tethering the extracellular domain to the surface of a plasma membrane of a cell. In some aspects, the anchor is a glycosylphosphatidyl-inositol (GPI) polypeptide. In some aspects, the anchor is a moiety used in protein lipidation, e.g., a moiety used in cysteine palmitoylation, glycine myristoylation, lysine fatty-acylation, cholesterol esterification, cysteine prenylation, or serine fatty-acylation.

In some aspects, the tag can be directly or indirectly visualized, or otherwise detected. For example, the tag may comprise a moiety that can be detected using an antibody or an antibody fragment, e.g., may be a glycoprotein D (gD) polypeptide. In some aspects, the tag comprises a fluorescent protein.

iib. Cell surface interaction assay bait proteins

The bait protein (query protein) or bait proteins may comprise one or more fusion proteins (e.g., a library of bait fusion proteins) in which the ECD of a bait protein of interest is conjugated to one or more additional moieties such that the bait fusion protein is soluble. The additional moiety or moieties may also increase the avidity of the bait fusion protein for the prey protein, e.g., by multimerizing the bait protein ECD. Increasing avidity may increase the detection of low-affinity interactions. In some aspects, the additional moiety causes tetramerization of the bait protein ECD.

In some aspects, the bait fusion protein comprises an Avi tag, a cleavage sequence (e.g., a TEV cleavage sequence), and an Fc tag, such that the Fc tag can be cleaved from the protein upon addition of the enzyme TEV protease. To prepare this protein for a cell surface interaction assay, the Fc tag is cleaved, the Avi tag is biotinylated, and the biotinylated bait fusion protein is conjugated to a fluorescent streptavidin (SA), e.g., a streptavidin conjugated to allophycocyanin (APC), to form a tetramerized bait fusion protein detectable in a fluorescence assay.

iic. Expression

The prey fusion protein may be expressed (e.g., transfected, e.g., transiently transfected) in a cell. The cell may be a human cell, e.g., a COS7 cell. Transfected cells may be placed in a well, e.g., a well in a 384-well plate.

The bait fusion protein may be expressed (e.g., transfected, e.g., transiently transfected) in a cell, e.g., a mammalian cell. Bait fusion proteins may be purified using standard protocols, e.g., as described in Ramani et al., *Anal Biochem*, 420: 127-138, 2012.

iid. Assay for interaction

To perform the protein-protein interaction assay, a solution comprising the bait protein (e.g., the purified bait fusion protein conjugated to fluorescent SA) may be added to one or more wells containing cells expressing a prey protein (e.g., to one or more wells of a 384-well plate). The assay may then be incubated and washed one or more times to remove non-bound bait protein. The cells may then be fixed, e.g., with 4% paraformaldehyde, to preserve protein-protein interactions.

In some aspects, detecting an interaction comprises detecting a signal, e.g., a fluorescent signal, at a location on the solid surface that is above a threshold level (e.g., a signal indicating the presence of a query protein at the location, e.g., a signal from a moiety comprised by the bait fusion protein (e.g., multimerized query protein)). The signal may be directly or indirectly visualizable or otherwise detectable. In some aspects, the detecting is semi-automated or automated. The interaction may be a transient interaction and/or a low-affinity interaction, e.g., a micromolar-affinity interaction.

In aspects in which the bait fusion protein (e.g., a multimerized query protein) comprises a fluorescent SA, interaction between the bait fusion protein and the prey fusion protein may be detected by fluorescence microscopy. Relatively high fluorescence indicates that the bait fusion protein is present, i.e., that the bait fusion protein and the prey fusion protein interact.

iie. Automated cell surface interaction screen

The extracellular interaction assay may be a high-throughput assay, e.g., a screen. A screen may include between 1 and more than 1500 prey fusion proteins (e.g., 1, more than 1, more than 10, more than 100, more than 250, more than 500, more than 750, more than 1000, more than 1250, or more than 1500 prey fusion proteins) and between 1 and more than 1500 bait fusion proteins (e.g., 1, more than 1, more than 10, more than 100, more than 250, more than 500, more than 750, more than 1000, more than 1250, or more than 1500 bait fusion proteins). In some aspects, the assay uses an integrated robotic system. In some aspects, the assay is performed in one or more 384-well plates. In some aspects, assays are assessed by a computational pipeline, e.g., a custom analysis module, to determine whether interaction has occurred.

iii. Surface plasmon resonance (SPR) assays

Protein-protein interactions may also be assayed using a surface plasmon resonance (SPR) assay. In some aspects, SPR assays are used to confirm or validate assays detected in an extracellular interaction assay or a cell surface interaction assay, e.g., a high-throughput extracellular interaction screen or a high-throughput cell surface interaction screen.

In some aspects, a prey protein is expressed as a fusion protein comprising the ECD of the protein conjugated to an additional moiety, e.g., an Fc tag. The prey fusion protein may be purified. The prey protein may be immobilized on a sensor chip, e.g. a GLC or CM5 sensor chip, by amine coupling.

The bait protein may be provided in a soluble form, e.g., as an ECD fused to a soluble tag. The bait fusion protein may be purified.

B. Protein, vector, and cell libraries

Proteins assayed in the invention include cell surface proteins, e.g., STM receptors and IgSF proteins. Proteins may be full-length proteins (e.g., secreted proteins), one or more domains or regions of a full-length protein (e.g., an extracellular domain), or fusion proteins comprising one or more domains of a protein of interest and one or more additional polypeptide sequences. In some aspects, a protein is a fusion protein having an extracellular domain of a protein of interest, e.g., an STM receptor or an IgSF protein, and one or more additional polypeptide sequences, e.g., additional polypeptide sequences that allow the protein to be used in an assay. Proteins may be grouped into "libraries," i.e., collections of proteins in a particular class (i.e., STM receptors or IgSF proteins) having a shared format, construction, or modification (e.g., fusion proteins comprising the ECD of the protein of interest and the same or similar additional polypeptide sequences). Particular examples of libraries are described below.

i. Extracellular domains

In some aspects, the protein is expressed as one or more domains of the full-length protein, e.g., an extracellular domain (ECD). An ECD is a domain of a protein that is predicted to be localized outside of the plasma membrane of the cell. This domain of the protein is thus available to interact with the extracellular environment, e.g., interact with soluble proteins and ECDs of other proteins on the cell or on an adjacent cell. In some aspects, the ECD is soluble.

The ECD or ECDs of a protein may be identified by bioinformatics analysis, e.g., by analysis of UniProt annotations. For example, the boundaries of the ECD may be identified relative to the boundary of an adjacent predicted transmembrane region, e.g., a transmembrane helix. In some aspects, the presence of an extracellular domain may be predicted by the presence of a domain, sequence, or motif that indicates that the protein is trafficked to the plasma membrane, e.g., a signal sequence or a glycosylphosphatidylinositol (GPI) linkage site.

In some aspects, the extracellular domain is expressed in the context of a full-length protein. In other aspects, the extracellular domain is expressed as an isolated extracellular domain, e.g., a sequence of amino acid residues comprising only the amino acid residues of a protein that are predicted to be extracellular. In some aspects, the isolated extracellular domain is expressed in a fusion protein.

ia. ECD fusion proteins

In some aspects, the isolated ECD is included in a fusion protein, e.g., is expressed as part of a polypeptide chain comprising one or more other polypeptide sequences. The isolated ECD may be fused directly or indirectly to one or more moieties that confer or increase one or more desirable properties, e.g., solubility, ease of expression, ease of capture, or multimerization. In some aspects, the ECD fusion protein may be for use in an assay, e.g., extracellular interaction assay, a cell surface interaction assay, or a surface plasmon resonance assay.

In some aspects, the ECD fusion protein is a monomer. In other aspects, the ECD fusion protein is a multimer, e.g., a tetramer or a pentamer. In some aspects, the ECD is fused to a human IgG. In some aspects, the ECD is fused to a human Fc tag. In some aspects, the ECD is fused to an Avi tag. In some aspects, the ECD is fused to a polyhistidine (His) tag. In some aspects, the ECD is fused to a (GPI)-gD (gDGPI) tag. In other aspects, the ECD is fused to the pentamerization domain of rat cartilaginous oligomeric matrix protein (COMP) and the β-lactamase protein, e.g., as described in Bushell et al., *Genome Res*, 18: 622-630, 2008.

In some aspects, the ECD fusion protein further includes a cleavage sequence, e.g., a TEV cleavage sequence, to allow selective removal of one or more domains. In some instances, an ECD fusion protein having an Avi tag and an Fc tag cleavable at a cleavage sequence is further processed to remove the Fc tag, to biotinylate the Avi tag, and to fuse the biotinylated ECD fusion protein to a fluorescent streptavidin (SA), e.g., to form a tetramerized ECD fusion protein. In some instances, the isolated ECD or ECD fusion protein is purified.

In some aspects, a fusion protein comprises the full sequence of the protein (e.g., the full sequence of a secreted protein, e.g., a secreted IgSF protein) fused to one or more of the other polypeptide sequences described herein.

ii. STM receptors

Single transmembrane (STM) receptor proteins are a large category of membrane-bound receptors having a single domain passing through the plasma membrane. Many STM receptors are expressed on the cell surface, and thus may participate in the extracellular interactome. Exemplary STM

receptors are provided in Table 5, Table 7, and Table 8 and in Martinez-Martin et al., *Cell*, 174(5): 1158-1171, 2018 and Clark et al., *Genome Res*, 13: 2265-2270, 2003.

STM receptors included in the STM library were identified by bioinformatics analysis, e.g., by using algorithms for the prediction of protein features, e.g., protein domains and subcellular localizations. Exemplary algorithms for predicting protein domains and/or subcellular localizations include the TMHMM and SignalP Servers (University of Denmark) and Phobius (Centre Stockholm Bioinformatics).

In some aspects, the STM receptor has the UniProt annotation "leucine-rich," "cysteine-rich," "ITIM/ITAM" (immunoreceptor tyrosine-based inhibition motif/immunoreceptor tyrosine-based activation motif), "TNFR" (tumor necrosis factor receptor), "TLR/ILR" (Toll-like receptor/interleukin receptor), "semaphorin," "Kinase-like," "Ig-like" (immunoglobulin-like), "fibronectin," "ephrin," "EGF," "cytokineR," or "cadherin".

iia. STM receptor library for extracellular interaction assays

In some aspects, the invention features an STM receptor library for use in an extracellular interaction assay. Proteins included in this library are provided in Table 5 and are "prey" fusion proteins constructed as described in Section IIA*(ia)* herein.

iib. STM receptor library for cell surface interaction assays

In some aspects, the invention features an STM receptor library for use in a cell surface interaction assay. Proteins included in this library are provided in Table 7 and are "prey" fusion proteins constructed as described in Section IIA*(iia)* herein.

Polypeptide library

In some aspects, the invention features a collection of polypeptides (e.g., a polypeptide library), wherein each polypeptide comprises an extracellular domain, a tag, and an anchor, and wherein the collection of polypeptides comprises the extracellular domains of all or a subset of the proteins of Table 7. In some aspects, the anchor is at N-terminus of the polypeptide and the extracellular domain is at the C-terminus of the polypeptide. In other aspects, the anchor is at the C-terminus of the polypeptide and the extracellular domain is at the N-terminus of the polypeptide. In some aspects, the collection of polypeptides comprises the extracellular domains of at least 81% of the proteins of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domains of at least 8%, at least 9%, at least 10%, at least 11%, at least 12%, at least 13%, at least 14%, at least 15%, at least 16%, at least 17%, at least 18%, at least 19%, at least 20%, at least 21%, at least 22%, at least 23%, at least 24%, at least 25%, at least 26%, at least 27%, at least 28%, at least 29%, at least 30%, at least 31%, at least 32%, at least 33%, at least 34%, at least 35%, at least 36%, at least 37%, at least 38%, at least 39%, at least 40%, at least 41%, at least 42%, at least 43%, at least 44%, at least 45%, at least 46%, at least 47%, at least 48%, at least 49%, at least 50%, at least 51%, at least 52%, at least 53%, at least 54%, at least 55%, at least 56%, at least 57%, at least 58%, at least 59%, at least 60%, at least 61%, at least 62%, at least 63%, at least 64%, at least 65%, at least 66%, at least 67%, at least 68%, at least 69%, at least 70%, at least 71%, at least 72%, at least 73%, at least 74%, at least 75%, at least 76%, at least 77%,

at least 78%, at least 79%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% of the proteins of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domains of at least 81% to 100% of the proteins of Table 7, e.g., comprises at least 85%, 90%, 95%, or 100% of (e.g., comprise all of) the proteins of Table 7, e.g., comprises the extracellular domains of 81%-85%, 83%-87%, 85%-89%, 87%-91%, 89%-93%, 91%-95%, 93%-97%, 95%-99%, or 100% of the proteins of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domains of at least 80% to 81% of the proteins of Table 7, e.g., comprises at least 80.1%, 80.2%, 80.3%, 80.4%, 80.5%, 80.6%, 80.7%, 80.75%, 80.8%, or 80.9% of the proteins of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domains of at least 100, at least 150, at least 200, at least 250, at least 300, at least 350, at least 400, at least 450, at least 500, at least 550, at least 600, at least 650, at least 700, at least 750, at least 800, at least 850, at least 900, at least 950, at least 1000, at least 1050, at least 1100, at least 1150, or all 1195 of the proteins of Table 7, e.g., comprise the extracellular domains of 100-150, 150-200, 200-250, 250-300, 300-350, 350-400, 400-450, 450-500, 500-550, 550-600, 600-650, 650-700, 750-800, 800-850, 850-900, 900-950, 950-1000, 1000-1050, 1050-1100, 1100-1150, or all 1195 of the polypeptides of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domains of at least 965 to at least 970 of the proteins of Table 7, e.g., comprises the extracellular domains of at least 965, 966, 967, 968, 969, or 970 of the proteins of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domain of at least one of the proteins of Table 17, e.g., comprises the extracellular domains of at least 2, at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, at least 110, at least 120, at least 130, at least 140, at least 150, at least 160, at least 170, at least 180, at least 190, at least 200, at least 210, at least 220, at least 230, or all 231 of the proteins of Table 17, e.g., comprise the extracellular domains of 1-5, 5-10, 10-15, 15-20, 20-25, 25-30, 30-35, 35-40, 40-45, 45-50, 50-55, 55-60, 60-65, 65-70, 70-75, 75-80, 80-85, 85-90, 90-95, 95-100, 101-105, 105-110, 110-115, 115-120, 120-125, 125-130, 130-135, 135-140, 140-145, 145-150, 150-155, 155-160, 160-165, 165-170, 170-175, 175-180, 180-185, 185-190, 190-195, 195-200, 200-205, 205-210, 210-215, 214-220, 220-225, 225-230, or all 231 of the polypeptides of Table 17.

In some aspects, the extracellular domain of the prey protein (e.g., STM protein) has a native conformation, e.g., a conformation observed in the wild-type protein. In some aspects, the extracellular domain of the prey protein (e.g., STM protein) comprises a native post-translational modification.

In some aspects, the cell is a mammalian cell, e.g., a COS7 cell.

In some aspects, the cell has been transiently transfected with a plasmid encoding the polypeptide.

Plasmid library

In some aspects, the invention comprises a collection of vectors (e.g., plasmids), each encoding a polypeptide comprising an extracellular domain, a tag, and an anchor, wherein the collection of polypeptides encoded by the vectors comprises the extracellular domains of all or a subset of the proteins of Table 7, e.g., encoding a collection of polypeptides comprising at least 8%, at least 9%, at least 10%, at least 11%, at least 12%, at least 13%, at least 14%, at least 15%, at least 16%, at least 17%, at least 18%, at least 19%, at least 20%, at least 21%, at least 22%, at least 23%, at least 24%, at least 25%, at least 26%, at least 27%, at least 28%, at least 29%, at least 30%, at least 31%, at least 32%, at least 33%, at least 34%, at least 35%, at least 36%, at least 37%, at least 38%, at least 39%, at least 40%, at least 41%, at least 42%, at least 43%, at least 44%, at least 45%, at least 46%, at least 47%, at least 48%, at least 49%, at least 50%, at least 51%, at least 52%, at least 53%, at least 54%, at least 55%, at least 56%, at least 57%, at least 58%, at least 59%, at least 60%, at least 61%, at least 62%, at least 63%, at least 64%, at least 65%, at least 66%, at least 67%, at least 68%, at least 69%, at least 70%, at least 71%, at least 72%, at least 73%, at least 74%, at least 75%, at least 76%, at least 77%, at least 78%, at least 79%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% of the proteins of Table 7. Exemplary collections of polypeptides that may be encoded by the plasmids are described in Section II*B*.

In some aspects, the collection of polypeptides encoded by the vectors comprises at least 81% of the proteins of Table 7, e.g., comprises the extracellular domains of at least 81% to 100% of the proteins of Table 7, e.g., comprises at least 85%, 90%, 95%, or 100% of (e.g., comprises all of) the proteins of Table 7, e.g., comprises the extracellular domains of 81%-85%, 83%-87%, 85%-89%, 87%-91%, 89%-93%, 91%-95%, 93%-97%, 95%-99%, or 100% of the proteins of Table 7.

In some aspects, the collection of polypeptides encoded by the vectors comprises the extracellular domains of at least 100, at least 150, at least 200, at least 250, at least 300, at least 350, at least 400, at least 450, at least 500, at least 550, at least 600, at least 650, at least 700, at least 750, at least 800, at least 850, at least 900, at least 950, at least 1000, at least 1050, at least 1100, at least 1150, or all 1195 of the proteins of Table 7.

In some aspects, the collection of polypeptides encoded by the vectors comprises at least 965 of the proteins of Table 7. In some aspects, the collection of polypeptides encoded by the vectors comprises the extracellular domains of at least 965 to at least 970 of the proteins of Table 7, e.g., comprises the extracellular domains of at least 965, 966, 967, 968, 969, or 970 of the proteins of Table 7.

In some aspects, the collection of polypeptides encoded by the vectors comprises the extracellular domain of at least one of the proteins of Table 17, e.g., comprises the extracellular domains of at least 2, at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, at least 110, at least 120, at least 130, at least 140, at least 150, at least 160, at least 170, at least 180, at least 190, at least 200, at least 210, at least 220, at least 230, or all 231 of the proteins of Table 17, e.g., comprise the extracellular domains of 1-5, 5-10, 10-15, 15-20, 20-25, 25-30, 30-35, 35-40, 40-45, 45-50, 50-55, 55-60, 60-65, 65-70, 70-75, 75-80, 80-85, 85-90, 90-95, 95-100, 101-105, 105-110, 110-115, 115-120, 120-125, 125-130, 130-135, 135-140, 140-145, 145-150, 150-155, 155-160, 160-

165, 165-170, 170-175, 175-180, 180-185, 185-190, 190-195, 195-200, 200-205, 205-210, 210-215, 214-220, 220-225, 225-230, or all 231 of the polypeptides of Table 7.

Cell library

In some aspects, the invention comprises a collection of cells that have been transformed with the above-described vectors (e.g., plasmids), i.e., have each been transformed with a vector encoding a polypeptide comprising an extracellular domain, a tag, and an anchor, wherein the collection of polypeptides encoded by the vectors comprises the extracellular domains of all or a subset of the proteins of Table 7, e.g., at least 8%, at least 9%, at least 10%, at least 11%, at least 12%, at least 13%, at least 14%, at least 15%, at least 16%, at least 17%, at least 18%, at least 19%, at least 20%, at least 21%, at least 22%, at least 23%, at least 24%, at least 25%, at least 26%, at least 27%, at least 28%, at least 29%, at least 30%, at least 31%, at least 32%, at least 33%, at least 34%, at least 35%, at least 36%, at least 37%, at least 38%, at least 39%, at least 40%, at least 41%, at least 42%, at least 43%, at least 44%, at least 45%, at least 46%, at least 47%, at least 48%, at least 49%, at least 50%, at least 51%, at least 52%, at least 53%, at least 54%, at least 55%, at least 56%, at least 57%, at least 58%, at least 59%, at least 60%, at least 61%, at least 62%, at least 63%, at least 64%, at least 65%, at least 66%, at least 67%, at least 68%, at least 69%, at least 70%, at least 71%, at least 72%, at least 73%, at least 74%, at least 75%, at least 76%, at least 77%, at least 78%, at least 79%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% of the proteins of Table 7. Exemplary collections of polypeptides that may be comprised by the cells are described in Section II*B*.

In some aspects, the collection of vectors comprised by the cells encodes the extracellular domains of at least 81% of the proteins of Table 7, e.g., comprises the extracellular domains of at least 81% to 100% of the proteins of Table 7, e.g., comprises at least 85%, 90%, 95%, or 100% of (e.g., comprises all of) the proteins of Table 7, e.g., comprises the extracellular domains of 81%-85%, 83%-87%, 85%-89%, 87%-91%, 89%-93%, 91%-95%, 93%-97%, 95%-99%, or 100% of the proteins of Table 7.

In some aspects, the collection of vectors comprised by the cells encodes the extracellular domains of at least of at least 100, at least 150, at least 200, at least 250, at least 300, at least 350, at least 400, at least 450, at least 500, at least 550, at least 600, at least 650, at least 700, at least 750, at least 800, at least 850, at least 900, at least 950, at least 1000, at least 1050, at least 1100, at least 1150, or all 1195 of the proteins of Table 7.

In some aspects, the collection of vectors comprised by the cells encodes at least 965 of the proteins of Table 7.

In some aspects, the collection of vectors comprised by the cells encodes the extracellular domains of at least 965 to at least 970 of the proteins of Table 7, e.g., comprises the extracellular domains of at least 965, 966, 967, 968, 969, or 970 of the proteins of Table 7.

In some aspects, the collection of vectors comprised by the cells encodes the extracellular domain of at least one of the proteins of Table 17, e.g., comprises the extracellular domains of at least 2, at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, at

least 100, at least 110, at least 120, at least 130, at least 140, at least 150, at least 160, at least 170, at least 180, at least 190, at least 200, at least 210, at least 220, at least 230, or all 231 of the proteins of Table 17, e.g., comprise the extracellular domains of 1-5, 5-10, 10-15, 15-20, 20-25, 25-30, 30-35, 35-40, 40-45, 45-50, 50-55, 55-60, 60-65, 65-70, 70-75, 75-80, 80-85, 85-90, 90-95, 95-100, 101-105, 105-110, 110-115, 115-120, 120-125, 125-130, 130-135, 135-140, 140-145, 145-150, 150-155, 155-160, 160-165, 165-170, 170-175, 175-180, 180-185, 185-190, 190-195, 195-200, 200-205, 205-210, 210-215, 214-220, 220-225, 225-230, or all 231 of the polypeptides of Table 17.

In some aspects, each cell of the collection of cells is capable of expressing the polypeptide encoded by the vector with which it has been transformed. In some aspects, each of a plurality of cells of the collection of cells is capable of expressing the polypeptide encoded by the vector with which it has been transformed.

iic. PDPN

Podoplanin (PDPN) is an STM receptor. PDPN may be highly expressed on the surface of fibroblasts (e.g., cancer-associated fibroblasts), lymphatic endothelial cells, and type I alveolar cells. PDPN is overexpressed in many tumor tissues, and its expression in tumor tissues is associated with poor prognosis. PDPN is known to act as a master regulator of actomyosin contractility in mouse fibroblasts via interaction with the C-type lectin receptor CLEC-2 (CLEC1B) (Astarita et al., *Nat Immunol,* 16: 75-84, 2015; Acton et al., *Nature,* 514: 498-502, 2014). In some aspects, PDPN acts as a regulator of actomyosin contractility in human CAFs.

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PDPN for cell surface interaction assay

In some aspects, the invention features a PDPN fusion protein for use in a cell surface interaction assay. This protein is a "bait" fusion protein constructed as described in Section IIA*(iib)* herein.

iii. IgSF proteins

The immunoglobulin superfamily (IgSF) is the largest family of secreted and cell surface-expressed proteins encoded by the human genome and the most highly represented extracellular protein domain in humans. IgSF proteins are known to function through the formation of homophilic and heterophilic complexes that mediate a wide array of functionalities, e.g., modulation of axon guidance, modulation of synaptic plasticity, control of cell migration, control of cell adhesion, and self vs. non-self recognition. As such, these proteins constitute a major focus for drug development efforts. Some IgSF proteins are expressed on the cell surface (e.g., transmembrane proteins); others are secreted. Exemplary IgSF proteins are provided in Table 4 and in Ozkan et al., *Cell*, 154(1): 228-239, 2013.

The Immunoglobulin Superfamily (IgSF) library comprises proteins having containing at least one immunoglobulin (Ig) domain or immunoglobulin fold, having the annotation "immunoglobin-like superfamily," e.g., in the SwissProt database, or otherwise indicated to have structural or functional similarity to such a protein. In some aspects, IgSF proteins are identified by the annotation "immunoglobulin-like domain superfamily" for the protein in the SwissProt database. In some aspects, IgSF proteins are identified based on the protein's participation in key biological activities.

In some aspects, the IgSF protein has the UniProt annotation "TFNR" (transcription factor-like nuclear regulator), "TLR/ILR (Toll-like receptor/interleukin receptor), "semaphorin," "Kinase-like," "IgSF/Ig-like fold," "Ig-like fold," "fibronectin," "ephrin," "EGF," "CytokineR," or "cadherin".

In some aspects, the IgSF superfamily protein is Programmed death ligand 1 (PD-L1; CD274), Programmed cell death 1 ligand 2 (PD-L2; CD274; PDCD1LG2), Receptor-type tyrosine-protein phosphatase delta (PTPRD), Receptor-type tyrosine-protein phosphatase S (PTPRS), Receptor-type tyrosine-protein phosphatase F (PTPRF), Neural cell adhesion molecule L1-like protein ("Close homolog of L1"; CHL1), Contactin 1 (CNTN1), Leukocyte immunoglobulin-like receptor subfamily B member 1 (LILRB1), Leukocyte immunoglobulin-like receptor subfamily B member 2 (LILRB2), Leukocyte immunoglobulin-like receptor subfamily B member 3 (LILRB3), Leukocyte immunoglobulin-like receptor subfamily B member 4 (LILRB4), Leukocyte immunoglobulin-like receptor subfamily B member 5 (LILRB5), MAM domain-containing glycosylphosphatidylinositol anchor protein 1 (MDGA1), or Tyrosine-protein kinase receptor AXL.

iiia. IgSF library for extracellular interaction assay

In some aspects, the invention features an IgSF receptor library for use in an extracellular interaction assay. Proteins included in this library are provided in Table 4 and are "bait" fusion proteins constructed as described in Section IIA*(ib)* herein.

iiib. IgSF proteins for cell surface interaction assay

In some aspects, the invention features IgSF receptors for use in a cell surface interaction assay. Proteins included in this library are provided in Table 4 and are "bait" fusion proteins constructed as described in Section IIA*(iib)* herein.

iv. Bait protein and prey protein libraries

In some aspects, the invention features a bait protein library comprising the proteins provided in Table 1. Proteins may be constructed as "bait" fusion proteins described in Section IIA*(ib)* or Section IIA*(iib)* herein.

In some aspects, the invention features a prey protein library comprising the proteins provided in Table 2. Proteins may be constructed as "prey" fusion proteins described in Section IIA*(ia)* or Section IIA*(iia)* herein.

C. Protein-protein interaction networks

In some aspects, interactions between bait proteins (Table 1) and prey proteins (Table 2) may be tested using extracellular interaction assays (including a high-throughput extracellular interaction screen), cell surface assays (including a high-throughput cell surface interaction screen), and surface plasmon resonance assays as described in Section IIA. In some aspects, the assay includes between 1 and more than 1500 prey proteins (e.g., 1, more than 1, more than 10, more than 100, more than 250, more than 500, more than 750, more than 1000, more than 1250, or more than 1500 prey proteins) and between 1 and more than 1500 bait proteins (e.g., 1, more than 1, more than 10, more than 100, more than 250,

more than 500, more than 750, more than 1000, more than 1250, or more than 1500 bait proteins. In some aspects, the assay identifies between 1 and 900 protein-protein interactions (e.g. 1, more than 1, more than 10, more than 100, more than 250, more than 500, more than 750, more than 850, or 900 protein-protein interactions. In some aspects, these analyses identify previously unrecognized communities of functionally related proteins, uncover binding partners for orphan proteins, and reveal receptor-ligand interactions prominently deregulated in cancer.

i. STM receptor – IgSF interactome

In some aspects, the IgSF proteins provided in Table 4 and the STM proteins provided in Table 5 are tested for interaction in a high-throughput extracellular interaction screen, as described in Section IIA*(ie)* herein. In some aspects, the IgSF proteins are constructed as a bait library (as in Section IIB*(iiia)*), and the STM proteins are constructed as a prey library (as in Section IIB*(iia)*). In some aspects, the detected interactions are assembled into a network. In some aspects, selected interactions are further tested, e.g., in a cell surface interaction screen (described in Section IIa*(ii)*) or an SPR assay (described in Section IIa*(iii)*).

ia. Proteins interacting with PD-L1 and/or PD-L2

The IgSF proteins PD-L1 (CD274) and PD-L2 (PDCD1LG2) are immune checkpoint proteins and play key roles in immunosuppressive functions that may result in tumor immune escape (Chen and Mellman, *Immunity*, 39: 1-10, 2013). Accordingly, therapies targeting PD-L1 have been a major focus of research. Antibody blockade of PD-L1 is a preferred immunotherapeutic strategy for the treatment of solid tumors; however, many patients do not respond or do not display durable responses to antibody blockade of PD-L1, indicating that therapies targeting other immunosuppressive pathways are needed.

In some aspects, the assays described herein may identify an interaction between PD-L1 and ephrin type-A receptor 3 (EPHA3). EPHA3 is a receptor tyrosine kinase activated by the binding of an ephrin protein and having roles in signal transduction and the control of multiple cellular processes, e.g., cell growth, migration, and adhesion (Lisabeth et al., *Cold Spring Harb Perspect Biol*, 5, 2013). EPHA3 has also been identified as one of the most frequently mutated genes in certain tumors (Andretta et al., *Sci Rep*, 7: 41576, 2017). The downstream effects of the interaction between PD-L1 and EPHA3 may therefore include modulation of immune checkpoint function, e.g., immunosuppression, and/or modulation of EPHA3 kinase functions.

In some aspects, the assays described herein may identify an interaction between PD-L2 and CEACAM4. The CEACAM family has been shown to have a role in regulation of the immune system: CEACAM1 has been identified as a ligand for the inhibitory receptor TIM-3 (Huang et al., *Nature*, 517: 386-390, 2002). The interaction between CEACAM4 and PD-L2 may contribute to PD-1-independent functions of PD-L2, e.g., functions described in Liu et al., *J Exp Med*, 197: 1721-1730, 2003, e.g., phagocytosis. The downstream effects of the interaction between PD-L2 and CEACAM4 may therefore include modulation of immune checkpoint function, e.g., immunosuppression (Delgado Tascon et al., *J Leukoc Biol*, 97: 521-531, 2015; Xiao et al., *J Exp Med*, 211: 943-959, 2014).

In some aspects, the assay or assays described herein may identify interactions between PD-L2 and CEACAM4; PD-L2 and ICAM5; PD-L2 and NECTIN3; PD-L2 and PSG9; and PD-L2 and TNFRSF11A.

ib. Proteins interacting with PTPR proteins

The PTPR proteins PTPRD, PTPRS, and PTPRF are receptor-type tyrosine-protein phosphatases. Tyrosine phosphorylation and dephosphorylation regulate a multitude of cellular processes, and aberrations in tyrosine phosphorylation/dephosphorylation are associated with tumor formation. In particular, PTPRD and PTPRS have been described as key modulators of nervous system processes, e.g., synapse formation and axonal growth, and have also been identified as tumor suppressors having a high mutation rate in neuroblastoma, glioma, colon cancer, and breast cancer (Veeriah et al., *Proc Natl Acad Sci USA*, 106: 9435-9440, 2009; Wang et al., *Hepatology*, 62: 1201-1214, 2015).

In some aspects, the assays described herein may identify interactions between PTPRS, PTPRD, and/or PTPRF and members of the SLIT and NTRK-like (SLITRK) family (e.g., SLITRK1, SLITRK2, SLITRK3, SLITRK4, and SLITRK6), and may also identify interactions between PTPRS, PTPRF, and/or PTPRD and members of the Leucine-rich repeat and fibronectin type III domain-containing protein (LRFN) family, Interleukin-1 receptor accessory protein (IL1RAP), and the related proteins IL1RAPL1 and IL1RAPL2. SLITRKs, LRFNs, and IL1RAP-like proteins have been implicated in nervous system disorders including tumors. For example, IL1RAP is required for IL-1 signaling as has been reported to be a biomarker for chronic myeloid leukemia stem cells (Zhao et al., *Int J Clin Exp Med*, 7: 4787-4798, 2014). The downstream effects of the identified interactions may therefore include changes in phosphatase activity, e.g., changes in tyrosine phosphorylation/dephosphorylation, e.g., tyrosine phosphorylation/dephosphorylation of proteins implicated in diseases including cancer.

In some aspects, the assay or assays may identify interactions between PTPRD and BMP5, CEACAM3, IL1RAP, IL1RAPL2, LECT1, LRFN5, SIRPG, SLITRK3, SLITRK4, SLITRK6, and TGFA. PTPRD has been associated with suppression of cell proliferation and STAT3 phosphorylation (Veeriah et al., *PNAS*, 106(23): 9435-9440, 2009; Peyser et al., *PLoS ONE*, 10.1371/journal.pone.0135750, 2015).

In some aspects, the assay or assays may identify interactions between PTPRS and C6orf25, IL1RAP, IL1RAPL1, IL1RAPL2, LRFN1, LRFN5, LRRC4B, NCAM1, SLITRK1, SLITRK2, SLITRK3, SLITRK4, and SLITRK6. PTPRS has been associated with inhibition of cell migration (Wang et al., *Hepatology*, 62(4): 1201-1214, 2015) and with activation of the PI3K signaling pathway (Suarez Pestana et al., *Oncogene*, 18: 4069-4079, 1999; Morris et al., *PNAS*, 108(47): 19024-19029, 2011).

In some aspects, the assay or assays may identify interactions between PTPRF and CD177, IL1RAP, and LRFN5. PTPRF has been associated with inhibition of cell migration and phosphorylation of EGFR (Du et al., *J Cell Sci*, 126: 1440-1453, 2013).

Proteins interacting with PTPRD mutants

In some aspects, the assay or assays may identify interactions between forms of PTPRD having one or more disease-relevant (e.g., cancer-relevant) mutations (PTPRD mutants), e.g., an amino acid

substitution mutation or an amino acid deletion mutation, and IL1RAP, IL1RAPL1, IL1RAPL2, LRFN4, LRFN5, LRRC4B, NTRK3, SLITRK1, SLITRK3, or SLITRK6. Disease-relevant variations in PTPRD (Table 9) occur in the immunoglobulin (IG) domains IG1, IG2, and IG3 and in the fibronectin (FN) domains FN1-FN8 of the PTPRD ECD (Fig. 6F). Specific amino acid substitution or deletion mutations include ΔG61 ΔE106 (IG1), G203E K204E (IG2), R232C R233C (IG2), P249L (IG3), G285E (IG3), E406K (FN1), S431L (FN2), R561Q (FN3), P666S (FN4), E755K (FN5), V892I (FN6), S912F (FN7), R995C (FN7), and R1088C (FN8). In some aspects, the PTPRD variant is expressed as a bait protein as described in Section IIA*(ib)* herein and assayed for interaction with a prey protein in an extracellular interaction assay as described in Section IIA*(i)* herein. In some aspects, the strength of the interaction between a PTPRD variant and a binding partner may be decreased relative to the strength of an interaction between a wild-type PTPRD protein and the binding partner. In other aspects, the strength of the interaction may be similar for the variant and wild-type PTPRD proteins.

ic. Proteins interacting with CHL1 and/or CNTN1

Neural cell adhesion molecule L1-like protein (CHL1) and Contactin 1 (CNTN1) are IgSF proteins that act as cell adhesion molecules (CAMs). Overexpression of CAMs is associated with poor prognosis in patents with cancers (Yan et al., *Cancer Res.,* 76(6), 1603-1614, 2016).

CHL1 is involved in neural cell adhesion and has roles in central nervous system (CNC) development. CHL1 has been associated with suppression of cell proliferation (Tang et al., *Oncogene,* doi: 10.1038/s41388-018-0648-7); suppression of tumor formation (Tang et al., *Oncogene,* doi: 10.1038/s41388-018-0648-7); and suppression of cell invasion (He et al., *Biochem Biophys Res Commun*, 438: 433-438, 2013).

In some aspects, the assays described herein may identify interactions between CHL1 and contactin 5 (CNTN5), L1 cell adhesion molecule (L1CAM), two proteins involved in cell adhesion, and B- and T-lymphocyte attenuator (BTLA).

Upregulation of CNTN1 is strongly associated with prostate cancer cell invasion. CNTN1 has been associated with suppression of cell proliferation; suppression of cell invasion (Yan et al., *Cancer Res*, 76(6): 1603-1614, 2016) and activation of the RhoA and AKT signaling pathways (Yan et al, *PLoS ONE*, 8(5): e65463, 2013; Chen et al., *Front Mol Neurosci*, 11, Article 422 (2018); Su et al., *Cancer Res*, 66(5): 2553-2561, 2006).

In some aspects, the assay or assays may identify interactions between CHL1 and SIRPA, CNTN1, CNTN5, L1CAM, and TMEM132A.

In some aspects, the assay or assays may identify an interaction between CNTN1 and CDH6, CHL1, FCGRT, PCDHB7, and SGCG. The downstream effects of the identified interactions may include modulation of cell adhesion, e.g., neural cell adhesion.

id. Proteins interacting with LILRB proteins

The leukocyte immunoglobulin-like receptor B proteins (LILRBs) are IgSF proteins characterized by the presence of cytosolic immunoreceptor tyrosine-based activating motifs (ITAM) or immunoreceptor tyrosine-based inhibitory motifs (ITIM) (Brown et al., *Tissue Antigens*, 64: 215-225, 2004). LILR proteins

may be activating or inhibitory receptors, are mainly expressed in myeloid cells and lymphocytes, and have been associated with roles in cancer, autoimmune disease, infectious disease, and macrophage phagocytosis.

In some aspects, the assays described herein may identify interactions between LILRB5 and low-density lipoprotein receptor (LDLR). LDLR mediates the endocytosis of low-density lipoprotein (LDL) and has been implicated in diseases including familial hypercholesterolemia and coronary artery disease.

The assays described herein may also identify interactions between identify interactions between LILRB1 and CLEC6A, CXADR, EDAR, FLT4, IL6R, ILDR1, and LILRA5. LILRB1 is a component of the MHC class 1-LILRB1 signaling axis, which has been shown to protect cells (e.g., tumor cells) from phagocytosis (Barkal et al., *Nature Immunol*, 19: 76-84, 2017). The downstream effects of the identified interactions may therefore include modulation of phagocytosis (Section IIIB(*vii*)). Downregulation of interactions involving LILRB1 may lead to increased phagocytosis, e.g., increased phagocytosis of tumor cells. LILRB1 has also been associated with osteoclast differentiation (Mori et al., J Immunol, 181(7): 4742-4751, 2008).

The assays described herein may also identify interactions between LILRB2 and IGSF8 and MOG. LILRB2 has been associated with M2 macrophage polarization (Chen et al., *J Clin Invest*, 128(12), 5647-5662).

The assays described herein may also identify interactions between LILRB3 and LRRC15 and LY6G6F. LILRB3 has been associated with osteoclast differentiation (Mori et al., J Immunol, 181(7): 4742-4751, 2008).

The assays described herein may also identify interactions between LILRB4 and CNTFR. LILRB4 has been associated with osteoclast differentiation (Mori et al., J Immunol, 181(7): 4742-4751, 2008).

In some aspects, the assay or assays may identify interactions between LILRB5 and APLP2, CD177, CLEC10A, LDLR, PILRA, and UNC5C.

ie. Proteins interacting with MDGA1

MAM domain containing glycosylphosphatidylinositol anchor 1 (MDGA1) is in IgSF protein that is expressed in the nervous system. In some aspects, the assay or assays described herein may identify interactions between MDGA1 and NLGN3 and NLGN4X.

if. Proteins interacting with AXL

The tyrosine-protein kinase receptor AXL is an IgSF protein that is an inhibitor of the innate immune response. Overexpression of AXL is associated with numerous cancers (e.g., colon cancer, esophageal cancer, thyroid cancer, breast cancer, lung cancer, liver cancer, and astrocytoma-glioblastoma (Verma et al., *Mol Cancer Ther*, 10(10): 1763-1773, 2011).

AXL has been associated with regulation of cell invasion (Verma et al., *Mol Cancer Ther*, 10(10): 1763-1773, 2011); regulation of the JAK/STAT pathway, regulation of the RAS/RAF/MAPK/ERK1/2 pathway, and PI3K signaling pathways (Verma et al., *Mol Cancer Ther*, 10(10): 1763-1773, 2011); changes in cell motility and morphology, e.g., formation of filopodia (Verma et al., *Mol Cancer Ther*, 10(10): 1763-1773, 2011); and regulation of the epithelial-mesenchymal transition (EMT) (Gjerdrum et al.,

PNAS, 107(3): 1124-1129, 2010; Divine et al.; *Oncotarget*, 7: 77291-77305, 2016; Rankin et al., *Cancer Res*, 70(19), 7570-7579, 2010; Chichon et al., *Oncogene*, 33: 4185-4192, 2013).

In some aspects, the assay or assays described herein may identify interactions between AXL and IL1RL1 and VSIG10L.

ig. Proteins interacting with LRRC4B

In some aspects, the assay or assays described herein may identify interactions between LRRC4B and BTN3A1 or BTN3A3.

ii. Interactions between STM receptors and PDPN

In some aspects, the STM proteins provided in Table 7 may be tested for interaction with PDPN in a high-throughput cell surface interaction screen, as described in Section IIA*(iie)* herein. PDPN may be constructed as a bait protein (as in Section IIB*(iic)*), and the STM proteins may be constructed as a prey library (as in Section IIB*(iib)*). In some aspects, selected interactions may be further tested with SPR assays (described in Section IIa*(iii)*).

Podoplanin (PDPN) is an STM receptor that acts as a regulator of actomyosin contractility in CAFs. In some aspects, the assays described herein may identify interactions between PDPN and cluster of differentiation 177 (CD177), a neutrophil receptor that has recently been identified as a marker of tumor-resident Tregs (Plitas et al., *Immunity*, 45: 1122-1134, 2016). In some aspects, the assay or assays may identify an interaction between PDPN and CD177, CLEC-2 (CLEC1B), and SIGLEC7.

In some aspects, the downstream effects of interaction with PDPN (e.g., interaction of CLEC-2 and/or CD177 with PDPN) may include increased fibroblast elongation (e.g., increased CAF elongation) and decreased fibroblast contractility (e.g., decreased CAF contractility) (Section IIIB*(i)*).

III. METHODS OF IDENTIFYING A MODULATOR OF A PROTEIN-PROTEIN INTERACTION

A. Assays for modulation of interaction

In some aspects, the invention features identifying a modulator of the interaction between a protein of Table 1 and a protein of Table 2, the method comprising: (a) providing a candidate modulator (e.g., a candidate modulator described in Section IV herein); (b) contacting a protein of Table 1 with a protein of Table 2 in the presence or absence of the candidate modulator under conditions permitting the binding of the protein of Table 1 to the protein of Table 2, wherein the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (c) measuring the binding of the protein of Table 1 to the protein of Table 2, wherein an increase or decrease in binding in the presence of the candidate modulator relative to binding in the absence of the candidate modulator identifies the candidate modulator as a modulator of the interaction between the protein of Table 1 and the protein of Table 2.

In some aspects, the candidate modulator is provided to a cell (e.g., a mammalian cell), to cell culture media, to conditioned media, and/or to a purified form of a protein of Table 1 and/or a protein of Table 2. In some aspects, the candidate modulator is provided at a concentration of at least 0.1 nM, 0.5 nM, 1 nM, 10 nM, 50 nM, 100 nM, 250 nM, 500 nM, 750 nM, 1 μM, 2 μM, 3 μM, 5 μM, or 10 μM. In some

aspects, the candidate modulator is provided at a concentration of between 0.1 nM and 10 μM. In some aspects, the candidate modulator is provided in a solution, e.g., in a soluble form.

In some aspects, the candidate modulator is identified as a modulator if the increase in binding is at least 70%. In some aspects, the increase in binding is at least 5%, at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 100%, or more than 100%. In some aspects, the increase in binding is at least 70%.

In some aspects, the candidate modulator is identified as a modulator if the decrease in binding is at least 70%. In some aspects, the decrease in binding is at least 5%, at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100%. In some aspects, the decrease in binding is at least 70%.

i. Assays for modulation of protein-protein interaction

In some aspects, the binding of the protein of Table 1 and the protein of Table 2 in the presence or absence of the candidate modulator is assessed in an assay for protein-protein interaction. Modulation of the interaction between the protein of Table 1 and the protein of Table 2 may be identified as an increase in protein-protein interaction in the presence of the modulator compared to protein-protein interaction in the absence of the modulator, e.g., an increase of 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 80%, 90%, 95%, 100%, or more than 100% in protein-protein interaction. Alternatively, modulation may be identified as a decrease in protein-protein interaction in the presence of the modulator compared to protein-protein interaction in the absence of the modulator, e.g., an decrease of 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 80%, 90%, 95%, or 100% in protein-protein interaction. The assay for protein-protein interaction may be, e.g., an SPR assay, a biolayer interferometry (BLI) assay, an enzyme-linked immunosorbent assay (ELISA), an extracellular interaction assay as described in Section IIA*i*, or a cell surface interaction assay as described in Section IIA*ii*.

ia. SPR assays for modulation of protein-protein interaction

In some aspects, the assay for protein-protein interaction is a surface plasmon resonance (SPR) assay, as described in Section IIA*iii* herein. In some aspects, modulation of the binding of the protein of Table 1 to the protein of Table 2 is measured as a difference in SPR signal response units (RU) in the presence compared to the absence of the modulator.

ib. BLI assays for modulation of protein-protein interaction

In some aspects, the assay for protein-protein interaction is a BLI assay. In some aspects, the BLI assay is performed using isolated ECDs, e.g., isolated ECDs as described in Section IIB*(i)* herein. In some aspects, modulation of the binding of the protein of Table 1 to the protein of Table 2 is measured as a difference in wavelength shift (Δλ) measured at a biosensor tip in the presence compared to the absence of the modulator.

ic. ELISA for modulation of protein-protein interaction

In some aspects, the assay for protein-protein interaction is an ELISA. In some aspects, a first protein is bound to a plate (e.g., directly bound to a plate or bound to a plate via an affinity tag recognized by an antibody bound to a plate) and a second protein is provided in a soluble form, e.g., as an isolated ECD as described in Section IIB*(i)* herein. An interaction between the first protein and the second protein may be detected by providing an antibody that binds to the second protein or to an affinity tag thereof, wherein the antibody can be detected, e.g., visualized, in an assay for presence of the antibody.

id Other assays for modulation of protein-protein interaction

In some aspects, the assay is an extracellular interaction assay, as described in Section IIA*i* herein. In some aspects, the assay is a cell surface interaction assay, as described in Section IIA*ii* herein. In some aspects, the assay is an isothermal titration calorimetry (ITC) assay, an assay comprising immunoprecipitation, or an assay comprising an ALPHASCREEN™ technology.

B. Assays for changes in downstream activity

In some aspects, the invention features a method of identifying a modulator of a downstream activity of a protein of Table 1, the method comprising: (a) providing a candidate modulator (e.g., a candidate modulator described in Section IV herein); (b) contacting the protein of Table 1 with a protein of Table 2 in the presence or absence of the candidate modulator under conditions permitting the binding of the protein of Table 1 to the protein of Table 2, wherein the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (c) measuring a downstream activity of the protein of Table 1 (e.g., CAF contractility, immune checkpoint inhibition, suppression of cell proliferation, modulation of target phosphorylation, inhibition of cell migration, suppression of tumor formation, suppression of cell invasion, macrophage polarization, regulation of phagocytosis, osteoclast differentiation, activation of a signaling pathway, or formation of filopodia), wherein a change in the downstream activity in the presence of the candidate modulator relative to the downstream activity in the absence of the candidate modulator identifies the candidate modulator as a modulator of the downstream activity of the protein of Table 1.

In some aspects, the invention features a method of identifying a modulator of a downstream activity of a protein of Table 2, the method comprising: (a) providing a candidate modulator (e.g., a candidate modulator described in Section IV herein); (b) contacting the protein of Table 2 with a protein of Table 1 in the presence or absence of the candidate modulator under conditions permitting the binding of the protein of Table 2 to the protein of Table 1, wherein the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (c) measuring a downstream activity (e.g., CAF contractility, immune checkpoint inhibition, suppression of cell proliferation, modulation of target phosphorylation, inhibition of cell migration, suppression of tumor formation, suppression of cell invasion, macrophage polarization, regulation of phagocytosis, osteoclast differentiation, activation of a signaling pathway, or formation of filopodia) of the protein of Table 2, wherein a change in the downstream activity in the presence of the candidate modulator relative to the downstream activity in the absence of the candidate modulator identifies the candidate modulator as a modulator of the downstream activity of the protein of Table 2.

In some aspects, the candidate modulator is provided at a concentration of at least 0.1 nM, 0.5 nM, 1 nM, 10 nM, 50 nM, 100 nM, 250 nM, 500 nM, 750 nM, 1 μM, 2 μM, 3 μM, 5 μM, or 10 μM. In some aspects, the candidate modulator is provided at a concentration of between 0.1 nM and 10 μM. In some aspects, the candidate modulator is provided at a range of concentrations, e.g., as in Fig. 4F. In some aspects, the candidate modulator is provided is provided in a solution, e.g., in a soluble form. In some aspects, the candidate modulator is provided to an organism comprising the protein of Table 1 and the protein of Table 2, to a tissue comprising the protein of Table 1 and the protein of Table 2, to a cell (e.g., a mammalian cell), to cell culture media, to conditioned media, and/or to a purified form of a protein of Table 1 and/or a protein of Table 2.

In some aspects, the candidate modulator is identified as a modulator if the increase in the downstream activity of the protein of Table 1 or the protein of Table 2 is at least 30%. In some aspects, the increase in the downstream activity is at least 5%, at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 100%, or more than 100%. In some aspects, the increase in the downstream activity is at least 30%.

In some aspects, the candidate modulator is identified as a modulator if the decrease in the downstream activity of the protein of Table 1 or the protein of Table 2 is at least 30%. In some aspects, the decrease in the downstream activity is at least 5%, at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100%. In some aspects, the decrease in downstream activity is at least 30%.

In some aspects, the downstream activity of the protein of Table 1 or the protein of Table 2 is assessed in one or more assays, as described below.

In some aspects, the downstream activity is an activity relating to the development or progression of a disease, e.g., a cancer.

i. CAF contractility

In some aspects, the downstream activity is cancer-associated fibroblast (CAF) actomyosin contractility (CAF contractility). In some aspects, the protein of Table 1 is PDPN and the downstream activity is CAF contractility. In some aspects, the protein of Table 1 is PDPN, the protein of Table 2 is CD177, and the downstream activity is CAF contractility.

In some aspects, the assay for CAF contractility is a gel contraction assay. In this assay, a population of fibroblast cells (e.g., cancer-associated fibroblast cells) (e.g., 100,000 cells) comprising at least one of the protein of Table 1 and the protein of Table 2 are mixed into a Matrigel-collagen mixture and placed into a well, e.g., a well in a 96-well plate. In aspects wherein the individual cell does not comprise both the protein of Table 1 and the protein of Table 2, the protein not comprised by the cell may be provided on another cell (e.g., a mammalian cell, e.g., a neutrophil or a T cell) or may be provided in or added to the Matrigel-collagen media or the cell culture media. The cell may additionally be treated with the modulator, e.g., by addition to the Matrigel-collagen media or the cell culture media. After the gels set for 20 minutes, the gel is detached from the sides of the well and cell culture media is added. Gels are incubated, e.g., for 72 hours, before imaging. Contractility of the population of cells is measured by comparing the well diameter and the final gel diameter. Increased or decreased contractility is calculated

by comparing the gel contraction of cells to which the modulator is provided with that of cells to which the modulator has not been provided. In some instances, the population of cells that is treated with the modulator has decreased gel contraction relative to a population of cells that has not been treated with the modulator, e.g., CAF contractility is decreased in the presence of the modulator. In some aspects, CAF contractility is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a gel contraction assay. In some aspects, CAF contractility is decreased by at least 30% in the presence of the modulator as measured in a gel contraction assay. In some aspects, CAF contractility is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, or at least 80% as measured in a gel contraction assay.

In other aspects, CAF contractility is measured using a 3D gel elongation assay, e.g., an assay as described in Example 8*B*. In this assay, a fibroblast cell, (e.g., a CAF) comprises at least one of the protein of Table 1 and the protein of Table 2. In aspects wherein the cell does not comprise both the protein of Table 1 and the protein of Table 2, the protein not comprised by the cell may be provided on another cell (e.g., a mammalian cell, e.g., a neutrophil or a T cell) or may be provided in or added to the cell culture media. The cell may additionally be treated with the modulator, e.g., by addition to the cell culture media. Decreased contractility of the fibroblast cell is indicated by increased elongation of the cell in the 3D gel relative to an isotype control (Figs. 17A-17D). In some instances, the cell that is treated with the modulator is elongated relative to a control cell, e.g., CAF contractility is decreased in the presence of the modulator. In some aspects, CAF contractility is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a 3D gel elongation assay. In some aspects, CAF contractility is decreased by at least 30% in the presence of the modulator as measured in a 3D gel elongation assay. Morphology index may be calculated as in Astarita et al., *Nat Immunol,* 16: 75-84, 2015. In some aspects, the morphology index is calculated using the equation $perimeter^2/4\pi$ x area, wherein "perimeter" is the perimeter of the cell and "area" is the area of the cell. In some aspects, the morphology index of the cell is between 10 and 30, e.g., is 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30.

ii. Immune checkpoint inhibition

In some aspects, the downstream activity is immune checkpoint inhibition. In some aspects, the protein of Table 1 is PD-L1 and the downstream activity is immune checkpoint inhibition. In some aspects, the protein of Table 1 is PD-L1, the protein of Table 2 is EPHA3, and the downstream activity is immune checkpoint inhibition.

In other aspects, the protein of Table 1 is PD-L2 and the downstream activity is immune checkpoint inhibition. In some aspects, the protein of Table 1 is PD-L2, the protein of Table 2 is CEACAM4, ICAM5, NECTIN3, PSG9, or TNFRSF11A, and the downstream activity is immune checkpoint inhibition.

In some aspects, the assay for immune checkpoint inhibition is a cell-based assay, e.g., a cell-based assay as described in Skalniak et al., *Oncotarget*, 8: 72167-72181, 2017. In some aspects, the assay for immune checkpoint inhibition is an assay described in Mariathasan et al., *Nature*, 554: 544-548.

In some aspects, the cells assayed are additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, immune checkpoint inhibition is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator. In some aspects, immune checkpoint inhibition is increased by at least 30% in the presence of the modulator.

iii. Suppression of cell proliferation

In some aspects, the downstream activity is suppression of cell proliferation. In some aspects, the protein of Table 1 is PTPRD and the downstream activity is suppression of cell proliferation. In some aspects, the protein of Table 1 is PTPRD, the protein of Table 2 is BMP5, CEACAM3, IL1RAP, IL1RAPL2, LECT1, LRFN5, SIRPG, SLITRK3, SLITRK4, SLITRK6, or TGFA, and the downstream activity is suppression of cell proliferation. In some aspects, the PTPRD protein comprises a G203E and K204E; R232C and R233C; P249L; G285E; E406K; S431L; R561Q; P666S; E755K; V892I; S912F; R995C; or R1088C amino acid substitution mutation or a ΔG61 ΔE106 amino acid deletion mutation and the downstream activity is suppression of cell proliferation.

In other aspects, the protein of Table 1 is CNTN1 and the downstream activity is suppression of cell proliferation. In some aspects, the protein of Table 1 is CNTN1, the protein of Table 2 is CDH6, CHL1, FCGRT, PCDHB7, or SGCG, and the downstream activity is suppression of cell proliferation.

In yet other aspects, the protein of Table 1 is CHL1 and the downstream activity is suppression of cell proliferation. In some aspects, the protein of Table 1 is CHL1, the protein of Table 2 is CNTN1, CNTN5, SIRPA, L1CAM, or TMEM132A, and the downstream activity is suppression of cell proliferation.

In some aspects, the assay for suppression of cell proliferation is a colony formation assay, e.g., a colony formation assay as described in Yan et al., *Cancer Res*, 76(6): 1603-1614, 2016 or Ognibene et al., *Oncotarget*, 9(40): 25903-25921, 2018. In some aspects, the cells assayed in the colony formation assay are additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, cell proliferation is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a colony formation assay. In some aspects, cell proliferation is decreased by at least 30% in the presence of the modulator as measured in a colony formation assay.

In some aspects, the assay for suppression of cell proliferation is a cell proliferation assay, e.g., a cell proliferation assay as described in Yan et al., *Cancer Res*, 76(6): 1603-1614, 2016. In some aspects, the cells assayed in the cell proliferation assay are additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, cell proliferation is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a cell proliferation assay. In some aspects, cell proliferation is decreased by at least 30% in the presence of the modulator as measured in a cell proliferation assay.

iv. Modulation of target phosphorylation

In some aspects, the downstream activity is phosphorylation of or suppression of phosphorylation of a target protein, e.g., phosphorylation of EGFR or suppression of STAT3 phosphorylation. In some aspects, the protein of Table 1 is PTPRD and the downstream activity is suppression of STAT3 phosphorylation. In some aspects, the protein of Table 1 is PTPRD, the protein of Table 2 is BMP5, CEACAM3, IL1RAP, IL1RAPL2, LECT1, LRFN5, SIRPG, SLITRK3, SLITRK4, SLITRK6, or TGFA, and the downstream activity is suppression of STAT3 phosphorylation. In some aspects, the PTPRD protein comprises a G203E and K204E; R232C and R233C; P249L; G285E; E406K; S431L; R561Q; P666S; E755K; V892I; S912F; R995C; or R1088C amino acid substitution mutation or a ΔG61 ΔE106 amino acid deletion mutation and the downstream activity is suppression of STAT3 phosphorylation.

In some aspects, the assay for suppression of STAT3 phosphorylation is a Western blot for phosphorylated STAT3, e.g., a Western blot as described in Veeriah et al., *PNAS*, 106(23): 9435-9440, 2009 or Peyser et al., *PLoS ONE*, 10.1371/journal.pone.0135750, 2015. In some aspects, the cell assayed in the Western blot is additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, suppression of STAT3 phosphorylation is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a Western blot for phosphorylated STAT3. In some aspects, suppression of STAT3 phosphorylation is increased by at least 30% in the presence of the modulator as measured in a Western blot for phosphorylated STAT3.

In some aspects, suppression of STAT3 phosphorylation is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a Western blot for phosphorylated STAT3. In some aspects, suppression of STAT3 phosphorylation is decreased by at least 30% in the presence of the modulator as measured in a Western blot for phosphorylated STAT3.

In other aspects, the protein of Table 1 is PTPRF and the downstream activity is phosphorylation of EGFR. In some aspects, the protein of Table 1 is PTPRF, the protein of Table 2 is CD177, IL1RAP, or LRFN5, and the downstream activity is phosphorylation of EGFR.

In some aspects, the assay for phosphorylation of EGFR is a Western blot for phosphorylated EGFR, e.g., a Western blot as described in Du et al., *J Cell Sci*, 126: 1440-1453, 2013. In some aspects, the cell assayed in the Western blot is additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, phosphorylation of EGFR is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a Western blot for phosphorylated EGFR. In some aspects, phosphorylation of EGFR is decreased by at least 30% in the presence of the modulator as measured in a Western blot for phosphorylated EGFR.

In some aspects, phosphorylation of EGFR is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a Western blot for phosphorylated EGFR. In some aspects, phosphorylation of EGFR is increased by at least 30% in the presence of the modulator as measured in a Western blot for phosphorylated EGFR.

In other aspects, the protein of Table 1 is AXL and the downstream activity is phosphorylation of AXL. In some aspects, the protein of Table 1 is AXL, the protein of Table 2 is IL1RL1 or VSIG10L, and the downstream activity is phosphorylation of AXL.

In some aspects, the assay for phosphorylation of AXL is a Western blot for phosphorylated AXL. In some aspects, the cell assayed in the Western blot is additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, phosphorylation of AXL is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a Western blot for phosphorylated AXL. In some aspects, phosphorylation of AXL is decreased by at least 30% in the presence of the modulator as measured in a Western blot for phosphorylated AXL.

In some aspects, phosphorylation of AXL is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a Western blot for phosphorylated AXL. In some aspects, phosphorylation of AXL is increased by at least 30% in the presence of the modulator as measured in a Western blot for phosphorylated AXL.

v. Inhibition of cell migration

In some aspects, the downstream activity is inhibition of cell migration. In some aspects, the protein of Table 1 is PTPRF and the downstream activity is inhibition of cell migration. In some aspects, the protein of Table 1 is PTPRF, the protein of Table 2 is CD177, IL1RAP, or LRFN5, and the downstream activity is inhibition of cell migration.

In some aspects, the downstream activity is inhibition of cell migration. In some aspects, the protein of Table 1 is PTPRS and the downstream activity is inhibition of cell migration. In some aspects, the protein of Table 1 is PTPRS, the protein of Table 2 is C6orf25, IL1RAP, IL1RAPL1, IL1RAPL2, LRFN1, LRFN5, LRRC4B, NCAM1, SLITRK1, SLITRK2, SLITRK3, SLITRK4, or SLITRK6, and the downstream activity is inhibition of cell migration.

In some aspects, the assay for inhibition of cell migration is a cell migration assay, e.g., a cell migration assay as described in Du et al., *J Cell Sci*, 126: 1440-1453, 2013. In some aspects, the cell assayed in the cell migration assay is additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, inhibition of cell migration is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a cell migration assay. In some aspects, inhibition of cell migration is decreased by at least 30% in the presence of the modulator as measured in a cell migration assay.

vi. Suppression of tumor formation

In some aspects, the downstream activity is suppression of tumor formation. In some aspects, the protein of Table 1 is CHL1 and the downstream activity is suppression of tumor formation. In some aspects, the protein of Table 1 is CHL1, the protein of Table 2 is CNTN1, CNTN5, SIRPA, L1CAM, or TMEM132A, and the downstream activity is suppression of tumor formation.

In some aspects, the assay for suppression of tumor formation is an *in vitro* tumorigenicity assay, e.g., a tumorigenicity assay as described in Tang et al., *Oncogene,* doi: 10.1038/s41388-018-0648-7, 2019, e.g., an XTT cell proliferation assay, a foci formation assay, a colony formation assay in soft agar, or a tumor formation assay in nude mice. In some aspects, the cell assayed in the tumorigenicity assay is additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, suppression of tumor formation is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a tumorigenicity assay. In some aspects, suppression of tumor formation is increased by at least 30% in the presence of the modulator as measured in a tumorigenicity assay.

vii. Suppression of cell invasion

In some aspects, the downstream activity is cell invasion. In some aspects, the protein of Table 1 is CNTN1 and the downstream activity is cell invasion. In some aspects, the protein of Table 1 is CNTN1, the protein of Table 2 is CDH6, CHL1, FCGRT, PCDHB7, or SGCG, and the downstream activity is cell invasion.

In other aspects, the protein of Table 1 is AXL and the downstream activity is cell invasion. In some aspects, the protein of Table 1 is AXL, the protein of Table 2 is IL1RL1 or VSIG10L, and the downstream activity is cell invasion.

In yet other aspects, the protein of Table 1 is CHL1 and the downstream activity is cell invasion. In some aspects, the protein of Table 1 is CHL1, the protein of Table 2 is CNTN1, CNTN5, SIRPA, L1CAM, or TMEM132A, and the downstream activity is cell invasion.

In some aspects, the assay for cell invasion is a gel invasion assay, e.g., a gel invasion assay as described in Yan et al., Cancer Res, 76(6): 1603-1614, 2016 or He et al., *Biochem Biophys Res Commun*, 438: 433-438, 2013. In some aspects, the cell assayed in the gel invasion assay is additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, cell invasion is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in a gel invasion assay. In some aspects, cell invasion is decreased by at least 30% in the presence of the modulator as measured in a gel invasion assay.

viii. Macrophage polarization and phagocytic function

In some aspects, the downstream activity is suppression of the phagocytic function of phagocytes (e.g., macrophages), e.g., antibody-dependent cellular phagocytosis (suppression of phagocytosis). In some aspects, the protein of Table 1 is LILRB1 and the downstream activity is suppression of phagocytosis. In some aspects, the protein of Table 1 is LILRB1, the protein of Table 2 is CLEC6A, CXADR, EDAR, FLT4, IL6R, ILDR1, or LILRA5, and the downstream activity is suppression of phagocytosis.

Phagocytic function may be measured as, e.g., the proportion of macrophages comprising a fluorescent signal, wherein the presence of fluorescence indicates phagocytosis of a fluorescently labeled target cell. A representative assay for phagocytosis is described in Barkal et al., *Nature Immunol*, 19: 76-

84, 2017. In some aspects, suppression of phagocytosis is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in an assay for phagocytosis. In some aspects, suppression of phagocytosis is decreased by at least 30% in the presence of the modulator as measured in an assay for phagocytosis.

In some aspects, suppression of phagocytosis is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in an assay for phagocytosis. In some aspects, suppression of phagocytosis is increased by at least 30% in the presence of the modulator as measured in an assay for phagocytosis.

In some aspects, the downstream activity is promotion of M2 macrophage polarization. In some aspects, the protein of Table 1 is LILRB2 and the downstream activity is promotion of M2 macrophage polarization. In some aspects, the protein of Table 1 is LILRB2, the protein of Table 2 is IGSF8 or MOG, and the downstream activity is promotion of M2 macrophage polarization. M2 macrophage polarization may be assessed as in Chen et al., *J Clin Invest*, 128(12), 5647-5662. In some aspects, M2 macrophage polarization is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator. In some aspects, M2 macrophage polarization is decreased by at least 30% in the presence of the modulator.

In some aspects, M2 macrophage polarization is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator. In some aspects, M2 macrophage polarization is increased by at least 30% in the presence of the modulator.

ix. Osteoclast differentiation

In some aspects, the downstream activity is osteoclast differentiation.

In some aspects, the protein of Table 1 is LILRB1 and the downstream activity is osteoclast differentiation. In some aspects, the protein of Table 1 is LILRB1, the protein of Table 2 is CLEC6A, CXADR, EDAR, FLT4, IL6R, ILDR1, or LILRA5, and the downstream activity is osteoclast differentiation.

In some aspects, the protein of Table 1 is LILRB3 and the downstream activity is osteoclast differentiation. In some aspects, the protein of Table 1 is LILRB3, the protein of Table 2 is LRRC15 or LY6G6F, and the downstream activity is osteoclast differentiation.

In some aspects, the protein of Table 1 is LILRB4 and the downstream activity is osteoclast differentiation. In some aspects, the protein of Table 1 is LILRB4, the protein of Table 2 is CNTFR and the downstream activity is osteoclast differentiation.

In some aspects, the assay for osteoclast differentiation is an assay for multinucleated cells positive for tartrate-resistant acid phosphatase (TRAP) staining (TRAP+ multinucleated cells). TRAP+ status and multiple nuclei (e.g., three or more nuclei) are indicators that a cell is an osteoclast. A representative assay for TRAP+ multinucleated cells is provided in Mori et al., J Immunol, 181(7): 4742-4751, 2008. In some aspects, the cell assayed in the TRAP+ multinucleated cell assay is additionally treated with the modulator, e.g., by addition to the cell culture media. In some aspects, osteoclast

differentiation is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in an assay for TRAP+ multinucleated cells. In some aspects, osteoclast differentiation is decreased by at least 30% in the presence of the modulator as measured in an assay for TRAP+ multinucleated cells.

In other aspects, osteoclast differentiation is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator as measured in an assay for TRAP+ multinucleated cells. In some aspects, osteoclast differentiation is increased by at least 30% in the presence of the modulator as measured in an assay for TRAP+ multinucleated cells.

x. Activation of signaling pathways

In some aspects, the downstream activity is activation of a signaling pathway. In some aspects, the protein of Table 1 is AXL and the downstream activity is activation of the RAS/RAF/MAPK/ERK1/2 pathway, activation of the JAK/STAT pathway, or activation of the PI3K signaling pathway. In some aspects, the protein of Table 1 is AXL, the protein of Table 2 is IL1RL1 or VSIG10L, and the downstream activity is activation of the RAS/RAF/MAPK/ERK1/2 pathway, activation of the JAK/STAT pathway, or activation of the PI3K signaling pathway.

In some aspects, the protein of Table 1 is PTPRS and the downstream activity is activation of the PI3K signaling pathway. In some aspects, the protein of Table 1 is PTPRS, the protein of Table 2 is C6orf25, IL1RAP, IL1RAPL1, IL1RAPL2, LRFN1, LRFN5, LRRC4B, NCAM1, SLITRK1, SLITRK2, SLITRK3, SLITRK4, or SLITRK6, and the downstream activity is activation of the PI3K signaling pathway.

In other aspects, the protein of Table 1 is CNTN1 and the downstream activity is activation of the RhoA pathway or the Akt pathway. In some aspects, the protein of Table 1 is CNTN1, the protein of Table 2 is CDH6, CHL1, FCGRT, PCDHB7, or SGCG, and the downstream activity is activation of the RhoA pathway or the Akt pathway.

In some aspects, activation of the RAS/RAF/MAPK/ERK1/2 pathway, activation of the JAK/STAT pathway, activation of the RhoA pathway, activation of the Akt pathway, or activation of the PI3K signaling pathway is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator. In some aspects, activation of the RAS/RAF/MAPK/ERK1/2 pathway, activation of the JAK/STAT pathway, activation of the RhoA pathway, activation of the Akt pathway, or activation of the PI3K signaling pathway is decreased by at least 30% in the presence of the modulator.

In some aspects, activation of the RAS/RAF/MAPK/ERK1/2 pathway, activation of the JAK/STAT pathway, activation of the RhoA pathway, activation of the Akt pathway, or activation of the PI3K signaling pathway is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator. In some aspects, activation of the RAS/RAF/MAPK/ERK1/2 pathway, activation of the JAK/STAT pathway, activation of the RhoA pathway, activation of the Akt pathway, or activation of the PI3K signaling pathway is increased by at least 30% in the presence of the modulator.

xi. Formation of filopodia

In some aspects, the downstream activity is formation of filopodia. In some aspects, the protein of Table 1 is AXL and the downstream activity is formation of filopodia. In some aspects, the protein of Table 1 is AXL, the protein of Table 2 is IL1RL1 or VSIG10L, and the downstream activity is formation of filopodia. In some aspects, formation of filopodia is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator. In some aspects, formation of filopodia is decreased by at least 30% in the presence of the modulator.

xii. Regulation of the EMT

In some aspects, the downstream activity is inhibition of the epithelial-mesenchymal transition (EMT). EMT increases the migratory and survival attributes of carcinoma cells, thus facilitating malignant progression (Gjerdrum et al., *PNAS*, 107(3): 1124-1129, 2010). In some aspects, the protein of Table 1 is AXL and the downstream activity is inhibition of the EMT. In some aspects, the protein of Table 1 is AXL, the protein of Table 2 is IL1RL1 or VSIG10L, and the downstream activity is inhibition of the EMT. EMT may be quantified as described in Gjerdrum et al., *PNAS*, 107(3): 1124-1129, 2010. In some aspects, inhibition of the EMT is increased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator. In some aspects, inhibition of the EMT is increased by at least 30% in the presence of the modulator.

xii. Tumor growth

In some aspects, the downstream activity is tumor growth. In some aspects, the protein of Table 1 is PDPN, the protein of Table 2 is CD177, and the downstream activity is tumor growth. In some aspects, tumor growth is decreased by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% in the presence of the modulator. In some aspects, tumor growth is decreased by at least 30% in the presence of the modulator.

IV. MODULATORS OF PROTEIN-PROTEIN INTERACTIONS

In some aspects, the disclosure features an isolated modulator of the interaction between a protein of Table 1 and a protein of Table 2, wherein: (a) the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (b) the modulator causes an increase or decrease in the binding of the protein of Table 1 to the protein of Table 2 relative to binding in the absence of the modulator.

In some aspects, the disclosure features an isolated modulator of the downstream activity of a protein of Table 1 or a protein of Table 2, wherein (a) the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and (b) the modulator causes a change in the downstream activity of the protein of Table 1 or the protein of Table 2 relative to downstream activity in the absence of the modulator.

In some aspects, the modulator is an inhibitor or an activator of the downstream activity of the protein of Table 1 or Table 2.

In some aspects, the change in the downstream activity is an increase or a decrease in the amount, strength, or duration of the downstream activity, e.g., a downstream activity described in Section III*B* herein, e.g., CAF contractility, immune checkpoint inhibition, suppression of cell proliferation, modulation of target phosphorylation, inhibition of cell migration, suppression of tumor formation, suppression of cell invasion, macrophage polarization, regulation of phagocytosis, osteoclast differentiation, activation of a signaling pathway, or formation of filopodia.

A. Small molecules

In some aspects, the modulator or candidate modulator is a small molecule. Small molecules are molecules other than binding polypeptides or antibodies as defined herein that may bind, preferably specifically, to a protein of Table 1 and/or a protein of Table 2. Binding small molecules may be identified and chemically synthesized using known methodology (see, e.g., PCT Publication Nos. WO00/00823 and WO00/39585). Binding small molecules are usually less than about 2000 daltons in size (e.g., less than about 2000, 1500, 750, 500, 250 or 200 daltons in size), wherein such organic small molecules that are capable of binding, preferably specifically, to a polypeptide as described herein may be identified without undue experimentation using well known techniques. In this regard, it is noted that techniques for screening small molecule libraries for molecules that are capable of binding to a polypeptide target are well known in the art (*see, e.g.*, PCT Publication Nos. WO00/00823 and WO00/39585). Binding small molecules may be, for example, aldehydes, ketones, oximes, hydrazones, semicarbazones, carbazides, primary amines, secondary amines, tertiary amines, N-substituted hydrazines, hydrazides, alcohols, ethers, thiols, thioethers, disulfides, carboxylic acids, esters, amides, ureas, carbamates, carbonates, ketals, thioketals, acetals, thioacetals, aryl halides, aryl sulfonates, alkyl halides, alkyl sulfonates, aromatic compounds, heterocyclic compounds, anilines, alkenes, alkynes, diols, amino alcohols, oxazolidines, oxazolines, thiazolidines, thiazolines, enamines, sulfonamides, epoxides, aziridines, isocyanates, sulfonyl chlorides, diazo compounds, acid chlorides, or the like.

In some aspects, the binding of a protein of Table 1 and a protein of Table 2 is decreased (e.g., decreased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%) in the presence of the small molecule. In some aspects, the binding of a protein of Table 1 and a protein of Table 2 is increased (e.g., increased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more than 100%) in the presence of the small molecule. In some aspects, a downstream activity (e.g., a downstream activity described in Section III*B* herein, e.g., CAF contractility, immune checkpoint inhibition, suppression of cell proliferation, modulation of target phosphorylation, inhibition of cell migration, suppression of tumor formation, suppression of cell invasion, macrophage polarization, regulation of phagocytosis, osteoclast differentiation, activation of a signaling pathway, or formation of filopodia) of the protein of Table 1 and/or the protein of Table 2 is decreased (e.g., decreased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%) in the presence of the small molecule. In some aspects, a downstream activity (e.g., a downstream activity described in Section III*B* herein) of the protein of Table 1 and/or the protein of Table 2 is increased (e.g., increased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more than 100%) in the presence of the small molecule.

B. Antibodies and antigen-binding fragments

In some aspects, the modulator or candidate modulator is an antibody or an antigen-binding fragment thereof binding a protein of Table 1 and/or a protein of Table 2. In some aspects, the antigen-binding fragment is a bis-Fab, an Fv, a Fab, a Fab'-SH, a $F(ab')_2$, a diabody, a linear antibody, an scFv, an ScFab, a VH domain, or a VHH domain.

In some aspects, the binding of a protein of Table 1 and a protein of Table 2 is decreased (e.g., decreased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%) in the presence of the antibody or antigen-binding fragment. In some aspects, the binding of a protein of Table 1 and a protein of Table 2 is increased (e.g., increased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more than 100%) in the presence of the antibody or antigen-binding fragment. In some aspects, a downstream activity (e.g., a downstream activity described in Section III*B* herein, e.g., CAF contractility, immune checkpoint inhibition, suppression of cell proliferation, modulation of target phosphorylation, inhibition of cell migration, suppression of tumor formation, suppression of cell invasion, macrophage polarization, regulation of phagocytosis, osteoclast differentiation, activation of a signaling pathway, or formation of filopodia) of the protein of Table 1 and/or the protein of Table 2 is decreased (e.g., decreased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%) in the presence of the antibody or antigen-binding fragment. In some aspects, a downstream activity (e.g., a downstream activity described in Section III*B* herein) of the protein of Table 1 and/or the protein of Table 2 is increased (e.g., increased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more than 100%) in the presence of the antibody or antigen-binding fragment.

C. Peptides

In some aspects, the modulator or candidate modulator is a peptide that binds to a protein of Table 1 and/or a protein of Table 2. The peptide may be the peptide may be naturally occurring or may be engineered. In some aspects, the peptide is a fragment of the protein of Table 1, the protein of Table 2, or another protein that binds to the protein of Table 1 or the protein of Table 2. The peptide may bind the binding partner with equal, less, or greater affinity than the full-length protein. In some aspects, the peptide performs all functions of the full-length protein. In other aspects, the peptide does not perform all functions of the full-length protein.

In some aspects, the binding of a protein of Table 1 and a protein of Table 2 is decreased (e.g., decreased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%) in the presence of the peptide. In some aspects, the binding of a protein of Table 1 and a protein of Table 2 is increased (e.g., increased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more than 100%) in the presence of the peptide. In some aspects, a downstream activity (e.g., a downstream activity described in Section III*B* herein, e.g., CAF contractility, immune checkpoint inhibition, suppression of cell proliferation, modulation of target phosphorylation, inhibition of cell migration, suppression of tumor formation, suppression of cell invasion, macrophage polarization, regulation of phagocytosis, osteoclast differentiation, activation of a signaling pathway, or formation of filopodia) of the protein of Table 1 and/or the protein of Table 2 is decreased (e.g., decreased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%) in the presence of the peptide. In some aspects, a downstream activity (e.g., a

downstream activity described in Section III*B* herein) of the protein of Table 1 and/or the protein of Table 2 is increased (e.g., increased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more than 100%) in the presence of the peptide.

D. Mimics

In some aspects, the modulator or candidate modulator is a mimic, e.g., a molecular mimic, that binds to a protein of Table 1 and/or a protein of Table 2. The mimic may be a molecular mimic of the protein of Table 1, the protein of Table 2, or another protein that binds to the protein of Table 1 or the protein of Table 2. In some aspects, the mimic may perform all functions of the mimicked polypeptide. In other aspects, the mimic does not perform all functions of the mimicked polypeptide.

In some aspects, the binding of a protein of Table 1 and a protein of Table 2 is decreased (e.g., decreased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%) in the presence of the mimic. In some aspects, the binding of a protein of Table 1 and a protein of Table 2 is increased (e.g., increased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more than 100%) in the presence of the mimic. In some aspects, a downstream activity (e.g., a downstream activity described in Section III*B* herein, e.g., CAF contractility, immune checkpoint inhibition, suppression of cell proliferation, modulation of target phosphorylation, inhibition of cell migration, suppression of tumor formation, suppression of cell invasion, macrophage polarization, regulation of phagocytosis, osteoclast differentiation, activation of a signaling pathway, or formation of filopodia) of the protein of Table 1 and/or the protein of Table 2 is decreased (e.g., decreased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%) in the presence of the mimic. In some aspects, a downstream activity (e.g., a downstream activity described in Section III*B* herein) of the protein of Table 1 and/or the protein of Table 2 is increased (e.g., increased by 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more than 100%) in the presence of the mimic.

V. METHODS OF TREATMENT COMPRISING MODULATORS OF IDENTIFIED PROTEIN-PROTEIN INTERACTIONS

In some aspects, a modulator of a protein-protein interaction described in Section II*C* herein is used to treat or delay progression of a pathological state, disease, disorder, or condition, e.g., a cancer.

In some aspects, the modulator increases or decreases the amount, strength, or duration of a downstream activity described in Section III*B* herein, e.g., CAF contractility, immune checkpoint inhibition, suppression of cell proliferation, modulation of target phosphorylation, inhibition of cell migration, suppression of tumor formation, suppression of cell invasion, macrophage polarization, regulation of phagocytosis, osteoclast differentiation, activation of a signaling pathway, or formation of filopodia, in an individual to whom the modulator has been administered.

A. Cancers

In some aspects, a modulator of a protein-protein interaction described in Section II*C* herein (e.g., a small molecule, an antibody, an antigen-binding fragment, a peptide, a mimic, an antisense oligonucleotide, or an siRNA) is used to treat or delay progression of a cancer in a subject in need

thereof. In some aspects, the subject is a human. The cancer may be a solid tumor cancer or a non-solid tumor cancer. Solid cancer tumors include, but are not limited to a bladder cancer, a melanoma, a breast cancer, a colorectal cancer, a lung cancer, a head and neck cancer, a kidney cancer, an ovarian cancer, a pancreatic cancer, or a prostate cancer, or metastatic forms thereof. In some aspects, the cancer is a bladder cancer. Further aspects of bladder cancer include urothelial carcinoma, muscle invasive bladder cancer (MIBC), or non-muscle invasive bladder cancer (NMIBC). In some aspects, the bladder cancer is a metastatic urothelial carcinoma (mUC). In some aspects, the cancer is a breast cancer. Further aspects of breast cancer include a hormone receptor-positive (HR+) breast cancer, e.g., an estrogen receptor-positive (ER+) breast cancer, a progesterone receptor-positive (PR+) breast cancer, or an ER+/PR+ breast cancer. Other aspects of breast cancer include a HER2-positive (HER2+) breast cancer. Yet other aspects of breast cancer include a triple-negative breast cancer (TNBC). In some aspects, the breast cancer is an early breast cancer. In some aspects, the cancer is a lung cancer. Further aspects of lung cancer include an epidermal growth factor receptor-positive (EGFR+) lung cancer. Other aspects of lung cancer include an epidermal growth factor receptor-negative (EGFR-) lung cancer. Yet other aspects of lung cancer include a non-small cell lung cancer, e.g., a squamous lung cancer or a non-squamous lung cancer. Other aspects of lung cancer include a small cell lung cancer. In some aspects, the cancer is a head and neck cancer. Further aspects of head and neck cancer include a squamous cell carcinoma of the head & neck (SCCHN). In some aspects, the cancer is a kidney cancer. Further aspects of kidney cancer include a renal cell carcinoma (RCC). In some aspects, the cancer is a liver cancer. Further aspects of liver cancer include a hepatocellular carcinoma. In some aspects, the cancer is a prostate cancer. Further aspects of prostate cancer include a castration-resistant prostate cancer (CRPC). In some aspects, the cancer is a metastatic form of a solid tumor. In some aspects, the metastatic form of a solid tumor is a metastatic form of a melanoma, a breast cancer, a colorectal cancer, a lung cancer, a head and neck cancer, a bladder cancer, a kidney cancer, an ovarian cancer, a pancreatic cancer, or a prostate cancer. In some aspects, the cancer is a metastatic urothelial carcinoma (mUC). In some aspects, the cancer is a non-solid tumor cancer. Non-solid tumor cancers include, but are not limited to, a B-cell lymphoma. Further aspects of B-cell lymphoma include, e.g., a chronic lymphocytic leukemia (CLL), a diffuse large B-cell lymphoma (DLBCL), a follicular lymphoma, myelodysplastic syndrome (MDS), a non-Hodgkin lymphoma (NHL), an acute lymphoblastic leukemia (ALL), a multiple myeloma, an acute myeloid leukemia (AML), or a mycosis fungoides (MF). In some aspects, the cancer is a colorectal cancer.

B. Methods of delivery

The compositions utilized in the methods described herein (e.g., a modulator of a protein-protein interaction described in Section II*C,* e.g., a small molecule, an antibody, an antigen-binding fragment, a peptide, a mimic, an antisense oligonucleotide, or an siRNA) can be administered by any suitable method, including, for example, intravenously, intramuscularly, subcutaneously, intradermally, percutaneously, intraarterially, intraperitoneally, intralesionally, intracranially, intraarticularly, intraprostatically, intrapleurally, intratracheally, intrathecally, intranasally, intravaginally, intrarectally, topically, intratumorally, peritoneally, subconjunctivally, intravesicularly, mucosally, intrapericardially, intraumbilically, intraocularly, intraorbitally, orally, transdermally, intravitreally (e.g., by intravitreal

injection), by eye drop, by inhalation, by injection, by implantation, by infusion, by continuous infusion, by localized perfusion bathing target cells directly, by catheter, by lavage, in cremes, or in lipid compositions. The compositions utilized in the methods described herein can also be administered systemically or locally. The method of administration can vary depending on various factors (e.g., the compound or composition being administered and the severity of the condition, disease, or disorder being treated). In some aspects, a modulator of a protein-protein interaction is administered intravenously, intramuscularly, subcutaneously, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, or intranasally. Dosing can be by any suitable route, e.g., by injections, such as intravenous or subcutaneous injections, depending in part on whether the administration is brief or chronic. Various dosing schedules including but not limited to single or multiple administrations over various time-points, bolus administration, and pulse infusion are contemplated herein.

A modulator of a protein-protein interaction described herein (and any additional therapeutic agent) may be formulated, dosed, and administered in a fashion consistent with good medical practice. Factors for consideration in this context include the particular disorder being treated, the particular mammal being treated, the clinical condition of the individual patient, the cause of the disorder, the site of delivery of the agent, the method of administration, the scheduling of administration, and other factors known to medical practitioners. The modulator need not be, but is optionally formulated with and/or administered concurrently with one or more agents currently used to prevent or treat the disorder in question. The effective amount of such other agents depends on the amount of the modulator present in the formulation, the type of disorder or treatment, and other factors discussed above. These are generally used in the same dosages and with administration routes as described herein, or about from 1 to 99% of the dosages described herein, or in any dosage and by any route that is empirically/clinically determined to be appropriate.

VI. METHODS OF TREATMENT COMPRISING PD-L1 AXIS BINDING ANTAGONISTS

A. Markers for responsiveness to atezolizumab

In some aspects, the invention comprises a method of identifying an individual having a cancer treatable with a PD-L1 axis binding antagonist (e.g., a cancer that is more likely to be treatable with a PD-L1 axis binding antagonist), the method comprising determining an expression level of a first member and a second member of at least one of the gene pairs of Table 15 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual having a cancer treatable with a PD-L1 axis binding antagonist.

In some aspects, the invention comprises a method of identifying an individual having a cancer who may benefit from a treatment comprising a PD-L1 axis binding antagonist, the method comprising determining an expression level of a first member and a second member of at least one of the gene pairs of Table 15 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the

gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment comprising a PD-L1 axis binding antagonist.

In some aspects, the invention comprises a method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of a first member and a second member at least one of the gene pairs of Table 15 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment comprising a PD-L1 axis binding antagonist.

In some aspects, the individual has an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level and the method further comprises administering to the individual an effective amount of a PD-L1 axis binding antagonist.

In some aspects, the invention comprises a method of treating an individual having a cancer, the method comprising: (a) determining an expression level of a first member and a second member at least one of the gene pairs of Table 15 in a sample from the individual, wherein the expression level of the first member of the gene pair is above a first reference expression level and the expression level of the second member of the gene pair is above a second reference expression level; and (b) administering an effective amount of a PD-L1 axis binding antagonist to the individual.

In some aspects, the invention comprises a method of treating an individual having a cancer, the method comprising administering a PD-L1 axis binding antagonist to an individual who has been determined to have an expression level of a first member of a gene pair of Table 15 that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level.

In some aspects, the benefit comprises an extension in the individual's overall survival (OS) as compared to treatment without the PD-L1 axis binding antagonist. In other aspects, the benefit may comprise, e.g., an increase in time to recurrence or a reduced duration of treatment as compared to treatment without the PD-L1 axis binding antagonist.

In some aspects, the first member of the gene pair is SIGLEC6 and the second member of the gene pair is NCR1.

In some aspects, the first member of the gene pair is BTN3A1 and the second member of the gene pair is LRRC4B.

In some aspects, the first member of the gene pair is CD80 and the second member of the gene pair is CTLA4.

In some aspects, the first member of the gene pair is BTN3A3 and the second member of the gene pair is LRRC4B.

In some aspects, the first member of the gene pair is NCR1 and the second member of the gene pair is SIGLEC8.

In some aspects, the first member of the gene pair is CNTFR and the second member of the gene pair is LILRB4.

In some aspects, the first member of the gene pair is FGFR3 and the second member of the gene pair is LRRTM2.

In some aspects, the first member of the gene pair is FGFR4 and the second member of the gene pair is SIGLEC15.

In some aspects, the first member of the gene pair is FGFR1 and the second member of the gene pair is KL.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is TRHDE.

In some aspects, the first member of the gene pair is CTLA4 and the second member of the gene pair is PCDHGB4.

In some aspects, the first member of the gene pair is CTLA4 and the second member of the gene pair is FAM200A.

In some aspects, the first member of the gene pair is CA12 and the second member of the gene pair is SIGLEC6.

In some aspects, the first member of the gene pair is ILDR2 and the second member of the gene pair is CLEC12B.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is ITLN1.

In some aspects, the first member of the gene pair is CADM1 and the second member of the gene pair is CRTAM.

In some aspects, the first member of the gene pair is CD79B and the second member of the gene pair is CD244.

In some aspects, the first member of the gene pair is DAG1 and the second member of the gene pair is EFNB1.

B. Markers for lack of responsiveness to atezolizumab

In some aspects, the invention comprises a method of identifying an individual having a cancer who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist, the method comprising determining an expression level of a first member and a second member of at least one of the gene pairs of Table 16 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist.

In some aspects, the invention comprises a method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of a first member and a second member at least one of the gene pairs of Table 16 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist.

In some aspects, the invention comprises a method of identifying an individual having a cancer who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist, the method comprising determining an expression level of a first member and a second member of at least one of the gene pairs of Table 16 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies an individual having a cancer resistant to treatment with a PD-L1 axis binding antagonist.

In some aspects, the invention comprises a method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of a first member and a second member at least one of the gene pairs of Table 16 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies an individual having a cancer resistant to treatment with a PD-L1 axis binding antagonist.

In some aspects, the individual has an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level and the method comprises administering to the individual an effective amount of a treatment other than or in addition to a PD-L1 axis binding antagonist.

In some aspects, the benefit comprises an extension in the individual's overall survival (OS) as compared to treatment without the treatment other than or in addition to a PD-L1 axis binding antagonist.

In some aspects, the sample from the individual is obtained from the individual prior to administration of an anti-cancer therapy. In some aspects, the sample from the individual is obtained from the individual after administration of an anti-cancer therapy.

In some aspects, the sample from the individual is a tumor tissue sample or a tumor fluid sample, e.g., a formalin-fixed and paraffin-embedded (FFPE) sample, an archival sample, a fresh sample, or a frozen sample.

In some aspects, (a) the expression level of the first member and the second member of the gene pair in the sample is a protein expression level; or (b) the expression level of the first member and the second member of the gene pair in the sample is an mRNA expression level.

In some aspects, the expression level of the first member and the second member of the gene pair in the sample is a mRNA expression level of the first member and the second member of the gene pair, respectively. In some aspects, the mRNA expression level of the first member and the second member of the gene pair is determined by *in situ* hybridization (ISH), RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, FISH, or a combination thereof. In some aspects, the RNA-seq is TruSeq RNA Access technology (Illumina®).

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is EVC2.

In some aspects, the first member of the gene pair is GPC4 and the second member of the gene pair is FGFRL1.

In some aspects, the first member of the gene pair is EFNB3 and the second member of the gene pair is EPHB4.

In some aspects, the first member of the gene pair is PTPRD and the second member of the gene pair is LRFN4.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is AQPEP.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is DSG4.

In some aspects, the first member of the gene pair is LDLR and the second member of the gene pair is LILRB5.

In some aspects, the first member of the gene pair is EFNB3 and the second member of the gene pair is EPHB3.

In some aspects, the first member of the gene pair is PLXNB3 and the second member of the gene pair is SEMA4G.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is EPHB6.

In some aspects, the first member of the gene pair is FLT4 and the second member of the gene pair is FLRT2.

In some aspects, the first member of the gene pair is FLT1 and the second member of the gene pair is ELFN1.

In some aspects, the first member of the gene pair is GPC4 and the second member of the gene pair is FGFR4.

In some aspects, the first member of the gene pair is GPC3 and the second member of the gene pair is TNFRSF11B.

In some aspects, the first member of the gene pair is FGFR4 and the second member of the gene pair is GPC6.

In some aspects, the first member of the gene pair is PLXNB1 and the second member of the gene pair is SEMA4B.

In some aspects, the first member of the gene pair is EDA and the second member of the gene pair is EDAR.

In some aspects, the first member of the gene pair is FGFR4 and the second member of the gene pair is NRXN2.

In some aspects, the first member of the gene pair is SEMA4D and the second member of the gene pair is PLXNB2.

In some aspects, the first member of the gene pair is FLT4 and the second member of the gene pair is NRP2.

In some aspects, the first member of the gene pair is FGFR4 and the second member of the gene pair is GPC3.

In some aspects, the first member of the gene pair is FGFR2 and the second member of the gene pair is RAMP1.

In some aspects, the first member of the gene pair is AXL1 and the second member of the gene pair is IL1RL1.

In some aspects, the first member of the gene pair is CD320 and the second member of the gene pair is IGSF5.

In some aspects, the first member of the gene pair is CD59 and the second member of the gene pair is STAB1.

In some aspects, the first member of the gene pair is CNTN3 and the second member of the gene pair is PTPRG.

In some aspects, the first member of the gene pair is EFNB1 and the second member of the gene pair is EPHA3.

In some aspects, the first member of the gene pair is EFNB3 and the second member of the gene pair is EPHB2.

In some aspects, the first member of the gene pair is EGF and the second member of the gene pair is TNFRSF11B.

In some aspects, the first member of the gene pair is ENPEP and the second member of the gene pair is SLITRK1.

In some aspects, the first member of the gene pair is FCGR3B and the second member of the gene pair is EDA2R.

In some aspects, the first member of the gene pair is IL20RA and the second member of the gene pair is CLEC14A.

In some aspects, the first member of the gene pair is IL6R and the second member of the gene pair is BTNL9.

In some aspects, the first member of the gene pair is IZUMO1 and the second member of the gene pair is LILRA5.

In some aspects, the first member of the gene pair is NGFR and the second member of the gene pair is LRRTM3.

In some aspects, the first member of the gene pair is NTM and the second member of the gene pair is AMIGO2.

In some aspects, the first member of the gene pair is PCDHB3 and the second member of the gene pair is IGSF11.

In some aspects, the first member of the gene pair is PTGFRN and the second member of the gene pair is TMEM59L.

In some aspects, the first member of the gene pair is TREM1 and the second member of the gene pair is VSIG8.

C. Reference expression levels

In some aspects, the reference expression level for the first member of the protein pair (i.e., the first reference expression level) is a pre-assigned expression level and the reference expression level for the first member of the protein pair (i.e., the second reference expression level) is a pre-assigned reference expression level.

In some aspects, the first reference expression level is between about 0.1 to about 0.5 counts per million (CPM), e.g, between about 0.15 to about 0.4 CPM, between about 0.2 to 0.3 CPM, or between about 0.225 to about 0.275 CPM.

In some aspects, the second reference expression level is between about 0.1 to about 0.5 counts per million (CPM), e.g, between about 0.15 to about 0.4 CPM, between about 0.2 to 0.3 CPM, or between about 0.225 to about 0.275 CPM.

In some aspects, the first reference expression level is between about 0.25 to about 0.5 counts per million (CPM) and the second reference expression level is between about 0.25 to about 0.5 CPM.

In some aspects, the first reference expression level is 0.25 CPM. In some aspects, the second reference expression level is 0.25 CPM. In some aspects, the first reference expression level is 0.25 CPM and the second reference expression level is 0.25 CPM.

In some aspects, the first reference expression level and the second reference expression level are expression levels of the first member and the second member of the gene pair, respectively, in a reference population of individuals having a cancer, e.g., a urinary tract cancer, e.g., a urinary tract carcinoma, e.g., a metastatic urothelial carcinoma (mUC).

D. Cancers

In some aspects, a PD-L1 axis binding antagonist is used to treat or delay progression of a cancer, e.g., a urinary tract cancer, in a subject in need thereof. In some aspects, the subject is a human. Urinary tract cancers include urothelial carcinomas (UC), non-urothelial carcinomas of the urinary tract, and carcinomas of the urinary tract having mixed histology. Non-urothelial carcinomas of the urinary tract include all subtypes listed in the World Health Organization classification, e.g., a squamous cell carcinoma, a verrucous carcinoma, an adenocarcinoma, a glandular carcinoma, a carcinoma of the Bellini collecting duct, a neuroendocrine carcinoma, or a small cell carcinoma. The adenocarcinoma may be an enteric adenocarcinoma, a mucinous adenocarcinoma, a signet-ring cell adenocarcinoma, or a clear cell adenocarcinoma. Urinary tract cancers may be located in the bladder, the renal pelvis, the ureter, or the urethra. In some aspects, the urinary tract cancer (e.g., urothelial carcinoma, non-urothelial carcinoma, or carcinoma of the urinary tract having mixed histology) is locally advanced, e.g., stage T4b N_{any} or T_{any} N2–3, according to the TNM classification, at the onset of treatment. In some aspects, the urinary tract cancer is a metastatic urothelial carcinoma (mUC), a metastatic form of a non-urothelial carcinoma of the urinary tract, or a metastatic form of a carcinoma of the urinary tract having mixed histology. In some aspects, the urinary tract cancer is TNM stage M1, according to the TNM classification, at the onset of treatment.

E. Immune checkpoint inhibitors

In some aspects, the methods of the invention include use of a PD-L1 axis binding antagonist, which may be a PD-1 binding antagonist, a PD-L1 binding antagonist, or a PD-L2 binding antagonist. PD-1 (programmed death 1) is also referred to in the art as "programmed cell death 1," "PDCD1," "CD279," and "SLEB2." An exemplary human PD-1 is shown in UniProtKB/Swiss-Prot Accession No. Q15116. PD-L1 (programmed death ligand 1) is also referred to in the art as "programmed cell death 1 ligand 1," "PDCD1LG1," "CD274," "B7-H," and "PDL1." An exemplary human PD-L1 is shown in

UniProtKB/Swiss-Prot Accession No. Q9NZQ7.1. PD-L2 (programmed death ligand 2) is also referred to in the art as "programmed cell death 1 ligand 2," "PDCD1LG2," "CD273," "B7-DC," "Btdc," and "PDL2." An exemplary human PD-L2 is shown in UniProtKB/Swiss-Prot Accession No. Q9BQ51. In some instances, PD-1, PD-L1, and PD-L2 are human PD-1, PD-L1 and PD-L2.

In some aspects, the PD-1 binding antagonist is a molecule that inhibits the binding of PD-1 to its ligand binding partners. In a specific aspect the PD-1 ligand binding partners are PD-L1 and/or PD-L2. In another instance, a PD-L1 binding antagonist is a molecule that inhibits the binding of PD-L1 to its binding ligands. In a specific aspect, PD-L1 binding partners are PD-1 and/or B7-1. In another instance, the PD-L2 binding antagonist is a molecule that inhibits the binding of PD-L2 to its ligand binding partners. In a specific aspect, the PD-L2 binding ligand partner is PD-1. The antagonist may be an antibody, an antigen binding fragment thereof, an immunoadhesin, a fusion protein, or oligopeptide.

In some aspects, the PD-1 binding antagonist is an anti-PD-1 antibody (e.g., a human antibody, a humanized antibody, or a chimeric antibody), for example, as described below. In some aspects, the anti-PD-1 antibody is selected from the group consisting of MDX-1106 (nivolumab), MK-3475 (pembrolizumab), MEDI-0680 (AMP-514), PDR001, REGN2810, and BGB-108. MDX-1106, also known as MDX- 1106-04, ONO-4538, BMS-936558, or nivolumab, is an anti-PD-1 antibody described in WO2006/121168. MK-3475, also known as pembrolizumab or lambrolizumab, is an anti-PD-1 antibody described in WO 2009/114335. In some instances, the PD-1 binding antagonist is an immunoadhesin (e.g., an immunoadhesin comprising an extracellular or PD-1 binding portion of PD-L1 or PD-L2 fused to a constant region (e.g., an Fc region of an immunoglobulin sequence). In some instances, the PD-1 binding antagonist is AMP-224. AMP-224, also known as B7-DCIg, is a PD-L2-Fc fusion soluble receptor described in WO 2010/027827 and WO 2011/066342.

In some aspects, the anti-PD-1 antibody is MDX-1106. Alternative names for "MDX-1106" include MDX-1106-04, ONO-4538, BMS-936558, and nivolumab. In some aspects, the anti-PD-1 antibody is nivolumab (CAS Registry Number: 946414-94-4). In a still further aspect, provided is an isolated anti-PD-1 antibody comprising a heavy chain variable region comprising the heavy chain variable region amino acid sequence from SEQ ID NO: 1 and/or a light chain variable region comprising the light chain variable region amino acid sequence from SEQ ID NO: 2. In a still further aspect, provided is an isolated anti-PD-1 antibody comprising a heavy chain and/or a light chain sequence, wherein:

(a) the heavy chain sequence has at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to the heavy chain sequence:

QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWYDGSKRYYADSVKGR
FTISRDNSKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAA
LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTK
VDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGV
EVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLP
PSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEG
NVFSCSVMHEALHNHYTQKSLSLSLGK (SEQ ID NO: 1), and

(b) the light chain sequences has at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to the light chain sequence:
EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTD
FTLTISSLEPEDFAVYYCQQSSNWPRTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP
REAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN
RGEC (SEQ ID NO: 2).

In some aspects, the PD-L1 axis binding antagonist is a PD-L2 binding antagonist. In some aspects, the PD-L2 binding antagonist is an anti-PD-L2 antibody (e.g., a human antibody, a humanized antibody, or a chimeric antibody). In some aspects, the PD-L2 binding antagonist is an immunoadhesin.

In some aspects, the PD-L1 binding antagonist is an anti-PD-L1 antibody, for example, as described below. In some aspects, the anti-PD-L1 antibody is capable of inhibiting binding between PD-L1 and PD-1 and/or between PD-L1 and B7-1. In some aspects, the anti-PD-L1 antibody is a monoclonal antibody. In some aspects, the anti-PD-L1 antibody is an antibody fragment selected from the group consisting of Fab, Fab'-SH, Fv, scFv, and $(Fab')_2$ fragments. In some aspects, the anti-PD-L1 antibody is a humanized antibody. In some aspects, the anti-PD-L1 antibody is a human antibody. In some aspects, the anti-PD-L1 antibody is selected from the group consisting of YW243.55.S70, MPDL3280A (atezolizumab), MDX-1105, and MEDI4736 (durvalumab), and MSB0010718C (avelumab). Antibody YW243.55.S70 is an anti-PD-L1 described in WO 2010/077634. MDX-1105, also known as BMS-936559, is an anti-PD-L1 antibody described in WO2007/005874. MEDI4736 (durvalumab) is an anti-PD-L1 monoclonal antibody described in WO2011/066389 and US2013/034559. Examples of anti-PD-L1 antibodies useful for the methods of this invention, and methods for making thereof are described in PCT patent application WO 2010/077634, WO 2007/005874, WO 2011/066389, U.S. Pat. No. 8,217,149, and US 2013/034559, which are incorporated herein by reference.

Anti-PD-L1 antibodies described in WO 2010/077634 A1 and US 8,217,149 may be used in the methods described herein. In some aspects, the anti-PD-L1 antibody comprises a heavy chain variable region sequence of SEQ ID NO: 3 and/or a light chain variable region sequence of SEQ ID NO: 4. In a still further aspect, provided is an isolated anti-PD-L1 antibody comprising a heavy chain variable region and/or a light chain variable region sequence, wherein:

(a) the heavy chain sequence has at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to the heavy chain sequence:
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWVRQAPGKGLEWVAWISPYGGSTYYADSVKGRF
TISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGTLVTVSS (SEQ ID NO: 3), and

(b) the light chain sequence has at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to the light chain sequence:
DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCQQYLYHPATFGQGTKVEIKR (SEQ ID NO: 4).

In one aspect, the anti-PD-L1 antibody comprises a heavy chain variable region comprising an HVR-H1, HVR-H2 and HVR-H3 sequence, wherein:

(a) the HVR-H1 sequence is GFTFSX$_1$SWIH (SEQ ID NO: 5);

(b) the HVR-H2 sequence is AWIX$_2$PYGGSX$_3$YYADSVKG (SEQ ID NO: 6);

(c) the HVR-H3 sequence is RHWPGGFDY (SEQ ID NO: 7);

further wherein: X$_1$ is D or G; X$_2$ is S or L; X$_3$ is T or S. In one specific aspect, X$_1$ is D; X$_2$ is S and X$_3$ is T. In another aspect, the polypeptide further comprises variable region heavy chain framework sequences juxtaposed between the HVRs according to the formula: (FR-H1)-(HVR-H1)-(FR-H2)-(HVR-H2)-(FR-H3)-(HVR-H3)-(FR-H4). In yet another aspect, the framework sequences are derived from human consensus framework sequences. In a further aspect, the framework sequences are VH subgroup III consensus framework. In a still further aspect, at least one of the framework sequences is the following:

FR-H1 is EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO: 8)

FR-H2 is WVRQAPGKGLEWV (SEQ ID NO: 9)

FR-H3 is RFTISADTSKNTAYLQMNSLRAEDTAVYYCAR (SEQ ID NO: 10)

FR-H4 is WGQGTLVTVSS (SEQ ID NO: 11).

In a still further aspect, the heavy chain polypeptide is further combined with a variable region light chain comprising an HVR-L1, HVR-L2 and HVR-L3, wherein:

(a) the HVR-L1 sequence is RASQX$_4$X$_5$X$_6$TX$_7$X$_8$A (SEQ ID NO: 12);

(b) the HVR-L2 sequence is SASX$_9$LX$_{10}$S, (SEQ ID NO: 13);

(c) the HVR-L3 sequence is QQX$_{11}$X$_{12}$X$_{13}$X$_{14}$PX$_{15}$T (SEQ ID NO: 14);

wherein: X$_4$ is D or V; X$_5$ is V or I; X$_6$ is S or N; X$_7$ is A or F; X$_8$ is V or L; X$_9$ is F or T; X$_{10}$ is Y or A; X$_{11}$ is Y, G, F, or S; X$_{12}$ is L, Y, F or W; X$_{13}$ is Y, N, A, T, G, F or I; X$_{14}$ is H, V, P, T or I; X$_{15}$ is A, W, R, P or T. In a still further aspect, X$_4$ is D; X$_5$ is V; X$_6$ is S; X$_7$ is A; X$_8$ is V; X$_9$ is F; X$_{10}$ is Y; X$_{11}$ is Y; X$_{12}$ is L; X$_{13}$ is Y; X$_{14}$ is H; X$_{15}$ is A.

In a still further aspect, the light chain further comprises variable region light chain framework sequences juxtaposed between the HVRs according to the formula: (FR-L1)-(HVR-L1)-(FR-L2)-(HVR-L2)-(FR-L3)-(HVR-L3)-(FR-L4). In a still further aspect, the framework sequences are derived from human consensus framework sequences. In a still further aspect, the framework sequences are VL kappa I consensus framework. In a still further aspect, at least one of the framework sequence is the following:

FR-L1 is DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 15)

FR-L2 is WYQQKPGKAPKLLIY (SEQ ID NO: 16)

FR-L3 is GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 17)

FR-L4 is FGQGTKVEIKR (SEQ ID NO: 18).

In another aspect, provided is an isolated anti-PD-L1 antibody or antigen binding fragment comprising a heavy chain and a light chain variable region sequence, wherein:

(a) the heavy chain comprises an HVR-H1, HVR-H2 and HVR-H3, wherein further:

(i) the HVR-H1 sequence is GFTFSX$_1$SWIH; (SEQ ID NO: 5)

(ii) the HVR-H2 sequence is AWIX$_2$PYGGSX$_3$YYADSVKG (SEQ ID NO: 6)

(iii) the HVR-H3 sequence is RHWPGGFDY, and (SEQ ID NO: 7)

(b) the light chain comprises an HVR-L1, HVR-L2 and HVR-L3, wherein further:

(i) the HVR-L1 sequence is $RASQX_4X_5X_6TX_7X_8A$ (SEQ ID NO: 12)

(ii) the HVR-L2 sequence is $SASX_9LX_{10}S$; and (SEQ ID NO: 13)

(iii) the HVR-L3 sequence is $QQX_{11}X_{12}X_{13}X_{14}PX_{15}T$; (SEQ ID NO: 14)

wherein: X_1 is D or G; X_2 is S or L; X_3 is T or S; X_4 is D or V; X_5 is V or I; X_6 is S or N; X_7 is A or F; X_8 is V or L; X_9 is F or T; X_{10} is Y or A; X_{11} is Y, G, F, or S; X_{12} is L, Y, F or W; X_{13} is Y, N, A, T, G, F or I; X_{14} is H, V, P, T or I; X_{15} is A, W, R, P or T. In a specific aspect, X_1 is D; X_2 is S and X_3 is T. In another aspect, X_4 is D; X_5 is V; X_6 is S; X_7 is A; X_8 is V; X_9 is F; X_{10} is Y; X_{11} is Y; X_{12} is L; X_{13} is Y; X_{14} is H; X_{15} is A. In yet another aspect, X_1 is D; X_2 is S and X_3 is T, X_4 is D; X_5 is V; X_6 is S; X_7 is A; X_8 is V; X_9 is F; X_{10} is Y; X_{11} is Y; X_{12} is L; X_{13} is Y; X_{14} is H and X_{15} is A.

In a further aspect, the heavy chain variable region comprises one or more framework sequences juxtaposed between the HVRs as: (FR-H1)-(HVR-H1)-(FR-H2)-(HVR-H2)-(FR-H3)-(HVR-H3)-(FR-H4), and the light chain variable regions comprises one or more framework sequences juxtaposed between the HVRs as: (FR-L1)-(HVR-L1)-(FR-L2)-(HVR-L2)-(FR-L3)-(HVR-L3)-(FR-L4). In a still further aspect, the framework sequences are derived from human consensus framework sequences. In a still further aspect, the heavy chain framework sequences are derived from a Kabat subgroup I, II, or III sequence. In a still further aspect, the heavy chain framework sequence is a VH subgroup III consensus framework. In a still further aspect, one or more of the heavy chain framework sequences are set forth as SEQ ID NOs: 8, 9, 10, and 11. In a still further aspect, the light chain framework sequences are derived from a Kabat kappa I, II, II or IV subgroup sequence. In a still further aspect, the light chain framework sequences are VL kappa I consensus framework. In a still further aspect, one or more of the light chain framework sequences are set forth as SEQ ID NOs: 15, 16, 17, and 18.

In a still further specific aspect, the antibody further comprises a human or murine constant region. In a still further aspect, the human constant region is selected from the group consisting of IgG1, IgG2, IgG2, IgG3, and IgG4. In a still further specific aspect, the human constant region is IgG1. In a still further aspect, the murine constant region is selected from the group consisting of IgG1, IgG2A, IgG2B, and IgG3. In a still further aspect, the murine constant region in IgG2A. In a still further specific aspect, the antibody has reduced or minimal effector function. In a still further specific aspect, the minimal effector function results from an "effector-less Fc mutation" or aglycosylation mutation. In still a further aspect, the effector-less Fc mutation is an N297A or D265A/N297A substitution in the constant region.

In yet another aspect, provided is an anti-PD-L1 antibody comprising a heavy chain and a light chain variable region sequence, wherein:

(a) the heavy chain further comprises an HVR-H1, HVR-H2 and an HVR-H3 sequence having at least 85% sequence identity to GFTFSDSWIH (SEQ ID NO: 19), AWISPYGGSTYYADSVKG (SEQ ID NO: 20) and RHWPGGFDY (SEQ ID NO: 21), respectively, or

(b) the light chain further comprises an HVR-L1, HVR-L2 and an HVR-L3 sequence having at least 85% sequence identity to RASQDVSTAVA (SEQ ID NO: 22), SASFLYS (SEQ ID NO: 23) and QQYLYHPAT (SEQ ID NO: 24), respectively.

In a specific aspect, the sequence identity is 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100%.

In another aspect, the heavy chain variable region comprises one or more framework sequences juxtaposed between the HVRs as: (FR-H1)-(HVR-H1)-(FR-H2)-(HVR-H2)-(FR-H3)-(HVR-H3)-(FR-H4), and the light chain variable regions comprises one or more framework sequences juxtaposed between the HVRs as: (FR-L1)-(HVR-L1)-(FR-L2)-(HVR-L2)-(FR-L3)-(HVR-L3)-(FR-L4). In yet another aspect, the framework sequences are derived from human consensus framework sequences. In a still further aspect, the heavy chain framework sequences are derived from a Kabat subgroup I, II, or III sequence. In a still further aspect, the heavy chain framework sequence is a VH subgroup III consensus framework. In a still further aspect, one or more of the heavy chain framework sequences are set forth as SEQ ID NOs: 8, 9, 10, and 11. In a still further aspect, the light chain framework sequences are derived from a Kabat kappa I, II, II, or IV subgroup sequence. In a still further aspect, the light chain framework sequences are VL kappa I consensus framework. In a still further aspect, one or more of the light chain framework sequences are set forth as SEQ ID NOs: 15, 16, 17, and 18.

In a further aspect, the heavy chain variable region comprises one or more framework sequences juxtaposed between the HVRs as: (FR-H1)-(HVR-H1)-(FR-H2)-(HVR-H2)-(FR-H3)-(HVR-H3)-(FR-H4), and the light chain variable regions comprises one or more framework sequences juxtaposed between the HVRs as: (FR-L1)-(HVR-L1)-(FR-L2)-(HVR-L2)-(FR-L3)-(HVR-L3)-(FR-L4). In a still further aspect, the framework sequences are derived from human consensus framework sequences. In a still further aspect, the heavy chain framework sequences are derived from a Kabat subgroup I, II, or III sequence. In a still further aspect, the heavy chain framework sequence is a VH subgroup III consensus framework. In a still further aspect, one or more of the heavy chain framework sequences is the following:

FR-H1	EVQLVESGGGLVQPGGSLRLSCAASGFTFS	(SEQ ID NO: 27)
FR-H2	WVRQAPGKGLEWVA	(SEQ ID NO: 28)
FR-H3	RFTISADTSKNTAYLQMNSLRAEDTAVYYCAR	(SEQ ID NO: 10)
FR-H4	WGQGTLVTVSS	(SEQ ID NO: 11).

In a still further aspect, the light chain framework sequences are derived from a Kabat kappa I, II, II or IV subgroup sequence. In a still further aspect, the light chain framework sequences are VL kappa I consensus framework. In a still further aspect, one or more of the light chain framework sequences is the following:

FR-L1	DIQMTQSPSSLSASVGDRVTITC	(SEQ ID NO: 15)
FR-L2	WYQQKPGKAPKLLIY	(SEQ ID NO: 16)
FR-L3	GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC	(SEQ ID NO: 17)
FR-L4	FGQGTKVEIK	(SEQ ID NO: 26).

In a still further specific aspect, the antibody further comprises a human or murine constant region. In a still further aspect, the human constant region is selected from the group consisting of IgG1, IgG2, IgG2, IgG3, and IgG4. In a still further specific aspect, the human constant region is IgG1. In a still further aspect, the murine constant region is selected from the group consisting of IgG1, IgG2A, IgG2B, and IgG3. In a still further aspect, the murine constant region in IgG2A. In a still further specific aspect, the antibody has reduced or minimal effector function. In a still further specific aspect, the minimal

effector function results from an "effector-less Fc mutation" or aglycosylation. In still a further aspect, the effector-less Fc mutation is an N297A or D265A/N297A substitution in the constant region.

In yet another aspect, provided is an anti-PD-L1 antibody comprising a heavy chain and a light chain variable region sequence, wherein:

(c) the heavy chain further comprises an HVR-H1, HVR-H2 and an HVR-H3 sequence having at least 85% sequence identity to GFTFSDSWIH (SEQ ID NO: 19), AWISPYGGSTYYADSVKG (SEQ ID NO: 20) and RHWPGGFDY (SEQ ID NO: 21), respectively, and/or

(d) the light chain further comprises an HVR-L1, HVR-L2 and an HVR-L3 sequence having at least 85% sequence identity to RASQDVSTAVA (SEQ ID NO: 22), SASFLYS (SEQ ID NO: 23) and QQYLYHPAT (SEQ ID NO: 24), respectively.

In a specific aspect, the sequence identity is 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100%.

In another aspect, the heavy chain variable region comprises one or more framework sequences juxtaposed between the HVRs as: (FR-H1)-(HVR-H1)-(FR-H2)-(HVR-H2)-(FR-H3)-(HVR-H3)-(FR-H4), and the light chain variable regions comprises one or more framework sequences juxtaposed between the HVRs as: (FR-L1)-(HVR-L1)-(FR-L2)-(HVR-L2)-(FR-L3)-(HVR-L3)-(FR-L4). In yet another aspect, the framework sequences are derived from human consensus framework sequences. In a still further aspect, the heavy chain framework sequences are derived from a Kabat subgroup I, II, or III sequence. In a still further aspect, the heavy chain framework sequence is a VH subgroup III consensus framework. In a still further aspect, one or more of the heavy chain framework sequences are set forth as SEQ ID NOs: 8, 9, 10, and WGQGTLVTVSSASTK (SEQ ID NO: 29).

In a still further aspect, the light chain framework sequences are derived from a Kabat kappa I, II, II or IV subgroup sequence. In a still further aspect, the light chain framework sequences are VL kappa I consensus framework. In a still further aspect, one or more of the light chain framework sequences are set forth as SEQ ID NOs: 15, 16, 17, and 18. In a still further specific aspect, the antibody further comprises a human or murine constant region. In a still further aspect, the human constant region is selected from the group consisting of IgG1, IgG2, IgG2, IgG3, and IgG4. In a still further specific aspect, the human constant region is IgG1. In a still further aspect, the murine constant region is selected from the group consisting of IgG1, IgG2A, IgG2B, and IgG3. In a still further aspect, the murine constant region in IgG2A. In a still further specific aspect, the antibody has reduced or minimal effector function. In a still further specific aspect, the minimal effector function results from an "effector-less Fc mutation" or aglycosylation. In still a further aspect, the effector-less Fc mutation is an N297A or D265A/N297A substitution in the constant region.

In a still further aspect, provided is an isolated anti-PD-L1 antibody comprising a heavy chain and a light chain variable region sequence, wherein:

(a) the heavy chain variable region sequence has at least 85% sequence identity to the sequence:

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWVRQAPGKGLEWVAWISPYGGSTYYADSVKGRF TISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGTLVTVSSASTK (SEQ ID NO: 25), or

(b) the light chain variable region sequence has at least 85% sequence identity to the sequence:
DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCQQYLYHPATFGQGTKVEIKR (SEQ ID NO: 4).

In some aspects, provided is an isolated anti-PD-L1 antibody comprising a heavy chain and a light chain variable region sequence, wherein the light chain variable region sequence has at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to the amino acid sequence of SEQ ID NO: 4. In some aspects, provided is an isolated anti-PD-L1 antibody comprising a heavy chain and a light chain variable region sequence, wherein the heavy chain variable region sequence has at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to the amino acid sequence of SEQ ID NO: 25. In some aspects, provided is an isolated anti-PD-L1 antibody comprising a heavy chain and a light chain variable region sequence, wherein the light chain variable region sequence has at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO: 4 and the heavy chain variable region sequence has at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO: 25. In some aspects, one, two, three, four, or five amino acid residues at the N-terminal of the heavy and/or light chain may be deleted, substituted or modified.

In a still further aspect, provided is an isolated anti-PD-L1 antibody comprising a heavy chain and a light chain sequence, wherein:

(a) the heavy chain sequence has at least 85% sequence identity to the heavy chain sequence:
EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHWVRQAPGKGLEWVAWISPYGGSTYYADSVKGRF
TISADTSKNTAYLQMNSLRAEDTAVYYCARRHWPGGFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTS
GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKP
SNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE
PQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 30), and/or

(b) the light chain sequences has at least 85% sequence identity to the light chain sequence:
DIQMTQSPSSLSASVGDRVTITCRASQDVSTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCQQYLYHPATFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP
REAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN
RGEC (SEQ ID NO: 31).

In some aspects, provided is an isolated anti-PD-L1 antibody comprising a heavy chain and a light chain sequence, wherein the light chain sequence has at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 31. In some aspects, provided is an isolated anti-PD-L1 antibody comprising a heavy chain and a light chain sequence, wherein the heavy chain sequence has at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 30. In some aspects, provided is an isolated anti-PD-L1 antibody comprising a heavy chain and a light chain sequence, wherein the light chain sequence has at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 31 and the heavy chain sequence has at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 30.

In some aspects, the isolated anti-PD-L1 antibody is aglycosylated. Glycosylation of antibodies is typically either N-linked or O-linked. N-linked refers to the attachment of the carbohydrate moiety to the side chain of an asparagine residue. The tripeptide sequences asparagine-X-serine and asparagine-X-threonine, where X is any amino acid except proline, are the recognition sequences for enzymatic attachment of the carbohydrate moiety to the asparagine side chain. Thus, the presence of either of these tripeptide sequences in a polypeptide creates a potential glycosylation site. O-linked glycosylation refers to the attachment of one of the sugars N-aceylgalactosamine, galactose, or xylose to a hydroxyamino acid, most commonly serine or threonine, although 5-hydroxyproline or 5-hydroxylysine may also be used. Removal of glycosylation sites form an antibody is conveniently accomplished by altering the amino acid sequence such that one of the above-described tripeptide sequences (for N-linked glycosylation sites) is removed. The alteration may be made by substitution of an asparagine, serine or threonine residue within the glycosylation site another amino acid residue (e.g., glycine, alanine or a conservative substitution).

In any of the aspects herein, the isolated anti-PD-L1 antibody can bind to a human PD-L1, for example a human PD-L1 as shown in UniProtKB/Swiss-Prot Accession No.Q9NZQ7.1, or a variant thereof.

In a still further aspect, provided is an isolated nucleic acid encoding any of the antibodies described herein. In some aspects, the nucleic acid further comprises a vector suitable for expression of the nucleic acid encoding any of the previously described anti-PD-L1 antibodies. In a still further specific aspect, the vector is in a host cell suitable for expression of the nucleic acid. In a still further specific aspect, the host cell is a eukaryotic cell or a prokaryotic cell. In a still further specific aspect, the eukaryotic cell is a mammalian cell, such as Chinese hamster ovary (CHO) cell.

The antibody or antigen binding fragment thereof, may be made using methods known in the art, for example, by a process comprising culturing a host cell containing nucleic acid encoding any of the

previously described anti-PD-L1 antibodies or antigen-binding fragments in a form suitable for expression, under conditions suitable to produce such antibody or fragment, and recovering the antibody or fragment.

It is expressly contemplated that such PD-L1 axis binding antagonist antibodies (e.g., anti-PD-L1 antibodies, anti-PD-1 antibodies, and anti-PD-L2 antibodies), or other antibodies described herein for use in any of the aspects enumerated above may have any of the features, singly or in combination.

In some aspects, the immune checkpoint inhibitor is an antagonist directed against a co-inhibitory molecule (e.g., a CTLA-4 antagonist (e.g., an anti-CTLA-4 antibody), a TIM-3 antagonist (e.g., an anti-TIM-3 antibody), or a LAG-3 antagonist (e.g., an anti-LAG-3 antibody)), or any combination thereof.

In some aspects, the immune checkpoint inhibitor is an antagonist directed against TIGIT (e.g., an anti-TIGIT antibody). Exemplary anti-TIGIT antibodies are described in US Patent Application Publication No. 2018/0186875 and in International Patent Application Publication No. WO 2017/053748, which are incorporated herein by reference in their entirety.

F. Methods of delivery

The compositions utilized in the methods described herein (e.g., PD-L1 axis binding antagonists) can be administered by any suitable method, e.g., as described in Section V*B* herein.

Immune checkpoint inhibitors (e.g., an immune checkpoint inhibitor described in Section VI*E* herein, e.g., an antibody, binding polypeptide, and/or small molecule) described herein (and any additional therapeutic agent) may be formulated, dosed, and administered in a fashion consistent with good medical practice. Factors for consideration in this context include the particular disorder being treated, the particular mammal being treated, the clinical condition of the individual, the cause of the disorder, the site of delivery of the agent, the method of administration, the scheduling of administration, and other factors known to medical practitioners. The immune checkpoint inhibitor need not be, but is optionally formulated with and/or administered concurrently with one or more agents currently used to prevent or treat the disorder in question. The effective amount of such other agents depends on the amount of the immune checkpoint inhibitor present in the formulation, the type of disorder or treatment, and other factors discussed above. These are generally used in the same dosages and with administration routes as described herein, or about from 1 to 99% of the dosages described herein, or in any dosage and by any route that is empirically/clinically determined to be appropriate.

For the treatment of a cancer, e.g., a cancer described in Section VI*D* herein e.g., a urinary tract cancer, the appropriate dosage of an immune checkpoint inhibitor, e.g., a PD-L1 axis binding antagonist, an antagonist directed against a co-inhibitory molecule (e.g., a CTLA-4 antagonist (e.g., an anti-CTLA-4 antibody), a TIM-3 antagonist (e.g., an anti-TIM-3 antibody), or a LAG-3 antagonist (e.g., an anti-LAG-3 antibody)), or any combination thereof, described herein (when used alone or in combination with one or more other additional therapeutic agents) will depend on the type of disease to be treated, the severity and course of the disease, whether the PD-L1 axis binding antagonist is administered for preventive or therapeutic purposes, previous therapy, the patient's clinical history and response to the PD-L1 axis binding antagonist, and the discretion of the attending physician. The immune checkpoint inhibitor is suitably administered to the individual at one time or over a series of treatments. One typical daily dosage might range from about 1 μg/kg to 100 mg/kg or more, depending on the factors mentioned

above. For repeated administrations over several days or longer, depending on the condition, the treatment would generally be sustained until a desired suppression of disease symptoms occurs. Such doses may be administered intermittently, e.g., every week or every three weeks (e.g., such that the individual receives, for example, from about two to about twenty, or e.g., about six doses of the immune checkpoint inhibitor). An initial higher loading dose, followed by one or more lower doses, may be administered. However, other dosage regimens may be useful. The progress of this therapy is easily monitored by conventional techniques and assays.

For example, as a general proposition, the therapeutically effective amount of an immune checkpoint inhibitor, for example, a PD-L1 axis binding antagonist antibody, an anti-CTLA-4 antibody, an anti-TIM-3 antibody, or an anti-LAG-3 antibody, administered to human will be in the range of about 0.01 to about 50 mg/kg of patient body weight, whether by one or more administrations. In some aspects, the antibody used is about 0.01 mg/kg to about 45 mg/kg, about 0.01 mg/kg to about 40 mg/kg, about 0.01 mg/kg to about 35 mg/kg, about 0.01 mg/kg to about 30 mg/kg, about 0.01 mg/kg to about 25 mg/kg, about 0.01 mg/kg to about 20 mg/kg, about 0.01 mg/kg to about 15 mg/kg, about 0.01 mg/kg to about 10 mg/kg, about 0.01 mg/kg to about 5 mg/kg, or about 0.01 mg/kg to about 1 mg/kg administered daily, weekly, every two weeks, every three weeks, or monthly, for example. In some aspects, the antibody is administered at 15 mg/kg. However, other dosage regimens may be useful. In one aspect, an anti-PD-L1 antibody described herein is administered to a human at a dose of about 100 mg, about 200 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg, about 1100 mg, about 1200 mg, about 1300 mg, about 1400 mg, about 1500 mg, about 1600 mg, about 1700 mg, or about 1800 mg on day 1 of 21-day cycles (every three weeks, q3w). In some aspects, anti-PD-L1 antibody MPDL3280A (atezolizumab) is administered at 1200 mg intravenously every three weeks (q3w). In some aspects, anti-PD-L1 antibody MPDL3280A (atezolizumab) is administered at 840 mg intravenously every two weeks (q2w). In some aspects, anti-PD-L1 antibody MPDL3280A (atezolizumab) is administered at 1680 mg intravenously every four weeks (q4w). The dose may be administered as a single dose or as multiple doses (e.g., 2 or 3 doses), such as infusions. The dose of the antibody administered in a combination treatment may be reduced as compared to a single treatment. The progress of this therapy is easily monitored by conventional techniques.

In some aspects, the individual has not been previously treated for the urinary tract cancer. In some aspects, the individual has previously been treated for the urinary tract cancer (e.g., a locally advanced or metastatic urinary tract carcinoma, e.g., a urothelial or non-urothelial carcinoma). In some aspects, the individual has previously been treated for the urinary tract cancer with a therapy comprising platinum (e.g., a therapy comprising gemcitabine and cisplatin; a therapy comprising gemcitabine and carboplatin; or a therapy comprising methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC)). In some aspects, the individual has previously been treated for the urinary tract cancer with a therapy that does not comprise platinum. In some aspects, the individual has not been previously administered an immune checkpoint inhibitor.

G. Additional therapeutic agents

In some aspects, the PD-L1 axis binding antagonist is used with one or more additional therapeutic agents, e.g., a combination therapy. In some aspects, the composition comprising the PD-L1 axis binding antagonist further comprises the additional therapeutic agent. In another aspect, the additional therapeutic agent is delivered in a separate composition. In some aspects, the one or more additional therapeutic agents comprise an immunomodulatory agent, an anti-neoplastic agent, a chemotherapeutic agent, a growth inhibitory agent, an anti-angiogenic agent, a radiation therapy, a cytotoxic agent, a cell-based therapy, or a combination thereof.

Combination therapies as described above encompass combined administration (wherein two or more therapeutic agents are included in the same or separate formulations) and separate administration (wherein administration of a PD-L1 axis binding antagonist can occur prior to, simultaneously, and/or following, administration of the additional therapeutic agent or agents). In one aspect, administration of a PD-L1 axis binding antagonist and administration of an additional therapeutic agent occur within about one month, or within about one, two or three weeks, or within about one, two, three, four, five, or six days, of each other.

VII. METHODS OF TREATMENT COMPRISING AGONISTS OF CD177 ACTIVITY

A. Methods of treatment

In some aspects, the invention comprises a method of treating an individual having a cancer comprising administering to the individual a treatment comprising an effective amount of an agonist of CD177 activity.

In some aspects, the invention comprises a method of identifying an individual having a cancer who may benefit from a treatment comprising an agonist of CD177 activity, the method comprising determining an expression level of podoplanin (PDPN) in a sample from the individual, wherein an expression level of PDPN in the sample that is above a reference PDPN expression level identifies the individual as one who may benefit from a treatment comprising an agonist of CD177 activity.

In some aspects, the invention comprises a method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of PDPN in a sample from the individual, wherein an expression level of PDPN in the sample that is above a reference PDPN expression level identifies the individual as one who may benefit from a treatment comprising an agonist of CD177 activity.

In some aspects, the individual has an expression level of PDPN in the sample that is above a reference PDPN expression level and the method further comprises administering to the individual an effective amount of an agonist of CD177 activity.

In some aspects, the invention comprises a method of treating an individual having a cancer, the method comprising (a) determining an expression level of PDPN in a sample from the individual, wherein the expression level of PDPN in the sample is above a reference PDPN expression level; and (b) administering to the individual an effective amount of an agonist of CD177 activity.

In some aspects, the invention comprises a method of treating an individual having a cancer, the method comprising administering to the individual an effective amount of an agonist of CD177 activity,

wherein the expression level of PDPN in a sample from the individual has been determined to be above a reference PDPN expression level.

In some aspects, the CD177 activity is inhibition of PDPN.

In some aspects, the sample from the individual is a tumor tissue sample or a tumor fluid sample, e.g., a formalin-fixed and paraffin-embedded (FFPE) sample, an archival sample, a fresh sample, or a frozen sample.

In some aspects, the expression level of PDPN in the sample is a protein expression level of PDPN or an RNA expression level of PDPN. In some aspects, the expression level of PDPN in the sample is an RNA expression level of PDPN. In some aspects, the RNA expression level of PDPN is determined by *in situ* hybridization (ISH), RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, FISH, or a combination thereof.

In some aspects, the benefit comprises an extension in the individual's recurrence-free survival (RFS) as compared to treatment without the agonist of CD177 activity. In other aspects, the benefit may comprise, e.g., an extension in the individual's overall survival (OS), an increase in time to recurrence, or a reduced duration of treatment as compared to treatment without the agonist of CD177 activity

B. Reference expression levels

In some aspects, the reference PDPN expression level is an expression level of PDPN in a population of individuals having a cancer, e.g., a population of individuals having a colorectal cancer (CRC).

In some aspects, the reference PDPN expression level is the 33rd percentile, the 35th percentile, the 40th percentile, the 45th percentile, the 50th percentile, the 55th percentile, the 60th percentile, the 65th percentile, the 66th percentile, the 70th percentile, the 75th percentile, the 80th percentile, the 85th percentile, the 90th percentile, the 95th percentile, or the 99th percentile of expression levels in the population of individuals having a cancer.

In some aspects, the reference PDPN expression level is the 50th percentile of expression levels in the population of individuals having a cancer.

In some aspects, the reference PDPN expression level is the median of expression levels in the population of individuals having a cancer.

In some aspects, the reference PDPN expression level is the 33rd percentile of expression levels in the population of individuals having a cancer.

In some aspects, the reference PDPN expression level is the 66th percentile of expression levels in the population of individuals having a cancer.

In some aspects, the PDPN expression levels of the population of individuals are divided into tertiles, and the reference PDPN expression level is the lowest value in the second tertile.

In some aspects, the PDPN expression levels of the population of individuals are divided into tertiles, and the reference PDPN expression level is the lowest value in the third tertile.

In some aspects, the reference PDPN expression level is a pre-assigned PDPN expression level.

C. Cancers

In some aspects, the cancer is a CRC, a squamous cell carcinoma of the head and neck, or a glioma.

In some aspects, the individual has a colorectal cancer (CRC). In some aspects, the individual has had surgical resection of a CRC. In some aspects, the CRC of the individual is a stage I, stage II, or stage III, or stage IV CRC, e.g., a stage II CRC or a stage IV CRC, according to the TNM classification system at the onset of treatment. In some aspects, the CRC of the individual is a left-sided tumor, i.e., a tumor occurring in the distal colon (e.g., the distal third of the transverse colon, the splenic flexure the descending colon, the sigmoid colon, or the rectum) or a right-sided tumor, i.e., a tumor occurring in the proximal colon (e.g., the proximal two-thirds of the transverse colon, the ascending colon, and the cecum).

In some aspects, the agonist of CD177 activity results in an increase in the binding of PDPN and CD177 relative to binding of the two proteins in the absence of the agonist.

In some aspects, the agonist of CD177 activity results in a change in a downstream activity of PDPN relative to the downstream activity in the absence of the agonist of CD177 activity. In some aspects, the change in the downstream activity is a decrease in tumor growth or a decrease in cancer-associated fibroblast (CAF) contractility.

D. Agonists of CD177 activity

In some aspects, the agonist of CD177 activity is a small molecule, an antibody or antigen-binding fragment thereof, a peptide, or a mimic.

In some aspects, the agonist of CD177 activity is a peptide, e.g., a CD177 peptide, e.g., an extracellular domain of CD177. The peptide may be multimerized, e.g., dimerized, trimerized, tetramerized, or pentamerized. In some aspects, the peptide is tetramerized, e.g., tetramerized using streptavidin.

In some aspects, the agonist of CD177 activity is an antibody or antigen-binding fragment thereof. In some aspects, the antibody or antigen-binding fragment thereof binds PDPN, e.g., is an antagonist antibody or antigen-binding fragment thereof that binds PDPN. In some aspects, the antibody or antigen-binding fragment thereof binds CD177, e.g., is an agonist antibody or antigen-binding fragment thereof that binds CD177.

In some aspects, the antigen-binding fragment is a bis-Fab, an Fv, a Fab, a Fab'-SH, a $F(ab')_2$, a diabody, a linear antibody, an scFv, an ScFab, a VH domain, or a VHH domain.

Agonists of CD177 activity may be identified, e.g., using the methods for identifying modulation of an interaction or the methods for identifying a change in a downstream activity of a protein described in Sections III*A* and III*B* herein. For example, methods including surface plasmon resonance (SPR), biolayer interferometry (BLI), ELISA, or extracellular or cell surface interactions, as described herein, could be used to identify a modulator that increases the interaction between CD177 and PDPN, i.e., an agonist of CD177 activity.

In aspects in which the agonist of CD177 activity is an antibody (e.g., a CD177 agonist antibody or a PDPN antagonist antibody), the antibody may be isolated by screening combinatorial libraries for antibodies with the desired activity or activities. For example, a variety of methods are known in the art

for generating phage display libraries and screening such libraries for antibodies possessing the desired binding characteristics. Such methods are reviewed, e.g., in Hoogenboom et al. in *Methods in Molecular Biology* 178:1-37 (O'Brien et al., ed., Human Press, Totowa, NJ, 2001) and further described, e.g., in the McCafferty et al., *Nature* 348:552-554; Clackson et al., *Nature* 352: 624-628 (1991); Marks et al., *J. Mol. Biol.* 222: 581-597 (1992); Marks and Bradbury, in *Methods in Molecular Biology* 248:161-175 (Lo, ed., Human Press, Totowa, NJ, 2003); Sidhu et al., *J. Mol. Biol.* 338(2): 299-310 (2004); Lee et al., *J. Mol. Biol.* 340(5): 1073-1093 (2004); Fellouse, *Proc. Natl. Acad. Sci. USA* 101(34): 12467-12472 (2004); and Lee et al., *J. Immunol. Methods* 284(1-2): 119-132(2004).

In certain phage display methods, repertoires of VH and VL genes are separately cloned by polymerase chain reaction (PCR) and recombined randomly in phage libraries, which can then be screened for antigen-binding phage as described in Winter et al., *Ann. Rev. Immunol.*, 12: 433-455 (1994). Phage typically display antibody fragments, either as single-chain Fv (scFv) fragments or as Fab fragments. Libraries from immunized sources provide high-affinity antibodies to the immunogen without the requirement of constructing hybridomas. Alternatively, the naive repertoire can be cloned (e.g., from human) to provide a single source of antibodies to a wide range of non-self and also self antigens without any immunization as described by Griffiths et al., *EMBO J,* 12: 725-734 (1993). Finally, naive libraries can also be made synthetically by cloning unrearranged V-gene segments from stem cells, and using PCR primers containing random sequence to encode the highly variable CDR3 regions and to accomplish rearrangement *in vitro*, as described by Hoogenboom and Winter, *J. Mol. Biol.*, 227: 381-388 (1992). Patent publications describing human antibody phage libraries include, for example: US Patent No. 5,750,373, and US Patent Publication Nos. 2005/0079574, 2005/0119455, 2005/0266000, 2007/0117126, 2007/0160598, 2007/0237764, 2007/0292936, and 2009/0002360.

E. Methods of delivery

The compositions utilized in the methods described herein (e.g., agonists of CD177 activity) can be administered by any suitable method, e.g., as described in Section V*B* herein.

F. Additional therapeutic agents

In some aspects, the agonist of CD177 activity is used with one or more additional therapeutic agents, e.g., a combination therapy, e.g., as described in Section VI*F* herein.

VIII. ARTICLES OF MANUFACTURE

In another aspect of the invention, an article of manufacture containing materials useful for the treatment, prevention, and/or diagnosis of the disorders described above is provided.

In some aspects, the invention comprises a solid surface or a set of solid surfaces (e.g., a multi-well plate or a set of multi-well plates) comprising a number of locations, each of the locations comprising a unique polypeptide from a collection of polypeptides, wherein each polypeptide comprises an extracellular domain, a tag, and an anchor, and wherein the collection of polypeptides comprises the extracellular domains of all or a subset of the proteins of Table 7. Exemplary collections of polypeptides are described in Section II*B*.

In some aspects, the invention comprises a solid surface or a set of solid surfaces (e.g., a multi-well plate or a set of multi-well plates) comprising a number of locations, each of the locations comprising a plasmid encoding a unique polypeptide as described above. In some aspects, the solid surface or set of solid surfaces has been stamped with the polypeptide.

In some aspects, the invention comprises a solid surface or a set of solid surfaces (e.g., a multi-well plate or a set of multi-well plates), each of the locations comprising a unique polypeptide from a collection of polypeptides, wherein the collection of polypeptides comprises the extracellular domains of all or a subset of the proteins of Table 7, wherein said polypeptides are immobilized to one or more solid surfaces, wherein each of the one or more of said polypeptides is immobilized to a distinct location (e.g., a distinctly interrogatable location, e.g., a location that can be interrogated distinctly by the methods described herein) on said one or more solid surfaces. The distinct location may be an area on a surface where a cell line is plated, e.g., a well.

In some aspects, the solid surface or set of solid surfaces together comprise at least 965 locations, each of the locations comprising a unique polypeptide from a collection of polypeptides, wherein each polypeptide comprises an extracellular domain, a tag, and an anchor, and wherein the collection of polypeptides comprises the extracellular domains of at least 81% of the proteins of Table 7.

In some aspects, the solid surface or set of solid surfaces comprises at least 100, at least 150, at least 200, at least 250, at least 300, at least 350, at least 400, at least 450, at least 500, at least 550, at least 600, at least 650, at least 700, at least 750, at least 800, at least 850, at least 900, at least 950, at least 1000, at least 1050, at least 1100, at least 1150, or 1195 locations, e.g., comprises 100-150, 150-200, 200-250, 250-300, 300-350, 350-400, 400-450, 450-500, 500-550, 550-600, 600-650, 650-700, 750-800, 800-850, 850-900, 900-950, 950-1000, 1000-1050, 1050-1100, 1100-1150, or 1195 locations, each comprising a unique polypeptide from the collection of polypeptides or a plasmid encoding such a polypeptide.

In some aspects, the collection of polypeptides comprises the extracellular domains of at least 8%, at least 9%, at least 10%, at least 11%, at least 12%, at least 13%, at least 14%, at least 15%, at least 16%, at least 17%, at least 18%, at least 19%, at least 20%, at least 21%, at least 22%, at least 23%, at least 24%, at least 25%, at least 26%, at least 27%, at least 28%, at least 29%, at least 30%, at least 31%, at least 32%, at least 33%, at least 34%, at least 35%, at least 36%, at least 37%, at least 38%, at least 39%, at least 40%, at least 41%, at least 42%, at least 43%, at least 44%, at least 45%, at least 46%, at least 47%, at least 48%, at least 49%, at least 50%, at least 51%, at least 52%, at least 53%, at least 54%, at least 55%, at least 56%, at least 57%, at least 58%, at least 59%, at least 60%, at least 61%, at least 62%, at least 63%, at least 64%, at least 65%, at least 66%, at least 67%, at least 68%, at least 69%, at least 70%, at least 71%, at least 72%, at least 73%, at least 74%, at least 75%, at least 76%, at least 77%, at least 78%, at least 79%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% of the proteins of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domains of at least 81% to 100% of the proteins of Table 7, e.g., comprises at least 85%, 90%, 95%, or 100% of (e.g.,

comprises all of) the proteins of Table 7, e.g., comprise the extracellular domains of 81%-85%, 83%-87%, 85%-89%, 87%-91%, 89%-93%, 91%-95%, 93%-97%, 95%-99%, or 100% of the proteins of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domains of at least 80% to 81% of the proteins of Table 7, e.g., comprises at least 80.1%, 80.2%, 80.3%, 80.4%, 80.5%, 80.6%, 80.7%, 80.75%, 80.8%, or 80.9% of the proteins of Table 7.

In some aspects, the collection of polypeptides comprises the extracellular domain of at least one of the proteins of Table 17, e.g., comprises the extracellular domains of at least 2, at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, at least 110, at least 120, at least 130, at least 140, at least 150, at least 160, at least 170, at least 180, at least 190, at least 200, at least 210, at least 220, at least 230, or all 231 of the proteins of Table 17, e.g., comprise the extracellular domains of 1-5, 5-10, 10-15, 15-20, 20-25, 25-30, 30-35, 35-40, 40-45, 45-50, 50-55, 55-60, 60-65, 65-70, 70-75, 75-80, 80-85, 85-90, 90-95, 95-100, 101-105, 105-110, 110-115, 115-120, 120-125, 125-130, 130-135, 135-140, 140-145, 145-150, 150-155, 155-160, 160-165, 165-170, 170-175, 175-180, 180-185, 185-190, 190-195, 195-200, 200-205, 205-210, 210-215, 214-220, 220-225, 225-230, or all 231 of the polypeptides of Table 17.

In some aspects, the invention comprises a set of containers (e.g., a set of vials), each vial comprising a plasmid encoding a unique polypeptide as described above.

IX. EXAMPLES

The following are examples of methods and compositions of the invention. It is understood that various other aspects may be practiced, given the general description provided above, and the examples are not intended to limit the scope of the claims.

Example 1. Assay for interactions between IgSF proteins and a human STM receptor library

Using a technology for unbiased detection of low-affinity interactions, a library containing most human single transmembrane (STM) receptors (1,226 receptors) was assayed for binding to 445 immunoglobulin superfamily (IgSF) proteins. IgSF proteins are known to function through formation of homo- and heterophilic complexes that mediate a wide array of functionalities, such as modulation of axon guidance or synaptic plasticity, control of cell migration and adhesion, and self vs. non-self recognition, and as such, these proteins constitute a major focus for drug development efforts.

A. IgSF query collection

The immunoglobulin superfamily (IgSF) collection (query collection) was defined by integrating functional annotations and computational predictions from various computational algorithms for prediction of protein features, followed by careful manual curation and review. First, a list of proteins a predicted "Immunoglobulin-like domain superfamily," according to InterPro (IPR036179), was downloaded from UniProt. This list was complemented with 98 selected proteins based on their participation in relevant biological functions, and was then further curated in light of evidence for extracellular domains and motifs relevant to receptor signaling functions, restricting it to a subset of 445 proteins (Clark et al., *Genome Res*, 13: 2265-2270, 2003; Daeron et al., *Immunol Rev*, 224: 11-43, 2008; Yap et al., *J Mol Biol*, 426:

945-961, 2014). The final query set includes 365 human IgSF proteins (≈82% of the IgSF, according to InterPro annotations) and 98 additional proteins, some of which are also annotated with 'Ig-like Fold' in SwissProt (Fig. 1A; Table 4). IgSF proteins were cloned as previously described (Bushell et al., *Genome Res*, 18: 622-630, 2008; Martinez-Martin et al., *Cell*, 174(5): 1158-1171, 2018). In brief, the ECD of each IgSF query protein was fused to the pentameric helical region of rat cartilage oligomeric matrix protein (COMP) and β-lactamase, increasing avidity and allowing a colorimetric readout upon addition of the substrate nitrocefin (Fig. 1B). All clones were synthesized using sequences codon-optimized for mammalian cell expression.

The power of this technology to detect receptor-ligand interactions characterized by a wide range of affinities, including transient interactions with micromolar K_D, has previously been demonstrated (Martinez-Martin et al., *Cell*, 174(5): 1158-1171, 2018). To further benchmark the sensitivity and reproducibility of this platform for detection of interactions between human receptors, PD-1/PDCD1 and PD-L2/PDCD1LG2 proteins were screened following the established procedure (Fig. 1B). Notably, all expected interactors were detected with high normalized signal (>0.75), high binding specificity and excellent reproducibility (Pearson's r >= 0.87) (Fig. 1C and Figs. 7C-7E), further demonstrating the robustness of the receptor interaction discovery platform.

B. Human STM receptor library

The list of single transmembrane (STM) receptors (prey library) was compiled by integrating functional annotations and computational predictions from various computational algorithms for prediction of protein features, followed by careful manual curation and review of published annotations (Clark et al., *Genome Res*, 13: 2265-2270, 2003; Martinez-Martin et al., *Cell*, 174(5): 1158-1171, 2018). The library consists of 1,266 unique human STM receptors (Table 5). STM receptors were expressed as extracellular domains (ECDs) fused to a human Fc tag (e.g., soluble ECDs). This facilitates protein expression, circumvents the need for solubilization in the presence of detergents, and allows robust capture on protein A-coated plates (Fig. 1B). In brief, the boundaries of the extracellular domain (ECD) were determined by predicting signal peptides and transmembrane helices or glycosylphosphatidylinositol (GPI)-linkage sites using publicly available servers for prediction of protein features (Phobius, TMHMM, SignalP3.0). The ECD of each receptor was synthesized and cloned into the pRK5 vector (Genentech) containing a C-terminal human Fc tag. For type II STM proteins, a HSV signal sequence was inserted upstream of an N-terminal Fc tag.

C. Cell culture and conditioned media generation

i. Cell culture

Conditioned media for the STM receptor library was prepared using Expi293F cells (Thermo-Fisher), a suspension cell line adapted from HEK293 cells (epithelial human cells, embryonic kidney). Cells were cultivated under the following conditions: 37°C, 8% CO_2, 80% humidity and 150 rpm agitation speed. Expi293 Expression Medium (Life Technologies) was used as the seed train and production media. The same cell line and culture conditions were used for expression of the secreted, pentameric IgSF proteins. COS7 cells (fibroblast cell line derived from monkey kidney tissue, purchased from ATCC)

or HEK-293 cells were used for transient expression of the relevant binding partners, expressed as full-length proteins (Genentech). Transfections were performed using Lipofectamine LTX with PLUS Reagent (Life Technologies) in Opti-MEM media (Life Technologies). Cells were cultured in DMEM media supplemented with 10% FBS, 2 mM L-glutamine, 100 U/mL penicillin and 100 µg/mL streptomycin in a 37°C humidified, 5% CO_2 incubator.

ii. Conditioned media generation

The collection of STM receptors (prey library; cloned as the extracellular domain (ECD) fused to a human Fc tag (ECD-Fc)) was transiently transfected in human cells for expression as soluble proteins in the conditioned media. Cell culture and instrumentation for cell transfection automation have been described in detail (Bos et al., *Biotechnol Bioeng,* 112: 1832-1842, 2015). In brief, transfections were performed using Expi293 (Life Technologies), a suspension-adapted HEK293 line. Expi293 Expression Medium (Life Technologies) was used as the seed train and production medium. Cells were cultivated as a seed train in flasks and grown at 37°C, 5% CO_2, and 150 rpm agitation speed in a humidified incubator before transient transfection. A Tecan EVO liquid handling system (Tecan) and integrated MultiDrop Combi reagent dispenser (Thermo Fisher) was utilized for all automated cell culture operations. The prey library was prepared using micro-scale 1 mL transient transfections, using an automated platform that has been recently described (Bos et al., *Biotechnol Bioeng,* 112: 1832-1842, 2015; Martinez-Martin et al., *Cell*, 174(5): 1158-1171, 2018). In brief, DNA was purified at the miniprep scale using a high throughput plasmid purification system, and 1 µg of DNA was dispensed in each well. For generation of conditioned media enriched in oligomeric query proteins, 30 mL transient transfections using a total of 30 µg in each well were carried out in 50 ml tubespins processed in batches of 96 for efficiency using a Biomek FX liquid handling robot (Beckman Coulter), essentially as described (Bos et al., *Biotechnol Bioeng,* 112: 1832-1842, 2015). 25 KDa Linear polyethylenimine (PEI) was used for the transient transfection procedures, and conditioned media were harvested 7 days post-transfection. Cells were removed by spinning at 3,000 rpm for 30 minutes, and supernatants were stored at 4°C until processed.

iii. Preparation of STM library-coated plates for protein-protein interaction screens

The receptor-ligand screening technology utilized was based on the avidity-based extracellular interaction (AVEXIS) method (Bushell et al., *Genome Res*, 18: 622-630, 2008), further adapted for automated high throughput screening in 384 well plate format (Martinez-Martin et al., *Cell*, 174(5): 1158-1171, 2018). In brief, to prepare the conditioned media for the high-throughput extracellular interaction screens, the STM prey library and IgSF query proteins were produced in a human expression system as described above in order to maximize addition of the relevant post-translational modifications. Cell transfections were performed as described, and cell cultures were grown for 7 days before removing the cells by centrifugation at 3,000 g for 30 min. Protein A-coated plates (Thermo Scientific) were used to capture the prey library from conditioned media by overnight incubation followed by storage at 4°C. A similar procedure was used to prepare the IgSF query proteins, which were assayed directly in the conditioned media without any capturing step. Prior to screening, the concentration of each pentameric IgSF receptor was normalized using β-lactamase activity in the conditioned media as readout. Briefly, a

dilution series of the supernatant was added to nitrocefin (0.125 mg/mL) and immediately transferred to a plate reader to record absorbance at 485 nm every minute for a total of 20 min. The expression levels for each query protein were normalized to threshold levels previously determined to identify interactions of ≤ 10 μM, as described (Bushell et al., *Genome Res*, 18: 622-630, 2008).

iv. Analysis of ECD-Fc receptor concentration in conditioned media

The concentration of each STM receptor (ECD-Fc) in the conditioned media utilized for the assays was measured using a human IgG, Fcγ time-resolved (TR)-FRET assay. AffiniPur F(ab')$_2$ Goat anti-Human IgG, Fcγ (Jackson ImmunoResearch) conjugated with Europium Cryptate (Cisbio Bioassays), and AlexaFluor647R-AffiniPur F(ab')$_2$ Donkey anti-Human IgG, Fcγ were used as donor and acceptor, respectively. Standards, controls and samples were diluted in assay diluent (PBS/0.5% BSA/0.05%Tween-20/15ppm Proclin) and added to 1536-well MaKO white plates (Aurora Biotechnologies). A combined donor and acceptor reagent solution was then added to each well. Plates were allowed to incubate at ambient temperature for 1 hour, followed by reading using a PHERAstar FS (BMG Labtech) plate reader with an excitation wavelength of 320 nm and emission wavelengths of 665 nm and 620 nm. The TR-FRET signal was reported as the ratio of the two emission wavelengths (665 nm/620 nm) multiplied by 10,000. Sample quantification was obtained by interpolating the results from a 5 parameter fit of the standard. Data was processed using a custom software.

D. Automated cell surface interaction screen

To systematically explore the interaction repertoire of the IgSF members, each query protein was individually screened against the entire library of STM receptors, which resulted in testing of ~600,000 binary binding events from over 2,000 individual 384-well plates (Fig. 8A).

Preparation of STM receptor library-coated plates and screening of the oligomeric IgSF proteins against the STM receptor library were performed using an integrated robotic system consisting of automated liquid handling devices (plate dispensers and washers), to allow for high throughput analysis of protein-protein interactions and minimize manual operations to improve screening data quality (Martinez-Martin et al., *Cell*, 174(5): 1158-1171, 2018). The system was a fully automated microplate assay system that consists of several devices integrated with a robotic arm. This system was configured with a Biomek FX liquid handler (Beckman Coulter) with a 384-channel pipette head for plate-to-plate sample transfer, a Thermo Cytomat 9 hotel carousel (Thermo Fisher Scientific) for storing assay plates and tip boxes, a BioTek EL406 combination washer/dispenser (BioTek) for washing and dispensing reagents to plates, and a BioTek MultiFlo dispenser (BioTek) for dispensing additional reagents. A TECAN Infinite M1000 multimode microplate reader (Tecan) was used to record signal from screening plates. The method was developed using Beckman Coulter SAMI software, which schedules the methods according to the number of assay plates in a run and controls the execution of the entire automated processes.

Every 384 well screening plate used in this study was configured with 16 wells reporting the maximal enzymatic absorbance potential of the query construct (used as positive control for automation procedures), 16 blank wells to report plate background (negative control), and 346 randomly spotted prey

proteins from the STM library. On average, this workflow allowed screening of up to 7 query proteins a day against a library consisting of 1,364 preys distributed over 4 screening plates (Fig. 7C). On the day of the screen, protein A-coated plates that had been incubated overnight with the conditioned media library were washed three times with PBS containing Ca^{2+} and Mg^{2+}. Subsequently, plates were inoculated with the conditioned media containing the pentamerized IgSF query protein (50 µL/well) and incubated at room temperature for 1 h. Plates were then washed with PBS to remove any unbound IgSF pentamer. Nitrocefin (50 µL/well) was added (Calbiochem). Nitrocefin hydrolysis, indicated by a color change, is observed in the presence of β-lactamase activity and indicated that the IgSF query protein was bound to the individual STM receptor captured in the well (Fig. 1B). Plates were incubated at room temperature (RT) for 1 h, and IgSF-STM receptor interactions were assessed by measuring absorbance at 485 nm.

Example 2. Analysis of IgSF extracellular interaction screen results and prediction of the IgSF interactome

To enable analysis of this large dataset and reliably identify non-specific (false positives) binders and compute a binding score in an automated manner, we developed a computational classification tool.

First, raw enzymatic absorbance values were corrected per screened plate by subtracting the plate's estimated background enzymatic absorbance (10%-ile) and subsequently scaling those values to the maximal enzymatic absorbance estimate (99.5%-ile) to derive a normalized absorbance value within the [0,1] range for each measured well. All absorbance controls and empty well values were filtered out and the normalized absorbance values were compiled in a query (row) by prey (column) data matrix. Using the data matrix, four predictive features were computed for each query-prey pair: 1) the normalized absorbance value 2) a query Z-score (Z-score across all preys on the 4 STM library plates for a single query); 3) a prey Z-score (Z-score per prey in the STM receptor library across all queries that were screened against it); and 4) a custom Specificity Score, computed as follows:

$A_N^{q,p} = Normalized\ query\ prey\ Absorbance$; $A_N^P = \sum_{i=1}^{q} A_N^{q,p} = Sum\ Prey\ Absorbance$;

$A_N^S = \sum_{i=1}^{p} A_N^P = Sum\ Screen\ Absorbance$; $S^{q,p} = \sqrt[2]{A_N^{q,p} * \frac{A_N^S}{A_N^P}} = Specificity\ Score$

A supervised random forest classifier, implemented in the Caret R package, was trained using all four features on a benchmark data set of compiled true positive receptor interactions from literature, observed "nonspecific" preys from orthogonal library screens (Table 14) and true negative interactions, sampled at a 1:10 positive to negative ratio from the data points below the 99-%-ile (Normalized Absorbance < 0.057) (Figs. 8C-8E). All absorbance controls were removed prior to training and prediction. The training function in Caret was configured with the following parameters: training set size 75%, test set size 25%, repeated cross-validation (N=10, R=10), multi-class predictions (Positive, Negative, Non-specific), grid-search parameter optimization for Random Forest (mtry=20, .ntree=30) and Accuracy as performance metric. The predicted 'highconfidence' IgSF interactome was defined by additionally filtering by the following class probabilities: P(Positive) >= 0.75, P(Non-specific) <= 0.25 and P(Negative) <= 0.05 (Figs. 2B and 8B). Finally, for representation and data integration purposes, all interactions identified with multiple prey constructs for identical STM receptors and bi-directionally

identified interactions were summarized into a non-directional, non-redundant list of unique binding partners.

This classification exercise resulted in 577 predicted high-confidence interactions between 440 unique IgSF and STM proteins, referred to as the "IgSF interactome" (Fig. 2A, Table 6). To facilitate data integration, analysis and visualization, the IgSF interactome was represented as a Cytoscape interaction network where "nodes" represent extracellular proteins and "edges" the interactions between them (Fig. 2A). The IgSF Interactome network is highly connected (Fig. 2A). Connectivity in biological networks has been the subject of many studies, which postulate that their scale-free properties contribute to robustness (Barabasi, *Science,* 325: 412-413, 2009). Indeed, a network analysis of the IgSF Interactome showed that each protein is connected on average to 2-3 neighboring proteins and that the topological coefficients follow a power-law distribution (Fig. 2C), a hallmark of scale-free networks. This suggests that the extracellular interactome is not made up of disconnected receptor-ligand pairs, but rather consists of modular components that have dense intra-connectivity and sparse, but relevant interconnectivity (Albert, *J Cell Sci*, 118: 4947-4957, 2005).

The IgSF interactome identified the remarkable number of 472 novel interactions, and recapitulated 105 previously documented interactions in the aggregate of Biogrid, Bioplex and STRING databases (Fig. 2D).

Example 3. Integration of IgSF interactome data with public datasets

A. IgSF interactome and Bioplex,Biogrid, and STRING datasets

The IgSF interactome dataset was compared to the Bioplex, Biogrid, and STRING datasets (Chatr-Aryamontri et al., *Nucleic Acids Res,* 45: D369-D379, 2016; Huttlin et al., *Nature*, 545: 505-509, 2017; Szklarczyk et al., *Nucleic Acids Res.*, 43: D447-452, 2015), currently the most systematically compiled resources for human protein interactions. The Bioplex dataset was downloaded from the Bioplex webpage (v2.0). The Biogrid dataset was downloaded from the Biogrid webpage (v3.4.160, physical interactions). The STRING dataset, including all STRING "evidence channels", was downloaded from the STRING website (v.10.5) and filtered to retain only interactions with a STRING "combined score > 0.7" based on the previously described weighted evidence channels (von Mering et al., *Nucleic Acids Res*, 33:D433-437, 2005). To compute the overlap percentages, all three protein interaction resources were restricted to the scope of binary interactions tested in this work, being the combinatorial set of all query by prey proteins. All network statistics were computed in Cytoscape (v.3.6.1) (Shannon et al., *Genome Res*, 13: 2498-2504, 2003).

In relative terms, our dataset showed the largest overlap with the STRING database (82/1,037) and the smallest overlap with the combined Bioplex in HEK293 and HCT116 cells (11/350), an important observation given the scale of the Bioplex effort (~120,000 interactions among nearly 15,000 proteins), and the fact the nearly all proteins studied in our work are also part of the Bioplex and STRING databases (Fig. 7A). Integration of protein localization information from the Human Protein Atlas revealed that the number of interactions between two extracellular proteins found in Bioplex is disproportionally low, with only ~1% of this dataset representing interactions between the set of extracellular proteins encoded by the human genome (Fig. 2E). The challenges of capturing plasma membrane-expressed proteins with a

standard AP-MS workflow and the Bioplex projects' focus on intracellular tagged constructs offer logical explanations for this observation, and further highlight the relevance of the present study to address interactions that take place in the extracellular environment. Finally, given that 238 STM proteins represented on the network were also included as query proteins, it was possible to detect these as reciprocal interactions in our screen. Indeed, 114 interactions (out of 316, ~36%) were observed both as query-prey and prey-query pair (Fig. 2F).

B. Network clustering by healthy tissue expression correlation

The inherent challenges associated with the study of plasma membrane proteins have importantly hindered a systematic exploration of functional relationships between human receptors. To our knowledge, only a few studies have attempted to classify cell receptors into functional families through predicting shared ligand interactions from sequence and structure features, and virtually all predictions lack experimental validation. To facilitate a functional interpretation of the IgSF interactome, we integrated healthy tissue mRNA expression profiles for all proteins (network nodes) in the IgSF interactome from the Genotype-Tissue Expression (GTEx) project (Pierson et al., *PLoS Comput Biol,* 11, e1004220, 2015).

Tissue expression correlations between node pairs in GTEx were calculated as the Spearman coefficient on the log2-transformed RPKM across all tissue detail categories. All test p-values were adjusted for multiple hypothesis testing using the Benjamini-Hochberg method. All heatmaps were plotted with the pheatmap R package. Unsupervised clustering was performed with the Euclidean distance and Ward linkage. All network statistics were computed in Cytoscape (v.3.6.1) (Shannon et al., *Genome Res*, 13: 2498-2504, 2003). Network clustering was also performed in Cytoscape using the Markov Clustering Algorithm (MCL), implemented in the ClusterMaker2 plugin, with the Spearman correlation coefficients as edge weights (inflation parameter = 1.4, stop if residual increases = False, number of iterations = 500). Gene Ontology (GO) enrichment statistics were computed per MCL cluster using the GOstats R package (Falcon and Gentleman, *Bioinformatics*, 23: 257-258, 2007). Significantly enriched GO Biological Process terms were determined by q-value < 0.05. All significant terms were manually curated and aggregated in the overarching categories depicted in Fig. 3A.

We hypothesized that modular components of connected IgSF and STM proteins are more likely to share a functional relationship and would be commonly expressed in the same tissue. In agreement with this hypothesis, the global tissue correlation coefficients for pairs of interacting proteins were indeed significantly higher compared to those of non-interacting pairs in our screen ($p < 1.2\ 10^{-20}$, one-sided Wilcoxon rank-sum test) (Figs. 3B and 9A). Given that there was a clear agreement between physical and co-expression associations, the expression correlation coefficients were used to inform clustering of the IgSF Interactome into modular components or 'communities' (Fig. 3A). As expected, co-expression coefficients were significantly higher within these communities, compared to all interactions between them (Fig. 9B).

The clustered Interactome displayed a number of tightly connected communities between closely related IgSF members, including the CEACAM proteins (Fig. 3A, cluster 18), the PVR/Nectin receptors (Fig. 3A, cluster 13), the Semaphorin/Plexin family (Fig. 3A, cluster 21) or the ephrin family of receptor

tyrosine kinases (RTK) (Fig. 3A, cluster 5), among others. The co-expression and clustering results also revealed strong associations for many previously unknown protein pairs including MDGA1/neuroligins or the immune receptor AXL and its putative binding partners, suggesting a physiological role for these interactions in those tissues. Next, all network communities were interrogated with a custom Gene Ontology (GO) enrichment analysis to attempt functional classification of the proteins within the Interactome communities. This enrichment analysis showed that all sizeable communities (n>2) captured biological associations relevant to known IgSF functions such as immune response regulation, nervous system development, signal transduction and intercellular communication, and enabled assignment of putative functionalities for protein poorly characterized proteins, based on association with relatively well studied binding partners (Fig. 3A).

Although interacting proteins had significantly more correlated tissue expression patterns compared to non-interacting pairs, the modest mean shift between both distributions suggested that this difference was driven by selected interactions and/or interactions in a specific tissue context. Indeed, within the top 5% most correlated interacting pairs, many known protein pairs showed more prominent correlation patterns in discrete tissues, such as Nectin1-Nectin 4 (Fig. 3C) or CEACAM5-CEACAM7 (Fig. 3D and Fig. 9C), which were highly correlated in skin and colon, respectively.

Interestingly, many of the novel interactions found in the IgSF Interactome dataset also displayed a similarly strong tissue-dependent association. For example, LILRA5 and LILRB1 were highly associated in blood (Fig. 3E and Fig. 9D); PTPRZ1 and CNTN1, in brain (Fig. 3F); NCR1 and SIGLEC7 (Fig. 9E), in multiple tissues; or CHL1 and L1CAM (Fig. 3G and Fig. 9F), strongly associated across tissues, suggesting a relevant role for these interactions in certain biological scenarios. We next asked whether these interactions could take place “in-trans” on cells, using a tetramerization-based approach for high sensitivity detection of putative binders expressed on the cell surface (Fig. 3H). These results demonstrated binding of NCR1 to specific members of the SIGLEC family (Fig. 3I), the interaction between CHL1 and L1CAM (Fig. 3J and Figs. 9G and 9H), as well as binding of CNTN1 to PTPRZ1 and the rest of putative binding partners (Fig. 3K and Figs. 9H and 9I). Co-immunoprecipitation studies showed that NCR1 interacted with all the newly identified binding partners in the context of the plasma membrane, further supporting a role for these interactions (Figs. 3L-3N). Together, these analyses enabled a description of possible functional associations between protein families that were previously undocumented, governed by co-expression of binding partners. Consequently, this effort empowers hypothesis driven studies of putative molecular functions for known and poorly characterized proteins, and provides a rationale for biologically relevant contexts where these proteins may function.

The GTEx dataset was downloaded from the GTEx Portal webpage (v7, reprocessed by our internal pipeline).

C. IgSF interactome and TCGA dataset

Perturbations in the extracellular interactomes are tightly associated with pathological processes including tumor growth and immunoevasion, often through uncharacterized mechanisms. Therefore, we sought to investigate which edges in our interactome connect nodes that are significantly deregulated

(up- or downregulated) in comparison to their gene expression in tumor tissue to adjacent normal tissue as reported in The Cancer Genome Atlas (TCGA).

Tumor versus matched adjacent normal differences in TCGA were assessed for all indications that had at least 3 matched normal samples (N=20 out of 33 indications). Differential expression was tested for all TCGA indications with at least three matched Tumor and Adjacent Normal samples using a two-sided t-test. All test p-values were adjusted for multiple hypothesis testing using the Benjamini-Hochberg method. All heatmaps were plotted with the pheatmap R package. Unsupervised clustering was performed with the Euclidean distance and Ward linkage. All network statistics were computed in Cytoscape (v.3.6.1) (Shannon et al., *Genome Res*, 13: 2498-2504, 2003). Network clustering was also performed in Cytoscape using the Markov Clustering Algorithm (MCL), implemented in the ClusterMaker2 plugin, with the Spearman correlation coefficients as edge weights (inflation parameter = 1.4, stop if residual increases = False, number of iterations = 500).

This analysis revealed that 398/485 nodes (~82%) connected by 543/703 edges (~75%) are jointly de-regulated in at least one TCGA indication (Fig. 6A), indicating that interactions involving IgSF and STM proteins are generally perturbed in tumors. We also observed that the number of deregulated nodes, as well as the number of edges connecting those, is highest in Lung Squamous Cell Carcinoma (LUSC), Colorectal Adeno Carcinoma (COAD) and Kidney Renal Carcinoma (KIRC) indications, where around 150 network genes are significantly overexpressed (Figs. 6B, and11A). This analysis confirmed and further validated that many relatively well-characterized interaction pairs are up-regulated in multiple shared TCGA indications, such as the inhibitory receptor CTLA4 and CD80 (5/19 indications), the PVR/nectin family (4/19 indications) or several members of the semaphorin and ephrin receptor families, among others (Fig. 6A). Conversely, these results also revealed that functionally related interaction pairs such as CADM2 and CADM3, FLRT2 and UNC5C (9/19 indications each) or some members of the PTPR family and their interacting partners, are jointly downregulated across multiple shared tumor types, consistently with their proposed functions as tumor suppressors. Interestingly, our analyses also highlighted such striking synonymous co-modulation patterns for many of the newly reported interactions in this study. Of note, a number of interacting pairs, such as the inhibitory receptor pairs CD300LF-CD300LG and LILRB4-CNTFR, or the co-stimulatory molecules ICOS-ICOSLG are negatively synchronized in (up- and down-regulated, respectively), suggesting that absence of these interactions may play a role in tumor progression. Finally, this analysis revealed that most proteins identified as hubs (nodes connected by 5 or more edges), including PTPRD, PTPRS, NTRK2, CNTN1 or CD300LG, are significantly downregulated across multiple indications (Figs. 6A-6D), suggesting that disruption of interactions mediated by these proteins may play a role in cancer progression, and potential roles for poorly characterized proteins such as the CD300 family of immune receptors.

The TCGA RNA-Seq data was downloaded from the NCI Genomic Data Commons PanCanAtlas Publications webpage.

Example 4. Methods for validation of binding partners

Selected interactions identified in Examples 1 and 2 were validated using one or more orthogonal techniques, e.g., surface plasmon resonance (SPR), biolayer interferometry, and co-immunoprecipitation (co-IP).

A. Surface plasmon resonance

Putative receptor-ligand interactions were analyzed by SPR using a Biacore 8K (GE Healthcare) or Proteon instrument (Biorad). Indicated proteins were immobilized on CM5 (GE Healthcare) or GLC (Biorad) sensor chips, respectively, using a standard amino coupling method. Analytes were run at the concentrations indicated in each case, in HBS-P buffer (0.01 M Hepes, 0.15 M NaCl and 0.005% surfactant P20, pH7.4) or in PBS-0.01 TWEEN® 20 when the Proteon instrument was used. For kinetic calculations, ligands were immobilized at low resonance units, and K_D values were calculated in equilibrium. For kinetics experiments, his-tagged recombinant proteins were used as analytes. In all cases, bulk refractive index changes were removed by subtracting the reference flow responses, and sensorgrams were analyzed using the Proteon BiaEvaluation software version 4.1 (Biorad).

B. Biolayer interferometry

Interactions between AXL and the binding partners IL1RL1 and Gas6 were assayed by biolayer interferometry using an Octet Red system, as previously described (Husain et al., *Mol Cell Proteomics*, 18: 2310-2323, 2019). Briefly, recombinant AXL, MERTK or Tyro3 ectodomains were biotinylated *in vitro* using the EZ-LINK™ Sulfo-NHS Biotinylation Kit (Thermo Scientific), and captured on streptavidin-coated sensors. These receptors were tested for binding to Gas6 or IL1RL1, expressed as recombinant ectodomains assayed in PBS buffer. Data were analyzed using Forte Pall (Port Washington, NY) software 9.0.

C. Recombinant proteins

The following proteins were purchased from Sino Biologicals: CNTFR, LDLR, SLITRK4, and BTN3A3. The following proteins were obtained from R&D Biosystems: CHL1, MCAM, SIRPA, CNTN1, SLITRK2, SLITRK3, LRFN5, EDAR, FLT4, PD-L1, PD-1, EPHA3, EPHA4, BTNA2A, BTN3A1, AXL, IL1RL1, VSIG10L, FLRT1, FLRT2, FLRT3, NCR1, MDGA1, TREML2, IGSF9B, LILRA3, Gas6, MERTK, and Tyro3. CEACAM4, expressed as ECD-Fc, was expressed in mammalian cells and purified in house using standard affinity chromatography techniques (Ramani et al., 2012).

D. Co-immunoprecipitation of novel binding partners

The following STM proteins were expressed as full-length proteins fused to a C-terminal HA tag: FAM187B, LRRC4B, LRRC4C, VSIG8, CDH9, ST14, TGOLN2, IGSF5, IL1RL1, VSIG10L, PD-L2, PD-L1, LILRA3, LILRB4, LILRB5, and NCR1. The following STM proteins were expressed as full-length proteins fused a C-terminal Flag tag: BTN2A1, BTN3A1, BTN3A2, BTN3A3, AXL, CD300A, CD300C, CD300LF, CEACAM4, EPHA3, IL6R, EDAR, ILDR1, CNTFR, LDLR, SIGLEC7, SIGLEC8, and CD4. HEK293 cells

were co-transfected with the relevant protein pairs (expressed as HA- and Flag-tagged fusions, respectively) using LIPOFECTAMINE™ LTX Reagent. Relatively low plasmid concentrations were used to avoid high overexpression of the proteins. Typically, 6 x 10^5 cells were seeded in M6 well plates and reverse transfected with 1 µg of a 1:1 DNA mixture. Cell lysates were washed with PBS and lysed ~18 hours post-transfection using RIPA buffer (50 mM Tris HCL pH 7.4, 150 mM NaCl, 2 mM EDTA, 0.5 (w/v) Na-deoxycholate, 0.1 % (w/v) SDS, 1 % (v/v) NP40). Equal amounts of the lysates were incubated with EZVIEW™ Red ANTI-FLAG® M2 Affinity Gel (Millipore Sigma) at 4°C overnight, following the manufacturer's instructions. The beads were extensively washed with lysis buffer and proteins were eluted using loading buffer SDS sample buffer (Thermo Fisher Scientific) using denaturing conditions. Immuno-precipitates were analyzed by western blotting using anti-Flag (Cell Signaling Technologies) and anti-HA antibodies (Abcam), using a LICOR instrument.

Example 5. Validation of EPHA3 and CEACAM4 binding partners

The functional interaction map (Fig. 3A) showed that related receptors within a protein family showed distinct binders or differential tissue expression relative to other members within the protein community. Two notable examples of such divergent behavior were the ephrin receptor EPHA3 and the cell surface protein CEACAM4, identified as binding partners for PD-L1 and PD-L2, respectively, within the immune regulatory cluster (Fig. 4A).

Interestingly, certain ephrin family members (EPHA3, EFNB1, EPHB4) displayed a more promiscuous expression pattern relative to the rest of the family (Figs. 10A and 10B). Similarly, the family of Carcinoembryonic antigen-related cell adhesion molecules (CEACAM) was distinctly divided into two tissue clusters, where the group consisting of CEACAM4, CEACAM3 and CEACAM8 showed significant overlap in tissue expression patterns with the immune regulatory cluster, including shared tissue co expression for CEACAM4 and PD-L2 (Figs. 10A and 10C).

To further investigate these putative immunoregulators, both interactions were studied by surface plasmon resonance (SPR) using purified recombinant proteins. Specific binding of EPHA3 to PD-L1 (Fig. 4E) and CEACAM4 to PD-L2 (Fig. 4B) with moderate binding affinities was confirmed (PD-L1/EPHA3: K_D: 2.8 x 10^{-8} ± 2.7; PD-L2/CEACAM4, K_D: 8.4 x 10^{-8} ± 69) (Figs. 10D and 10E), illustrating the capacity for robust and sensitive detection of receptor-ligand interactions through the discovery pipeline. SPR analysis also confirmed the newly identified interaction between the LILR family member LILRA3 and EPHA3 (Fig. 4C). PD-L1 interacted with its known binding partners PD-1 and PD-L2 expressed on cells, as well as EPHA3, whereas no interaction with a related member of the ephrin family or the CEACAM proteins tested was observed, further demonstrating the specificity of the PD-L1/EPHA3 interaction (Fig. 4F). In turn, PD-L2 bound to PD-L1 and PD-1 expressed on the cell surface, as well as with the new interactor CEACAM4. No binding to CEACAM5, a protein related to CEACAM4, or the PD-L1 binder EPHA3 was observed, corroborating a specific interaction between PD-L2 and CEACAM4 (Fig. 4F). Interestingly, the therapeutic antibody atezolizumab, known to block the PD-1/PD-L1 axis and thus currently used as immunotherapy for the treatment of solid tumors (Shah et al., *Hum Vaccin Immunother*, 14: 269-276, 2018), also competed the interaction with EPHA3 (Fig. 4D).

Example 6. Validation of PTPR binding partners

Functional clustering of the IgSF interactome network (Example 2) revealed a remarkable association between members of the receptor-type protein tyrosine phosphatase (PTPR) family and nervous system-related proteins, including the neurotrophin receptors (NTRK), the interleukin-1-receptor accessory proteins (ILRAP), the Slit and NTRK like family (Slitrk), and the Leucine Rich and Fibronectin Type III domain (LRFN) proteins. Interestingly, the netrin-G ligand-3 (NGL-3/LRRC4B) was also found to interact with PTPRs proteins as well as with specific members of the butyrophilin (BTN) family (Fig. 3A).

A. Cell surface interaction assays

The PTPR family is the largest family of plasma membrane-expressed receptor protein tyrosine phosphatases (Du and Grandis, *Chin J Cancer,* 34: 61-69, 2015). This community revealed complex association patterns between members of the PTPR family and four different families of nervous system-related proteins, including the Neurotrophin receptors (NTRK), the interleukin-1-receptor accessory proteins (ILRAP), the Slit and NTRK-like family (SLITRK), and the Leucine Rich and Fibronectin Type III domain (LRFN) proteins (Fig. 3A, cluster 1; Fig. 5A). In addition, the netrin-G ligand-3 (NGL-3/LRRC4B), known to interact with PTPRs proteins, was found to bind specific members of the butyrophilin family, an emerging family of therapeutically relevant immune receptors (Arnett and Viney, *Nat Rev Immunol,* 14: 559-569, 2014). To confirm and further study the complex connections between these protein families, PTPRD, PTPRS and PTPRF were expressed as cell surface proteins and tested for binding to their identified interaction partners, using the cell-based methodology described. These results confirmed the specific interaction between the SLITRK2 and SLITRK3 proteins and both PTPRD and PTPRS respectively (Fig. 5B). Additionally, direct binding of LFRN5 (Fig. 5C) and IL1RAP (Fig. 5D) proteins to all three family members PTPRD, PTPRS and PTPRF was observed. In line with these results, SPR analysis further confirmed PTPRD binding to SLITRK1, SLITRK4, LFRN1, LFRN4, IL1RAP and IL1RAPL1 proteins (Fig. 5F). Finally, to investigate whether SLITRK, IL1RAP and LRFN family members specifically recognize select PTP receptors or rather maintain the capacity for promiscuous crosstalk, we tested binding to eight members of the PTPR family. Interestingly, these assays confirmed selective PTPR recognition of its cognate ligands in the respective families (Figs. 12A-12D).

In addition, we confirmed binding of cell surface expressed LRRC4B to the butyrophilin proteins BTN3A1 and BTN3A3 (Figs. 5E, 5G and 5H), but not the homologous family member BTN2A2 (Fig. 12E), as predicted by the Interactome results. Of note, these new interactors were confirmed in co-immunoprecipitation studies (Figs. 5G and 5I), which also demonstrated the interaction between LRRC4B and BTN3A2 (Figure 5H). Further analysis of other members of the butyrophilin family, including BTN2A1 and BTN3A1 (Figs. 5G, 5J, and 12F) demonstrated specific binding to the newly identified interactors, indicating that these proteins can form complexes in the cell.

Taken together, this comprehensive validation effort corroborated interacting partners previously described for the PTPR family, identified new interactions between individual family members and to our knowledge, assessed for the first time between-family selectivity. Furthermore, receptor-specific interactors for a number of butyrophilin proteins are uncovered, shedding light on an otherwise poorly characterized and yet highly relevant immunoreceptor family.

B. Disease-relevant PTPRD variants

Although a few genes have been exhaustively characterized, most disease-associated mutations are poorly studied and the alterations in protein interactomes underlying disease remain mostly unknown, in part owing to very limited understanding of interacting networks. Emerging data indicate that PTPRD functions as a tumor suppressor and that genetic and/or epigenetic deregulation causing a loss-of-function phenotype may result in altered signaling transduction and increased tumor growth. In fact, PTPRD is frequently mutated in glioblastoma, malignant melanoma and lung adenocarcinoma among other tumors (Peyser et al., *PLoS* One, 10: e0135750, 2015; Veeriah et al., *Proc Natl Acad Sci* USA, 9435-9440, 2009). We therefore utilized the receptor interaction discovery pipeline, described previously in this study, to examine a collection of cancer-relevant PTPRD variants. We queried the Catalogue Of Somatic Mutations In Cancer (COSMIC) and the TCGA data portal as well as individually published studies to identify non-synonymous mutations relatively prevalent across tumor types (Table 9).

Interestingly, in addition to alterations in the protein tyrosine phosphatase domain, frequent mutations were located throughout the immunoglobulin (IG) and fibronectin (FN) domains that compose the ECD, suggesting an impact on the landscape of PTPRD interactions that mediate cell communication (Fig. 5K). To examine whether these cancer-relevant mutations would interfere with the interacting network described for PTPRD, a collection of 14 mutants representing all domains in the ECD were screened with the interaction discovery pipeline (Figs. 5K and 5L and Table 9). Overall, mutations in the FN domains did not substantially modify the PTPRD interaction repertoire, whereas mutations concentrated in the IG domain had a significant effect (Fig. 5L), showing a significant reduction in binding to most binding partners, in agreement with the reports so far and existing structures (Mohebiany et al., *FEBS* J, 280: 388-400, 2012; Veeriah et al., *Proc Natl Acad Sci* USA, 9435-9440, 2009).

Interestingly, most of the mutations studied significantly impact the interactions to LRRC4B and NTRK3, with mutations in IG1-3 and FN domains 1-3 completely abrogating binding, suggesting that selected interactions are generally perturbed in the context of the tumor. Conversely, binding to ILRAP family members IL1RAP, IL1RAPL1, and ILRAPL2 was not impaired or was only marginally impaired, with the exception of mutants in the IG1 and IG2 domains (Figs. 5K and 5L). Interestingly, we also observed that selected mutations selectively impact binding to specific family members. Within the SLITRK family, the R232C/R233C double mutation impaired binding to SLITRK1/3 proteins, whereas binding to SLITRK6 was generally comparable to *wt* PTRPD. Similarly, within the LRFN family, the G203E/K204E double mutant showed absence of binding to both LRFN4 and LRFN5, while the R232C/R233C double mutant showed a more significant reduction in binding to LRFN5 but not LRFN4 (Fig. 5L). These results suggest that the highly specific interaction network rewiring events identified by the PTPRD mutant screen may play a role in disease and suggest a broader scope of biological functions and signaling properties that had remained uncharacterized for PTPRD.

Example 7. Validation of CHL1 and CNTN1 binding partners

The IgSF interactome network (Example 2) revealed an association between the neural cell adhesion molecule CHL1 and the contactin family member CNTN1, two cell surface proteins that play

roles in extracellular matrix, cell adhesion and synapse formation in the nervous system (Fig. 3A). The interactions between CHL1 and CNTN1 and other interacting proteins were confirmed using cell surface interaction assays and further assayed using SPR.

A. Cell surface interaction assays

Cell surface interaction assays as described in Example 5*A* were conducted for CNTN1 and CHL1. CHL1 expressed on the cell surface was confirmed to interact with CNTN5 and L1CAM and to interact more weakly with the immune receptor BTLA (Fig. 11C).

CNTN1 expressed on the cell surface bound specifically to the soluble query PTPRZ1, but to no other related members of this receptor family, including PTPRD or PTPRS (Fig. 12D), which were found to associate to the LFRN, SLITRK, and IL1RAP proteins (Figs. 5A and 12A-12D). This result further highlights the accuracy of the binding profiles identified in the IgSF interactome screens and suggests that these receptors exert specific functions through selective recognition of binding partners.

B. SPR assays

Selected CNTN1 binders were assayed by SPR as described in Examples 4*C* and 4*D*. CNTN1 was expressed as an extracellular domain (ECD) fused to a human Fc tag and was immobilized on CM5 sensor chips. The analytes NRCAM, NFASC, MCAM, and CHL1 and a control were formulated as described in Example 4*B* and were injected at a concentration of 250 nM. These experiments demonstrated a direct interaction between CNTN1 and the nervous system proteins NRCAM, NFASC, MCAM, and CHL1 (Fig. 9I).

Example 8. Validation of LILR family binding partners

The LILR proteins are a family of emerging, yet poorly characterized immune receptors, some of which are known to bind to MHC class I. We focused on LILRB1, LILRB3, LILRB4 and LILRB5, receptors characterized by the presence of immunoreceptor tyrosine-based inhibitory motifs (ITIM) and thus having putative immunosuppressive functions (Brown et al., *Tissue Antigens,* 64: 215-225, 2004; van der Touw et al., *Cancer Immunol Immunother,* 66: 1079-1087, 2017).

Interestingly, our study identified LILR receptor-specific interactions, including binding of EDAR and LILRA5 to LILRB1, expressed on the plasma membrane; and specific interactions between CNTFR and LDLR with LILRB4 and LILRB5 receptors, respectively (Fig. 5N). Furthermore, EDAR (Fig. 4G), IL6R (Fig. 4H) and CNTFR (Fig. 4I) efficiently co-immunoprecipitated with LILRB1 and LILRB4, respectively, indicating that these new identified binding partners can take place in the context of the plasma membrane.

A. Cell surface interaction assays

Cell surface interaction assays as described in Example 5*A* were conducted for LILR family proteins and relevant binding partners. FLT4, EDAR, IL6R, CNTFR, and LDLR were expressed on the cell surface, and LILRB1, LILRB4, and LILRB5 were expressed as soluble multimerized proteins. These assays confirmed the interaction between LILRB1 and the receptors EDAR, IL6R and the vascular

endothelial growth factor receptor 3 VEGFR3 (FLT4), the interaction between LILRB4 and CNTFR, and the interaction between LILRB5 and LDLR (Fig. 11B).

B. Analysis of LILRB1 in network integrations

Integration of the IgSF network with TCGA (Example 3*C*) revealed a synchronic upregulation of both LILRB1 and the lymphangiogenesis receptor FLT4/VEGFR3, but not other LILRB1 interacting partners, across multiple tumor indications, a pattern that was particularly significant in renal cancer (Fig. 5M). These observations are also in agreement with annotations in the Protein Cell Atlas and with independent efforts that suggest that FLT4 is a negative prognostic in certain tumors. In addition, increasing evidence indicates that LILRB1 plays a critical role in immune responses. We and others have identified LILRB1 as a prominent viral target (Chan et al., *Proc Natl Acad Sci U S A,* 111: 2722-2727, 2014; Chapman et al., *Immunity,* 11: 603-613, 1999; Hirayasu et al., *Nat Microbiol,* 1: 16054, 2016; Martinez-Martin et al., *Nat Commun*, 7: 11473, 2016), and a recent study has demonstrated a central role for LILRB1 in controlling the phagocytic function of macrophages through recognition of MHC-I (Barkal et al., *Nat Immunol,* 19: 76-84, 2018), altogether indicating that LILRB1 represents a promising therapeutic target.

Example 9. IgSF interactome and cancer

The IgSF Interactome was evaluated in the context of transcriptionally profiled samples from a large phase 2 trial (IMvigor210) on metastatic urothelial cancer patients treated with the anti-PD-L1 therapeutic antibody atezolizumab. These findings revealed interacting protein communities associated with CD8+ T-effector (Teff) cell function and distinct tumor immunological phenotypes. Further investigation uncovered protein interaction signatures highly correlated with lack of response to treatment and survival, with improved predictive power for clinical outcome.

A. Differential gene expression in tumors

Tissue integrity during homeostasis is primarily dictated by the interactions between cell surface proteins and, consequently, perturbations of the extracellular interactome are tightly associated with pathological processes such as tumor growth and immune evasion. Understanding of how protein interaction networks are perturbed or rewired in disease significantly limited, fundamentally due to the poor coverage of extracellular interactomes. Thus, to connect genomic information and functional significance, differential mRNA expression data between tumor and adjacent normal tissue, as reported in TCGA, was incorporated into the IgSF interactome (Figs. 6A and Figs. 29A-29J). Remarkably, we observed that over 90% of the IgSF genes studied were significantly differentially expressed (two-sided t-test, $|\text{Log Fold-Change}| > 1$, $q < 0.05$) in at least one tumor indication (Fig. 6A). In fact, a systematic comparison between pairs of unrelated genes and the interacting pairs in the IgSF interactome reported in this study showed that the number of jointly dysregulated interactions was consistently higher within the IgSF across all TCGA indications (Fig. 6B). Notably, integration of the IgSF Interactome and TCGA highlighted interacting proteins that were jointly down-regulated in most tumors, including CADM3-CADM2, UNC5C-FLRT2, and some members of the PTPR family and their interacting partners,

observations that are consistent with tumor suppressor functions described for these genes (Bae et al., *Sci Rep*, 7: 272, 2017; Chang et al., *Clin Cancer Res,* 16: 5390-5401, 2010). Conversely, this analysis also confirmed and further supported the observation that well-characterized interacting pairs are commonly jointly up-regulated in multiple shared TCGA indications, including well-described immune receptor pairs such as CTLA4/CD80 or PD-1/PD-L1 (Figs. 6C and 6D). In addition, as illustrated by certain members of the LILR family, a number of interacting proteins were found to be differentially expressed in opposing directions (up- and downregulated, respectively) in multiple tumor indications (Figs. 29B and 29C), suggesting that disruption of these interactions may influence cell communication in the tumor microenvironment.

Next, we sought to investigate which interactions were correlated at the protein level, which may have been missed at the RNA level. To do so, the recently published proteomics resource for 375 cancer cell lines from the Cancer Cell Line Encyclopedia (CCLE) (Nusinow et al., *Cell,* 180: 387-402 e316, 2020) was integrated with the IgSF interactome. Similar to the observations made using GTEX, the Pearson correlations for the subset of interacting pairs was significantly higher compared to the complement of non-interacting pairs, albeit less outspoken (one-sided Wilcoxon rank-sum text, $p < 0.05$) and with overall lower correlation scores to their GTEX counterparts, likely due to the larger number of patients in GTEX than cell lines in the CCLE, and the typically larger amount of missing values in proteomics datasets. Nevertheless, comparison of the IgSF Interactome with protein expression also revealed many interactions that were strikingly correlated, such as CEACAM5 and CEACAM6 in large intestine lineages (Fig. 6F) and lung cancer cell lines (Fig. 29H); the newly validated protein pairs CNTN1-NRCAM in lung cell lines (Figs, 6G, 9H, and 9I); LRRC4B and BTN3A1 (Figs. 6H, 5H, and 5J); interactions between the UNC and FLRT families (Figs. 6I and 10A-10J), or the CNTN1-PTPRZ1 pair, which interestingly, showed a strong correlation in healthy brain tissue (Fig. 3A) as well as a strong association in hematopoietic and lymph cell lines (Fig. 6J), suggesting a yet uncharacterized role for these interactions in immune cells. Similarly, the IGSF3-PTGFRN pair, for the first time reported to interact in this study and largely of unknown function, showed prominent correlation across cancer cell line lineages (Figs. 6K, 6L, and 29E-29G). We also observed strong correlation for the TAM receptor AXL (Fig. 6M), a receptor tyrosine kinase and important regulator of innate immunity increasingly appreciated as a determinant of resistance in tumors (Zhu et al., *Mol Cancer,* 18: 153, 2020). Interestingly, AXL protein levels were significantly correlated with the new binding partner VSIG10L, capable of interacting in cis in the plasma membrane (Fig. 6N). Although there was no protein expression data available for the second putative interactor identified, IL1RL1, we were also able to confirm a specific interaction between AXL and IL1RL1 using multiple methods, suggesting new modulators for this important RTK (Figs. 6O-6Q).

Finally, tightly negatively correlated interactions were observed for protein pairs such as KIT-KITLG or ICOSLG-NTM in lung (Figs. 29I and 29J), patterns that might suggest an important suppressive role for these interactions (Chung et al., mSystems, 4, 2019).

Taken together, these findings indicate that extracellular protein interactions between IgSF and STM proteins are commonly perturbed in tumors, possibly reflecting differences in the immune cell infiltrate in the tumor, or an immune-evasive process by the tumor cells. Evaluation of the IgSF Interactome in the context of the TCGA enables elucidation of interacting protein networks impacted in

specific tumor types, offering molecular insights into specific pathways dysregulated in cancer and thus suggesting opportunities for therapeutic development.

B. Interaction signatures associated with T cell function and clinical outcome.

The development of cancer immunotherapies to reinvigorate pre-existing anti-tumoral responses signifies an unparalleled leap forward in the treatment of cancer. In particular, therapeutic antibodies that block inhibitory checkpoints, such as PD-1-PD-L1, have been shown to induce durable responses in patients with multiple cancers. Notwithstanding the measurable success of the checkpoint therapies, these responses only occur in a subset of the patients, suggesting the existence of unknown non-redundant pathways that influence tumorigenesis (Sharma et al., *Cell,* 168: 707-723, 2017). Thus, to comprehensively elucidate the receptor-ligand networks associated with clinical outcome and identify new determinants of resistance and response to therapy, the IgSF Interactome was studied in the context of a large cohort from a phase 2 trial (IMvigor210) which included 298 transcriptome samples from metastatic urothelial cancer patients treated with the PD-L1 blocking antibody atezolizumab (Mariathasan et al., *Nature,* 554: 544-548, 2018). Interestingly, subsets of IgSF Interactome proteins exhibited strong correlations with immune cold (or non-inflamed) or hot (inflamed) tumors, defined by a gene set associated with CD8+ T_{eff} cells (Mariathasan et al., 2018). Immune hot tumors were further stratified using a pan-fibroblast TGFb signature associated with stroma-high tumors. correlated with an immune excluded phenotype (Mariathasan et al., *Nature,* 554: 544-548, 2018). Notably, we observed that newly identified interacting pairs such as PD-L2/CEACAM4, LILRB1/IL6R, and LILRB4/CNTFR were strongly correlated with hot tumors, including interactions between NCR1 and the SIGLEC6 or SIGLEC8 proteins, or members of the SLITRK family that bound to PTPRD, which were predominantly associated with stroma-rich tumors (Fig. 28A). These immune receptor interactions were largely absent from immune cold tumors, in line with the notion that these tumors lack an active immune response (Chen and Mellman, *Nature,* 541: 321-330, 2017). Conversely, cell adhesion families including the semaphorin and the plexin receptors or UNC and FLTR proteins, alongside newly identified interactors for these families such as UNC5D or glypican-3 (GPC3), were prominently associated immune cold tumors (Fig. 28A). Such a T_{eff} cell signature has been shown to correlate with PD-L1 expression in immune cells and better response to treatment (Mariathasan et al., *Nature,* 554: 544-548, 2018). In line with this observation, our analysis highlighted interacting proteins that showed a clear association with the CD8+ T_{eff} gene set, including the PD-1/PD-L1 family, well-characterized immune receptors pairs such as CTLA4/CD80, CD28/CD86 and CD47/SIRPA, as well as newly identified proteins pairs such as PD-L1/EPHA3 or the LILRB1 binders EDAR and IL6R (Fig. 30A). On the contrary, certain protein communities were negatively correlated with the CD8+ T_{eff} genes, including pairs within the semaphorin/plexin family and the putative FLT1 interactors TREM2 and EPHB6 (Fig. 30A).

We then sought to investigate IgSF Interactome features beyond T_{eff} cell function, by first evaluating the association between the interacting protein pairs and clinical outcome. Patients were categorized in responders and non-responders to Atezolizumab, as previously described (Mariathasan et al., *Nature,* 554: 544-548, 2018). Approximately 80 protein interactions (~15% of the Interactome network) were significantly associated with either an improved or worsened clinical outcome for this

cohort (Fig. 28B and Tables 15 and 16). As expected, interactions within the CD80 and PD-1 families of immunoreceptors were strongly correlated with response to atezolizumab. In addition, new putative protein pairs such as NCR1/SIGLEC6, or the interactions between LRRC4B and specific butyrophylin members, were strongly correlated with response (Fig. 28B). Conversely, interactions within the semaphorin/plexin family, as well as specific PTPRD regulators such as LFRN4 and IL1RAP were significantly associated with lack of response to treatment (Fig. 28B). Next, we investigated whether interacting gene pairs showed a synergistic effect on the predicted clinical outcome by comparing the 'protein interaction' hazard ratio (HR), derived from their joint expression, to the hazard ratio of their individual gene expression. Notably, 137 protein pairs, representing ~25% of the IgSF Interactome network, showed a significantly exaggerated hazard ratio over single proteins (Fig. 28C). Protein pairs for which this synergistic effect was observed included SIGLEC6 and NCR1; BTN3A1 and LRRC4B; CD80 and CTLA4; BTN3A3 and LRRC4B; EFNB1 and TRHDE; CTLA4 and PCDHGB4; CTLA4 and FAM200A; CA12 and SIGLEC6; ILDR2 and CLEC12B; EFNB1 and ITLN1; CADM1 and CRTAM; CD79B and CD244; and DAG1 and EFNB1, associated with responsiveness to atezolizumab therapy, and EFNB1 and EVC2; GPC4 and FGFRL1; EFNB3 and EPHB4; PTPRD and LRFN4; EFNB1 and AQPEP; EFNB1 and DSG4; LDLR and LILRB5; EFNB3 and EPHB3; PLXNB3 and SEMA4G; EFNB1 and EPHB6; FLT4 and FLRT2; AXL1 and IL1RL1; CD320 and IGSF5; CD59 and STAB1; CNTN3 and PTPRG; EFNB1 and EPHA3; EFNB3 and EPHB2; EGF and TNFRSF11B; ENPEP and SLITRK1; FCGR3B and EDA2R; IL20RA and CLEC14A; IL6R and BTNL9; IZUMO1 and LILRA5; NGFR and LRRTM3; NTM and AMIGO2; PCDHB3 and IGSF11; PTGFRN and TMEM59L; and TREM1 and VSIG8, associated with lack of responsiveness to atezolizumab therapy.

Among those, we observed new interactions for proteins with well characterized roles in tumors, such as the vascular endothelial growth factor receptors FLT1 and FLT4, or the regulators of cell death and immune responses EDAR, TNFRSF11B and CD47. As expected, interactions within the PD-L1 family were associated with response to atezolizumab and overall survival (Figs. 30B and 30E). In addition, a number of the novel receptor interactions were also strongly correlated with response to treatment, illustrated by the LRRC4B/BTN3A1/BTN3A3 or NCR1/SIGLEC6 protein pairs (Figs. 30C and 30F and Tables 15 and 16).

Conversely, interactions within protein families such as the fibroblast growth factor receptor (FGFR) tyrosine kinases or members of the LILR family were identified as interactions significantly associated with lack of response (Fig. 28C and Tables 15 and 16). A prominent example of such synergistic interactions was ephrinB1 (EFNB1), for which we confirmed binding members within the Ephrin family, together with newly identified previously unrelated interactors (Fig. 30D). Multiple EFNB1 interactions, including EVC2, AQPEP and EPHB6, showed a significantly higher association with non-responders when both genes in the pair were expressed relative to each of the genes in isolation (Fig. 28D). Consistently, expression of the interacting protein pair was significantly associated with lack of response to treatment and poor prognosis, illustrated by synergistic predictive effect between EFNB1 and the Hedgehog signaling machinery protein EVC2 (Figs. 28E and 28F).

Collectively, the study of the IgSF Interactome in the context of a large cohort of patients defines a gene signature map associated with CD8+ T_{eff} function as well as specific tumor immunophenotypes,

providing unique insights into receptor function, crosstalk and association with cancer progression. Further, these results highlight protein communities associated with response to PD-L1 blockade, and identify interacting gene signatures with improved predictive power for clinical outcome.

Example 10. Correlation of CAF-expressed PDPN with poor outcomes in CRC patients

The tumor microenvironment (TME) consists of a mixture of tumor and nonmalignant cells, including non-hematopoietic stromal cell types such as blood endothelial cells (BECs), lymphatic endothelial cells (LECs), and cancer-associated fibroblasts (CAFs), as well as hematopoietic immune cells. The tumor cells and the stroma establish a dynamic crosstalk that plays a critical role in regulating tumor growth and progression (Turley et al., *Nat Rev Immunol*, 15: 669-682, 2015; Peranzoni et al., *Cell Mol Life Sci*, 70: 4431-4448, 2013). Although the relationship between the stroma and tumor-infiltrating immune cells remains far less understood, compelling evidence indicates that the stroma importantly influences anti-tumor immune responses and responsiveness to immunotherapies (Turley et al., *Nat Rev Immunol*, 15: 669-682, 2015). Fibroblasts, which constitute the majority of stromal cells within the TME, regulate the structure and function of the tissue via extracellular matrix (ECM) remodeling and secretion of a plethora of inflammatory factors. In addition, increasing evidence suggests that CAFs impair anti-tumor immunity, supporting tumor cell growth and dissemination (Turley et al., *Nat Rev Immunol*, 15: 669-682, 2015; Chen et al., *Nat Rev Drug Discov*, 18: 99-115). In line with this notion, a recent report demonstrated that CAFs are major drivers of increased metastasis in response to TGF-b and poor outcomes in colorectal cancer (CRC) (Calon et al., *Nat Genet*, 47: 320-329, 2015).

Notwithstanding the emerging role for CAFs and other stromal cells in immunosuppression and resistance to immunotherapy, the downstream molecular circuitry responsible for crosstalk between CAFs and tumor-infiltrating immune cells remains poorly understood. Numerous reports have shown that podoplanin (PDPN, gp38, Aggrus, or T1α), a single transmembrane (STM)-containing receptor predominantly expressed by CAFs and LECs, is over-expressed in tumors and is associated with poor prognosis (Astarita et al., *Nat Immunol*, 16: 75-84, 2015). However, the function of PDPN in the tumor unclear, and fundamental aspects of PDPN biology have remained largely uncharacterized. We have shown that in mouse lymph node fibroblasts, PDPN is a master regulator of actomyosin contractility and is inhibited by the C-type lectin receptor CLEC-2 (*Clec1b*), which is predominantly expressed in platelets and dendritic cells (Astarita et al., *Nat Immunol*, 16: 75-84, 2015; Acton et al., *Nature*, 514: 498-502, 2014). Upon inflammation, CLEC-2 attenuates PDPN-mediated contractility, resulting in reduced lymph node stiffness and enhanced immunity (Astarita et al., *Nat Immunol*, 16: 75-84, 2015). It is unknown whether PDPN functions similarly in human fibroblasts to confer contractility and mediate interactions with immune cells, particularly in the unique environment that surrounds solid tumors.

Here, a gene signature representing the presence of $PDPN^+$ CAFs was found to correlate with a significant reduction in patient survival, indicating that expression of PDPN in human fibroblasts may importantly influence tumor progression.

A. PDPN expressed by CAFs correlates with poor outcome in human CRC

PDPN expression is highly elevated in several cancers, including squamous cell carcinoma of the head and neck, gliomas, and colon cancers, and is associated with poor survival outcomes. These studies are largely based on immunohistochemistry analysis and do not always define the cellular source of PDPN. This distinction is important when considering the function of this protein as it can be expressed by tumor cells, LECs, CAFs, and even some immune cells, all of which exert different effects in the TME (Astarita et al., *Front Immunol*, 3: 283, 2012; Turley et al., *Nat Rev Immunol*, 15: 669-682, 2015). A recent report identified TGFb signaling in PDPN+FAP+ CAFs as a major driver of metastasis in CRC patients (Calon et al., *Nat Genet*, 47: 320-329, 2015).

Thus, to determine whether PDPN expression at the RNA level was a significant prognostic factor in CRC, bulk tumor gene expression and recurrence-free survival (RFS) data from two previously published human CRC studies were queried. In a cohort consisting of stage II patients (de Sousa et al., *Cell Stem Cell,* 9: 476-485, 2011) (GSE33113, n = 85), we found that PDPN expression was significantly associated with reduced survival (Fig. 13A). Similarly, in a larger CRC cohort that included patients from all stages (Marisa et al., *PLoS Med*, 10: e1001453, 2013) (GSE39582, n = 511), PDPN expression was again significantly associated with reduced RFS, both in the entire cohort and in stage II patients (Figs. 13B and 19A). In late stage disease, PDPN expression was a highly significant risk factor for stage IV (Fig. 19B), but not for stage III CRC patients (Table 10).

B. PDPN functions as a regulator of cell tension/contraction in primary human fibroblasts

In light of the significant association between PDPN expression and reduced survival in CRC, we next sought to determine the function of PDPN in primary fibroblasts isolated from CRC lesions. *Pdpn* -/- cells were generated using a Cas9-RNP-CRISPR system in primary human CAFs grown from cancerous colorectal tissue, which express high endogenous levels of PDPN (Fig. 26A). Upon seeding these cells into 3D collagen matrices, we observed that *Pdpn*-/- CAFs exhibited a markedly polarized morphology compared to WT CAFs, with an approximately 70% more elongated phenotype (Figs. 26B-26C). In addition, to test whether the PDPN deletion had other functional consequences, we performed a variety of assays to measure growth rate, the ability of cells to generate tension, and the ability of cells to adhere to surfaces. To test contraction, the CAFs were seeded into 3D matrices and were allowed contract the gels over a period of three days. Consistent with our hypothesis that PDPN is a master regulator of fibroblast contractility, the PDPN-deficient cells were significantly impaired in their ability to contract the gels (Fig. 26D). Finally, we examined whether a lack of PDPN affects the growth of these cells, given that fibroblast contractility can control cell growth and survival. Notably, *Pdpn*-/- fibroblasts grew significantly more slowly compared with WT cells (Fig. 26E). Altogether, these results indicate that PDPN plays a major role in actomyosin contractility in human cells and promotes fibroblast growth in a cell-autonomous manner.

C. Activated fibroblast signature

We next asked whether PDPN expression in the tumor microenvironment (TME) was associated primarily with fibroblasts or with tumor cells. We first curated a list of activated fibroblast genes (activated fibroblast signature) from the literature and our own data (Table 11) and used it to infer fibroblast levels in

bulk tumor RNA-seq data. We then utilized published DNA copy number-based tumor content data (Taylor et al., *Cancer Cell*, 33: 676-689, 2018) and investigated the association between PDPN expression, inferred fibroblast levels, and tumor content. We found that *PDPN* mRNA levels had a strong positive correlation with inferred activated fibroblast levels (Fig. 13D), but had a negative correlation with tumor content (Fig. 13C), indicating that PDPN expression in the TME comes largely from fibroblasts.

D. FAP$^+$ fibroblast signature

We next sought to capture the presence of cancer-associated fibroblasts (CAFs) at a finer level in RNA-seq datasets. We utilized data from a recent study that defined a role for FAP$^+$ stromal cells in driving CRC (Calon et al., *Nat Genet*, 47: 320-329, 2015). We performed differential expression tests among the four sorted cell populations of the study (FAP$^+$ fibroblasts, CD31$^+$ endothelial cells, immune cells (CD45$^+$ cells), and tumor cells (EpCAM$^+$ cells) and defined a FAP$^+$ fibroblast signature from the top 35 genes expressed only by fibroblasts and not by other cells (Table 12).

E. Association of activated fibroblast signature and FAP$^+$ fibroblast signature with survival

We then investigated whether the activated fibroblast signature and the FAP$^+$ fibroblast signature had prognostic value in human CRC. Both signatures were significantly associated with poor relapse-free survival (RFS) in both GSE33113 and GSE39582 (Figs. 13E-13F, 19C-19D). Because GSE33113 included only stage II patients, we then asked whether the stage II cohort in GSE39582 confirmed the signatures as negative prognostics. We found that both signatures were also associated with poor RFS in the GSE39582 stage II cohort (Figs. 19E-19F). Both fibroblast signatures remained significant predictors of RFS when included in multivariate models fit to all patients while controlling for stage (Table 10). These data indicate that PDPN is an indicator of poor outcomes in CRC and that PDPN-expressing fibroblasts in the TME contribute to tumor growth.

Example 11. Characterization of the extracellular interactome

In an effort to better understand PDPN function in CAFs and to overcome the limitations of most commonly used receptor-ligand screening approaches, we built a library representing most STM human receptors engineered for controlled display on the cell surface. Additionally, we developed a tetramer-based screening method to detect transient, low affinity interactions. Here, we utilized this new platform to study the STM interactome of PDPN in humans, and identified the neutrophil marker CD177 as a novel binding partner.

A. A new platform for controlled protein display on the plasma membrane and enhanced detection of transient receptor-ligand interactions

Protein interactions in the extracellular milieu are often characterized by transient, low affinity binding (K_D in the micromolar to millimolar range) that challenge identification by most commonly used approaches (Martinez-Martin, 2017). To facilitate detection of such interactions, we developed a tetramer-based method for enhanced protein multimerization and binding avidity. First, this approach was used to test interactions between the immune receptors PD-L1/CD274 and the poliovirus receptor PVR and their

respective ligands. Briefly, PD-L1 or PVR, the query proteins, were expressed as recombinant biotinylated ectodomains, and then tetramerized using fluorescent streptavidin to enable quantification of receptor-ligand interactions. Next, the monomeric or tetrameric PD-L1 or PVR were tested for binding to cells transiently expressing the relevant binding partners. Tetramerization of the query protein significantly enhanced detection of receptor-ligand interactions over the monomeric ectodomain, including micromolar affinity interactions such as PD-1-PD-L1 (Figs. 14A and 14B).

We first tested this protein library for expression on transiently transfected cells, using a semi-automated transfection procedure. Notably, from over 3,500 STM proteins analyzed for cell surface expression, medium to high cell surface expression levels were achieved for over 75% of the STM proteins, whereas only ~10% of the proteins did not show detectable expression on the plasma membrane, indicating that most of the receptors in the library are displayed on the cell surface and available for interaction with the relevant binding partners (Fig. 14D).

Next, we sought to utilize the newly developed ectodomain-gD-GPI STM protein collection (Fig. 14C) in combination with the tetramer-based screening to enhance discovery of receptor-ligand interactions in high throughput. To do so, a method for automated cell transfection and screening was implemented, followed by high content imaging for detection of fluorescent tetramer binding to the cell surface (Fig. 14E). We first used this platform to study the immune receptor B7-H3/CD276 for cell surface interactors (Fig. 14F). The interleukin-20 receptor subunit alpha (IL20-RA) was detected as an interactor, in agreement with recent findings (Husain et al., *Mol Cell Proteomics*, 18: 2310-2323, 2019). To demonstrate that the gD tag and GPI anchor did not impact detection of protein interactions at the cell surface, B7-H3 was also screened against a library of STM proteins that were expressed as full-length proteins in the absence of any tags (Fig. 14G). In line with the previous results, this assay identified IL20-RA as a high scoring hit, which demonstrates that the ectodomain-gD-GPI library is amenable for detection of protein interactions on the cell surface.

B. . gD-GPI-tagged human STM receptor library

A list of STM receptors was compiled using bioinformatic analysis using various algorithms for prediction of protein features, such as protein domains and subcellular localizations, followed by manual curation and review of published annotations. This list was used to create a library consisting of most human STM receptor proteins (Table 7). STM receptors were expressed as extracellular domains (ECDs) fused to a glycosylphosphatidyl-inositol (GPI) - glycoprotein D (gD) tag (gD-GPI) to enhance expression at the cell surface (Fig. 14E). The boundaries of the extracellular domain (ECD) were annotated as in Example 1*B*. The ECD of each receptor, containing its native signal sequence, was synthesized and cloned into a pRK5 vector (Genentech) in frame with a gD-GPI tag.

C. Tetramerized query protein

The query protein PDPN was expressed as the PDPN extracellular domain (ECD) fused to an avi tag allowing site-directed biotinylation, was biotinylated, and was tetramerized for increased binding avidity using fluorescent streptavidin (Fig. 14E). To tetramerize ECDs, allophycocyanin (APC)-conjugated streptavidin was purchased from Prozyme as custom vials, typically at a concentration of 2

mg/mL. Avi-tagged, biotinylated PDPN ECDs were tetramerized following the protocol provided by the NIH Tetramer Core Facility. In brief, APC-conjugated streptavidin was added over 10 time intervals to maximize tetramer formation versus dimeric or trimeric species. The amount of streptavidin added was calculated based on the molecular weight of the PDPN and the streptavidin reagent, assuming 100 % biotinylation. Streptavidin was added at room temperature with the samples protected from light, and tetramers were subsequently stored on ice until the assay was performed. Tetramers were prepared fresh on the day of the assay.

D. Automated single-clone, cell-based Receptor Discovery Platform

The library of human STM receptors was screened for interaction with PDPN using a cell surface receptor interaction screen (Fig. 14E), as described in Section 2A *(ii)* herein. The tetramerized PDPN construct of Example 8*B* was used as a query protein. The gD-GPI-tagged human STM receptor library of Example 8*A* was used as a prey library.

i. Transfection of cells

The library of STM human receptors was expressed on COS-7 cells. Cells were transiently transfected with individual receptor clones following a reverse transfection protocol using a semi-automated procedure. Lipofectamine LTX-Plus reagent (Life Technologies) was used for transfection, following manufacturer's instruction with minor modifications. Briefly, 25 µL of Lipofectamine LTX-Plus mixture in Opti-MEM medium (Thermo) was dispensed to 384 well microtiter plates containing 6 ng of DNA per well. The DNA-lipofectamine complexes were incubated for 30 min at 37 °C, and subsequently the cells (resuspended in DMEM media at 0.125 million cells/mL) were aliquoted in the assay plates using an automatic cell dispenser.

ii. Cell surface interaction screen

A cell surface interaction screen for PDPN binding partners was performed 48 h after transfection. A number of GFP-tagged clones were included to control for cell transfection efficiency. Analysis of PDPN ECD binding to the cell surface was performed using an integrated robotic system consisting of automated liquid handling devices (plate dispensers and washers), to allow for high throughput analysis of PPIs while minimizing manual operations to increase data quality. Growth media was removed from cell cultures and cells were washed an incubated with 1% bovine serum albumin (BSA) for 30 min. Following washing, the cells were incubated with the PDPN ECD tetramer for 45 min at 4°C. Cell surface binding was assayed in PBS containing 0.1 % BSA supplemented with calcium and magnesium. Following incubation with PDPN, the cells were washed and fixed with 4% PFA and stored at 4°C protected from light. Images were acquired from individual wells using a high content microscope (In Cell 6000, GE Healthcare) assisted by a robotic arm. Cell surface tetramer staining was represented as fluorescent signal intensities (Fig. 14E).

iii. Image processing

Image data were exported as tiff files and processed using the Developer Toolbox version X software. Images were analyzed using a custom analysis module, and segmentations were performed based on positive cell surface staining. Typically, events in the range of 10-500 signal/noise ratio may be considered "hits" in the analysis module. Minimal post-processing analysis and exclusion parameters were set up to obtain optimal outline of desired objects and minimize any background signals due to screening artifacts. PDPN binding to the cell surface was represented as signal/noise ratio (Fig. 14E).

A single novel binding PDPN binding partner, CD177 (NB1, PRV1), was identified (Fig. 14H). CD177 is a GPI-linked cell surface glycoprotein expressed in neutrophils and a minor fraction of intratumoral regulatory T cells (Tregs) (Plitas et al., *Immunity*, 45: 1122-1134, 2016).

Similar screens performed against a library consisting of most STM-like receptors expressed as full-length proteins confirmed interaction between PDPN and human CLEC-2 (Fig. 20A); CLEC-2 is a known PDPN binding partner in murine models (Astarita et al., *Nat Immunol*, 16: 75-84, 2015).

iv. Validation of interactions between PDPN and CD177 and CLEC-2

To further validate the interactions between PDPN and CD177 and CLEC-2, we assayed binding using surface plasmon resonance (SPR). SPR was measured using a Proteon XPR36 Instrument (Biorad) or a Biacore 3000 (GE Healthcare). The purified proteins (CD177 or CLEC-2, expressed as recombinant ECDs) were immobilized on GLC or CM5 sensor chips, respectively, using the amine coupling method. Avidity AVITAG™ (Avi)-tagged PDPN was run as a soluble analyte at the indicated concentrations in PBS containing 0.01% Tween-20 (when the Proteon Instrument was used), or HBS-P buffer (0.01M Hepes, 0.15 M NaCl, 0.005% surfactant P20, pH 7.4), for Biacore assays. Bulk refractive index changes were removed by substrating a reference flow response. For K_D calculations, 300-400 resonance units were immobilized, and kinetic data were fit to equilibrium or a Langmuir model to calculate kinetic parameters for CD177 and CLEC-2 binding, respectively. For kinetics calculations, Avi-tagged monomeric PDPN ectodomain was used as the analyte. All sensorgrams were analyzed with BiaEvaluation 4.1 (Biacore) or Proteon Manager 3.1.0.6 (Proteon) software.

These studies corroborated the interaction between PDPN and CD177 (Figs. 14I-14J) and between PDPN and CLEC-2 (Fig. 20B). Interestingly, PDPN interacted with CD177 with micromolar binding affinity (K_D = 3.3±0.7 μM), one order of magnitude lower than the affinity detected for CLEC-2 (K_D = 210±0.3 nM) (Fig. 14I), illustrating the sensitivity of our approach to detect protein-protein interactions (PPIs) of a range of affinities.

v. Assessment of interactions between mouse PDPN, CD177, and CLEC-2

We also used SPR to test whether mouse CD177 and PDPN would interact. We were able to recapitulate mouse CLEC-2 binding to PDPN, but were unable to detect any binding of mouse CD177 to mouse PDPN in a variety of formats (not shown), possibly due to the low sequence conservation in mouse and human CD177, suggesting that this interaction plays a relevant function specific to the human immune system.

Example 12. PDPN, CLEC-2, and CD177-expressing cells in the tumor microenvironment

Primary human blood and colon tissues were analyzed to determine which cell types express PDPN and CD177.

A. Blood samples

Blood samples were obtained from healthy donors under the Genentech blood donation program. Neutrophils were isolated from blood using the MACSExpress Neutrophil isolation kit (Miltenyi). Peripheral blood mononuclear cells (PBMCs) were purified from heparinized blood by Ficoll (Lymphoprep) gradient centrifugation, followed by isolation of T cells using the Pan T Cell isolation kit (Miltenyi).

B. CAFs

Primary human colorectal cancer-associated fibroblasts (CAFs) were purchased from Vitro Biopharma and grown in MSC-Gro low serum growth media (Vitro Biopharma) for a maximum of 5-6 passages. The HT-29 cells were purchased from ATCC and grown in McCoy's 5a media with 10% FBS. All cells were cultured at 37°C and 5% CO_2.

C. CD177 in blood and colon cells

i. CD177 expression in blood neutrophils

We first confirmed the reported expression of CD177 on neutrophils in the blood. As previously reported (Bai et al., *Blood*, 130: 2092-2100, 2017), we found that the percentage of neutrophils expressing CD177 varied widely between individuals, with an average of about 60% of neutrophils being $CD177^+$ (Fig. 15A).

ii. Expression of PDPN and CD177 in microarray data

We next investigated RNA expression of PDPN and CD177 in the GSE33113 and GSE39582 microarray datasets. Expression of PDPN was significantly higher in tumor tissue compared to normal tissue, and expression of CD177 was much lower than expression of PDPN in tumors (Figs. 22A-22B).

iii. Expression of PDPN and CD177 in cell compartments

We next examined the expression patterns of PDPN and CD177 in human blood and colon tissues from healthy individuals and colorectal cancer (CRC) patients. RNA expression of PDPN and CD177 was significantly higher in tumors compared with normal tissues in the TCGA data set (Figs. 22A and 22B). In the two data sets examined in Figs. 13A-13F, CD177 and PDPN were expressed, but it is impossible to discern the cell source of RNA in bulk tumor RNA data (Figs. 22C and 22D). Thus, to study expression and cellular distribution at the protein level, fresh human tissues were digested into single cell suspensions using a digestion protocol that allowed for good recovery of all cell types, including stromal cells and immune cells, with good viability. Fluorescence-activated cell sorting (FACS) was performed, and samples were gated as in Fig. 15B.

We found that normal adjacent colon tissue contained relatively few neutrophils, whereas tumors had a large influx of neutrophils (Figs. 15B-15C). As in the blood, tumor neutrophils expressed varying amounts of CD177, but the ratio of CD177$^+$ neutrophils was similar between the blood and tumor for an individual (Figs. 15D-15E). Interestingly, CD177$^+$ neutrophils were slightly enriched in the tumor relative to the adjacent normal tissue (Figs. 15D-15E).

As was previously reported (Plitas et al., *Immunity*, 45: 1122-1134, 2016), we also observed that a small proportion of tumor Tregs expressed CD177, whereas CD177 was rarely observed on Tregs in non-tumor tissue, blood, or tonsil (data not shown). These CD177$^+$ Tregs were much less abundant than CD177$^+$ neutrophils.

We then examined the non-hematopoietic stromal compartment. Gates were chosen to include events that were live (as indicated by absence of 7-AAD staining), were singlets, were CD45$^-$ (i.e., were not immune cells, and were EpCAM$^-$) (i.e., were not tumor cells) (Fig. 15F). We found that approximately 40% of cancer-associated fibroblasts (CAFs), defined as total CD31$^-$ stroma, were PDPN$^+$ (Fig. 15G). While PDPN was also expressed by some lymphatic endothelial cells (LECs) and a small percentage of macrophages, the levels of PDPN on a per-cell basis were significantly higher on CAFs (Fig. 15H), indicating that they are the major source of PDPN in the tumor microenvironment (TME). This finding confirms the conclusions drawn from our bioinformatics analysis (Fig. 13D). Additionally, PDPN staining on CAFs was 6-fold higher than staining on fibroblasts from adjacent normal tissue, and a higher percentage of cells were PDPN$^+$ (Figs. 15I-15J).

We also examined fibroblasts in colon samples from patients with diverticulitis, an inflammatory condition, using the methods describe above. Interestingly, the fibroblasts in these tissues also upregulated PDPN relative to the normal tumor-adjacent tissue (Figs. 15I-15J). This finding is in line with previous observations that PDPN can be upregulated by a variety of inflammatory stimuli, such as TGF-β and IL-6 (Astarita et al., *Front Immunol*, 3: 283, 2012).

Overall, these data confirm that CAFs are the major source of PDPN in tumor tissue and indicate that both PDPN$^+$ CAFs and CD177$^+$ neutrophils are enriched in colon tumor tissues.

D. IHC and immunofluorescence localization of PDPN and CD177

To examine the localization of PDPN$^+$ and CD177$^+$ cells within the TME, we performed dual immunohistochemistry (IHC) and immunofluorescence staining for PDPN and CD177 in human colon tissues from CRC tumors (CRC colon) and normal adjacent tissue (adj colon). In normal tissues, PDPN staining was largely restricted to lymphatic vessels, and few neutrophils were observed (Figs, 16A, 23A, and 23C). In contrast, in tumor samples, PDPN was strongly upregulated in CAFs in the surrounding tumor stroma (Figs. 16B-16C and 23B), whereas it was rarely observed on the tumor cells. The PDPN$^+$ fibroblasts were generally aligned, creating large swaths of stroma running between tumor beds (Figs. 16B-16C). These fibers tended to run parallel to the tumor beds. Overall, while only about 20% of normal colon cells displayed some PDPN staining, greater than 60% of the tumor samples did (Fig. 16E). Co-staining with myeloperoxidase (MPO) confirmed that the majority of the CD177$^+$ cells were neutrophils (Figs. 16D, and 23D); this data, in combination with the FACS analysis, revealed that most CD177 signal would come from neutrophils. Similarly to PDPN$^+$ cells and in agreement with our tissue analyses (Fig.

15D), the amount of CD177+ neutrophils was also greatly increased in the tumor samples, with over 60% of tumor samples exhibiting CD177+ staining (Fig. 16E). Some CD177+ cells were identified in peritumoral stroma, where they closely interacted with PDPN+ cells (Figs. 16B-16C); however, most PDPN+ cells were not in contact with a CD177+ cell, as they were located sparsely throughout the tumor microenvironment. Overall, these results indicate that CD177-expressing neutrophils can interact with CAFs expressing PDPN in CRC tissue, suggesting that this newly discovered molecular interaction may influence CAF functions.

Example 13. Functional effects of interactions between PDPN, CLEC-2, and CD177

We next investigated the functional effects of the interactions between PDPN and CD177 and between PDPN and CLEC-2 on actomyosin contractility in CAFs. We performed 3D elongation experiments as described in Example 10*B*. 100 nM of recombinant CLEC-2 or CD177 was added to the media. These experiments showed that both CLEC-2 and CD177 caused elongation of CAFs (Figs. 17A-17B).

To test whether the observed effects occurred when CD177 and CLEC-2 were expressed endogenously on a cell, we performed similar assays in which CAFs were co-cultured with primary neutrophils (CD177+ CLEC-2+) or with T cells (CD177- CLEC2-). CAFs were seeded with a 5:1 ratio of neutrophils (neut) or T cells isolated from blood. We observed that the neutrophils caused CAF elongation to a similar extent as the recombinant proteins, whereas the T cells did not (Fig. 17C).

To confirm whether this phenotype was true across multiple types of fibroblasts, we repeated this experiment with primary human fibroblasts from healthy colon, bladder, and ovarian tissues. We observed increased elongation only in the two fibroblasts that expressed PDPN, the colon and bladder fibroblasts (Figs. 17D- 17E). These results indicate that CLEC-2 and CD177 are acting through PDPN on the plasma membrane to modulate fibroblast elongation.

We next tested whether CLEC-2 and CD177 also inhibit CAF contractility. Both proteins inhibited contractility by about 50% (Fig. 17F).

Example 14. Phosphoproteomics analysis

Next, we sought to study the mechanism underlying CD177 modulation of PDPN functions in primary human CAFs isolated from CRC tissue, which express high endogenous levels of PDPN. First, we analyzed changes in the transcriptional profile of CAFs upon stimulation with CLEC-2 and CD177. No significant changes in the CAF transcriptome were observed (data not shown), suggesting that PDPN targeting may have a more rapid, transient impact on the CAF proteome. Thus, to comprehensively survey signaling pathways and effector proteins modulated by CD177 and CLEC-2, we performed global quantitation of the proteome and phospho-proteome using a deep, multiplexed proteomics approach.

Briefly, CAFs were stimulated with recombinant CD177 or CLEC-2 proteins for 2 min and 30 min, and the resulting whole cell extracts were subjected to global phosphorylation analysis using liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) (Fig. 18A). We utilized a proteomics profiling method that combines 10-plex tandem mass tag (TMT) labeling of proteome fractions for relative quantitation of phosphopeptides across all conditions, with strong cation exchange

fractionation and TiO2 phosphopeptide enrichment to allow for deep phosphoproteomics profiling. Global proteome profiling was also performed to assess protein abundance, followed by computational data processing for total protein and phosphosite quantitation, and finally statistical testing for relative differences between treatment groups (Beausoleil et al., *Nat Biotechnol*, 24: 1285-1292, 2006). Importantly, this method demonstrated that CD177 or CLEC-2 stimulation did not significantly alter the levels of total protein at 2 minutes or 30 minutes, and thus allowed us to conclude that the observed differential phosphorylation events could be attributed specifically to signaling changes, altogether enabling assessment of global protein levels for almost 3,000 (~70%) of the quantified phospho-sites (Figs. 18G and 24A). Changes in the global phosphoproteome were more prominent after 30 min stimulation compared with 2 min (Figs. 18B and 24F). At 2 min, 30 proteins were significantly modified by either CD177 or CLEC-2 (Fig. 18C), whereas about 300 phosphosites, corresponding to 226 proteins, were significantly regulated after 30 min stimulation with the PDPN binders (Fig. 18D).

To functionally categorize the pathways modulated by PDPN engagement, the phosphoproteins significantly regulated by CD177 or CLEC-2 were analyzed for enrichment in Gene Ontology (GO) terms. These results highlighted major roles for PDPN in cytoskeleton rearrangement, cell motility, extracellular matrix deposition, and secretory pathways, in line with previous data from our laboratory and others (Astarita et al., *Nat Immunol,* 16: 75-84, 2015; Acton et al., *Nature,* 514: 498-502, 2014; Martinez et al., *Cell Rep,* 29: 2810-2822 e2815,2019) (Figs. 18E and 24A). Important modulators of microtubule function, cytoskeleton organization, and transport processes were substantially modulated upon PDPN targeting, including plectin (PLEC), the microtubule-associated proteins MAP1S or MAP4, the guanine-nucleotide exchange factors GBF1 and RGH10, or the pleckstrin homology-like domain family B members 1 and 2 (PHLB1 and PHLB2), among others (Fig. 18F). Moreover, and interestingly, these data also suggested prominent alterations in cell growth and differentiation, as well as metabolic processes related to cellular stress and response to exogenous stimuli, biological processes that are relevant to CAF biology that have not been previously linked with PDPN (Fig. 18E). Several key modulators of these processes were significantly post-translationally modified upon CLEC-2 and CD177 stimulation, including a number of transcriptional regulators and RNA binding molecules such as MED1, WWTR1/TAZ, LARP1, and NCBP1 (Fig. 18F).

This global assessment of the phosphoproteome supports a critical role of PDPN signaling in altering CAF cell morphology and cytoskeleton rearrangement, as well as previously unappreciated processes such as cell growth. Furthermore, these data indicate that the binding of either CLEC-2 or CD177 can profoundly alter PDPN signaling into CAFs, indicating that the interactions of immune cells with CAFs could change the TME in previously unappreciated ways.

A. Phosphoproteomics methods

i. Proteomic sample preparation

CAFs were grown to ~70% confluency on 15 cm dishes. The day of the assay, the cells were starved for 2 hours, followed by stimulation with recombinant CLEC-2 or CD177 for 2 or 30 minutes (Table 13). Stimulations were performed at 37°C in serum free media. After stimulation, the cells were washed with ice-cold PBS and subsequently harvested and lysed in 20 mM HEPES pH 8.0, 9 M urea

containing 1 mM sodium orthovanadate, 2.5 mM sodium pyrophosphate, and 1 mM β-glycerophosphate. Lysates from 5 conditions were analyzed. These were: untreated, CLEC-2 treated for 2 min & 30 min, and CD177 treated for 2 min & 30 min. Two bioreplicates of each 5-plex experiment was performed and combined to make a 10-plex experiment. Samples were sonicated using a Misonix Microson XL sonicator followed by centrifugation at 20,000 g for 20 min at 15 °C. Protein concentration was measured using Bradford assay (BioRad). Proteins (1mg/condition) were reduced with 5 mM dithiothreitol (DTT) at 37 °C for 1h followed by alkylation with 15 mM iodoacetamide (IAA) at room temperature for 20 min in the dark. Samples were diluted to a final concentration of 2M urea prior to digestion with Lys-C (Wako, Japan) at an enzyme:substrate ratio (E:S) of 1:50 at 37°C for 4 h followed by tryptic (Promega) digestion at an E:S ratio of 1:50 at 37°C overnight. The peptide solution was acidified with 20% trifluoroacetic acid (TFA) prior to solid-phase extraction using C18 cartridge (50 mg absorbent) from Waters. Peptides were eluted with 2 x 0.5 mL of 40% acetonitrile (ACN)/0.1% TFA followed by peptide concentration measurement using a quantitative colorimetric peptide assay kit (Thermo). Equal amounts per condition were subjected to lyophilization overnight.

ii. TMT labeling

The peptide mixture was reconstituted in 1000 µL of HEPES (200 mM, pH 8.5) + 300 µL of ACN, and 100 µL of TMT reagent was added to each of the ten samples (each vial of TMT reagent (Thermo) was dissolved in 40 µL of ACN). Labeling was performed at RT for 1.5 h. A small portion (2 µL) from each condition was mixed, desalted, and analyzed to determine labeling efficiency as well as the relative protein abundance in each sample. The reaction was quenched with 100 µL of 5% hydroxylamine once labeling efficiency was determined to be at least 95%. Samples were mixed at equal amounts followed by acidification using 20% TFA and lyophilized overnight. The 10-plex TMT labeled peptide mixture was desalted using C18 cartridge (200 mg absorbent) from Waters. Sample was eluted with 3 x 1 mL of 60% ACN/0.1% TFA. A small amount (~0.5 mg) was saved for total protein profiling and ~6.5 mg was subjected to global phosphorylation analysis.

iii. Global phosphorylation & global protein analyses

Strong cation exchange (SCX) fractionation was performed using a PolySulfoethyl 4.6 mm ID x 200 mm, 5µm, 200Å column (The Nest Group) at a flow rate of 1 mL/min on the HP1100 HPLC system (Agilent Technologies). Sixteen fractions were collected and then desalted followed by phosphopeptide enrichment using the TiO2 enrichment Phos-TiO kit (GL Sciences). For protein profiling, the sample was subjected to high pH reverse phase fractionation, in which 96 fractions were collected and pooled into 24 fractions. Samples were desalted with C18 stagetip prior to mass spectrometry analysis.

iv. Mass spectrometry analysis

Desalted peptides were reconstituted in 2% ACN/0.1% formic acid (FA)/water and loaded onto a C18 column (1.7 µm BEH, 130 Å, 0.1 x 250 mm, New Objective) using a NanoAcquity UPLC system (Waters) at a flow rate of 0.7 µL/min. A gradient of 2% to 30% solvent B (0.1% FA/2% water/ACN) at 0.5 µL/min was applied over 155 min with a total analysis time of 180 min to separate the peptides. Peptides

were analyzed using an Orbitrap Fusion Lumos instrument (Thermo). Precursor ions (MS1) were analyzed in the Orbitrap (AGC target 1E6, 120,000 mass resolution, 50 ms maximum injection time) and 10 most abundant species were selected for fragmentation (MS2). Ions were filtered based on charge state ≥ 2 (z =2, 3 & 4-6) and monoisotopic peak assignment and dynamic exclusion (45 s ± 10 ppm) was enabled. Each precursor was isolated at a mass width of 0.5 Th followed by fragmentation using collision-induced dissociation (CID at 35 NCE), MS2 AGC target was set at 2.0E4 with a maximum injection time of 200 ms. Multiple fragment ions were isolated using synchronous precursor selection (SPS) prior to HCD (55 NCE, SPS notches = 8, AGC target = 2.0E5, maximum injection time of 150 ms) MS3 fragmentation and Orbitrap analysis at 50,000 resolution. For global phosphorylation analysis, a neutral loss of 79.97 Da was specified to activate a multistage activation allowing for better identification of phosphorylated species. In addition, MS3 maximum injection time was set to 350 ms.

v. Mass spectrometry data analysis

MS/MS data was searched using the Mascot search algorithm (Matrix Sciences) against a concatenated forward-reverse target-decoy database (downloaded from UniProt in June 2016) consisting of Homo sapiens proteins and common contaminant sequences. Spectra were assigned using a precursor mass tolerance of 50 ppm and fragment ion tolerance of 0.8 Da. Static modifications included carbamidomethyl cysteine (+57.0215 Da), TMT (229.1629 Da) on both the N-terminus of the peptides and lysine residues. Variable modification included oxidized methionine (+15.994 Da) and phosphorylation on serine, threonine and tyrosine residues (+79.9663 Da) for phosphorylation analysis. Trypsin specificity with up to 3 missed cleavages was specified. Peptide spectral matches were filtered at 5% false discovery rate (FDR) followed by protein filtering at 2% FDR. For phosphorylated species, the AScore algorithm was applied to determine the exact phosphorylation site localization16. MS3 TMT quantification was performed using Mojave module, filtering out TMT peaks in MS3 scans that summed to less than 30,000 across all 10 channels. Each peptide was quantified by summing the TMT signal for each sample from all PSMs. Finally, peptides shorter than 7 residues were filtered out.

vi. Mass spectrometry statistical analysis

For the global phospho-proteomics assay, all tryptic phospho-peptides covering identical phospho-site(s) were grouped under a single phospho-site group identifier, including groups that cover more than a single phospho-site. Then, for each phospho-site group (or protein in the global proteome assay) a model was fitted in MSstats v3.7.137 using a Tukey Median Polish summary on all quantified peptides across replicates with imputation of missing values below a censoring threshold of 28. Within MSstats, the model estimated fold change and statistical significance was computed for all compared treatment groups. Significantly altered phospho-site groups were determined by setting a threshold of $|Log2(Fold\text{-}Change)| > 1$ and p-value < 0.05. All subsets of significantly altered phospho-site groups were then annotated and tested for over-represented biological annotations (Gene Ontology, PFAM, and KEGG), within each group comparison, with the GoStats package (Falcon and Gentleman, 2007). Significant annotations were defined by a q-value < 0.05, group size > 2 and genome occurrence < 1000

threshold. The significant terms were then further manually grouped into simplified, non-redundant categories for biological process terminology and tested for over-representation with a Fisher's exact test.

Example 15. Enhancement of tumor growth by PDPN$^+$ CAFs is restrained by CD177

In light of our results showing that PDPN controls CAF growth and actomyosin contractility, and the prognostic significance of PDPN in CRC patients, we next decided to assess whether CRC CAFs could directly support tumor growth. A SW480 tumor cell line expressing red fluorescent protein was generated to enable quantification of tumor organoid growth. Tumor cells were grown alone or in co-culture with WT or PDPN-deficient CAFs, and the CAFs were assessed for their ability to promote tumor organoid growth. WT CAFs significantly enhanced tumor growth compared to tumor cells grown alone. Notably, the *Pdpn-/-* CAFs were significantly worse at supporting organoid growth, which indicates a central role for PDPN signaling in maintaining the tumor-supporting functions of CAFs (Figs. 27A and 27B). Next, given that CLEC-2 and CD177 significantly affected the morphology and contractility of CAFs, we sought to evaluate whether CD177 or CLEC-2 would impact the ability of the CAFs to support tumor organoid growth. To this end, tumor cells and CAF co-cultures were stimulated with CD177 and CLEC-2 to mimic interactions between CAFs and immune cells. Tumor organoid growth was evaluated in cultures for 17 days. Remarkably, the increased growth caused by PDPN+ CAFs was significantly decreased upon CD177 or CLEC-2 stimulation, indicating that these molecules inhibit PDPN functions and thereby limit the pro-tumorigenic potential of the CAFs (Figs. 27C and 27D).

A. Tumor organoid culture methods

To generate the 3D organoid cultures, 2,000 SW-480 tumor cells stably expressing red fluorescent protein (RFP) were seeded in 100 µL of MATRIGEL® Matrix (CORNING®, 356231) with or without 100,000 WT or *Pdpn-/-* CAFs. Tumor organoids were prepared as described previously (Dominguez et al., *Cancer Discov,* 10: 232-253, 2019). Briefly, the mixtures were plated in 24-well glass-bottom plates coated with 100 µL of the Matrigel® to prevent attachment of the cells to the coverslip. Next, 2 mL of the tumor cell growth media was added on top of the cultures following gel polymerization, and cultures were monitored for 12-17 days. For CLEC-2 and CD177 treatments, 150 nM of tetramerized CLEC-2 or CD177, provided as tetramers comprising biotinylated extracellular domains of CD177 or CLEC-2 conjugated to streptavidin, were added directly to the MATRIGEL®-cell mixture prior to plating. Additionally, 150 nM of each tetramer was supplemented in the media after plating the organoids, and tetramer additions were repeated every 72 h until day 15. The plates were imaged every 4 days on a NIKON® Ti-E inverted microscope with an automated stage (Applied Scientific Instrumentation), using a NIKON® 4X Plan Fluor objective (NA: 0.13). Images were recorded in tetramethylrhodamine (TRITC) and brightfield channels, and spheres representing tumor organoids were stitched and focused on a single maximum image projection with an extended depth of focus module (EDF, Nikon®). The total area of tumor organoids for each image was analyzed in MATLAB® (vR2018a, MATHWORKS®).

Table 1. Bait proteins

Bait name	Bait Entrez ID	Bait Uniprot ID	Bait sequence boundaries

ACVR1	90	Q04771	M1-E123
ACVR1B	91	P36896	M1-E126
ADAM17	6868	P78536	M1-N671
AGER	177	Q15109	M1-T340
ALCAM	214	Q13740	M1-K527
AMICA1	120425	Q86YT9	M1-Q274
AMIGO1	57463	Q86WK6	M1-A373
AMIGO2	347902	Q86SJ2	M1-T398
AMIGO3	386724	Q86WK7	M1-T383
AXL	558	P30530	M1-P449
BAMBI	25805	Q13145	M1-A152
BCAM	4059	P50895	M1-G548
BGN	633	P21810	M1-K367
BOC	91653	Q9BWV1	M1-Y855
BSG	682	P35613	M1-A323
BTLA	151888	Q7Z6A9	M1-P152
BTN1A1	696	Q13410	M1-T244
BTN2A1	11120	Q7KYR7	M1-P246
BTN2A3P	54718	Q96KV6	M1-P244
BTN3A1	11119	O00481	M1-A250
BTN3A2	11118	P78410	M1-P247
BTN3A3	10384	O00478	M1-P247
BTNL2	56244	Q9UIR0	M1-W455
BTNL3	10917	Q6UXE8	M1-S237
BTNL8	79908	Q6UX41	M1-K238
BTNL9	153579	Q6UXG8	M1-K256
BUTR1	100129094	A8MVZ5	M1-A255
C10orf54	64115	Q9H7M9	M1-A195
C19orf38	255809	A8MVS5	M1-L119
C6orf25	80739	O95866	M1-Q142
CADM1	23705	Q9BY67	M1-H374
CADM2	253559	Q8N3J6	M1-A368
CADM3	57863	Q8N126	M1-H330
CADM4	199731	Q8NFZ8	M1-A324
CD101	9398	Q93033	M1-P954

CD109	135228	Q6YHK3	M1-S1423
CD14	929	P08571	M1-N345
CD160	11126	O95971	M1-S160
CD163	9332	Q86VB7	S42-S1050
CD164	8763	Q04900	M1-D162
CD164L2	388611	Q6UWJ8	M1-S141
CD177	57126	Q8N6Q3	M1-G408
CD19	930	P15391	M1-K291
CD1A	909	P06126	M1-V300
CD1B	910	P29016	M1-S303
CD1C	911	P29017	M1-N303
CD1D	912	P15813	M1-S301
CD1E	913	P15812	M1-G303
CD2	914	P06729	M1-D209
CD200	4345	P41217	M1-G232
CD200R1	131450	Q8TD46	M1-K238
CD200R1L	344807	Q6Q8B3	M1-S237
CD22	933	P20273	M1-G685
CD226	10666	Q15762	M1-T250
CD244	51744	Q9BZW8	M1-P229
CD27	939	P26842	M1-R191
CD274	29126	Q9NZQ7	M1-R191
CD276	80381	Q5ZPR3	M1-A466
CD28	940	P10747	M1-P152
CD300A	11314	Q9UGN4	M1-P180
CD300C	10871	Q08708	M1-R183
CD300E	342510	Q496F6	M1-H173
CD300LB	124599	A8K4G0	M1-K147
CD300LD	100131439	Q6UXZ3	M1-H165
CD300LF	146722	Q8TDQ1	M1-S156
CD300LG	146894	Q6UXG3	M1-R247
CD320	51293	Q9NPF0	M1-G230
CD33	945	P20138	M1-G260
CD34	947	P28906	M1-T290
CD3D	915	P04234	M1-G106

CD3E	916	P07766	M1-D126
CD3G	917	P09693	M1-G117
CD4	920	P01730	M1-P396
CD40	958	P25942	M1-A194
CD47	961	Q08722	M1-N142
CD48	962	P09326	M1-S220
CD5	921	P06127	M1-T379
CD55	1604	P08174	M1-T352
CD58	965	P19256	M1-R215
CD59	966	P13987	M1-P128
CD6	923	P30203	M1-L402
CD7	924	P09564	M1-R143
CD79A	973	P11912	M1-G160
CD79B	974	P40259	M1-N242
CD80	941	P33681	M1-N242
CD83	9308	Q01151	M1-E144
CD84	8832	Q9UIB8	M1-G225
CD86	942	P42081	M1-P135
CD8A	925	P01732	M1-D182
CD8B	926	P10966	M1-P170
CD96-1	10225	P40200-1	M1-G518
CD96-2	10225	P40200-2	M1-G502
CDH11	1009	P55287	M1-T617
CDON	50937	Q4KMG0	M1-D963
CEACAM1	634	P13688	M1-A429
CEACAM16	388551	Q2WEN9	M1-G425
CEACAM19	56971	Q7Z692	M1-A160
CEACAM20	125931	Q6UY09	M1-A447
CEACAM21	90273	Q3KPI0	M1-G240
CEACAM3	1084	P40198	M1-G155
CEACAM4	1089	O75871	M1-G155
CEACAM5	1048	P06731	M1-A685
CEACAM6	4680	P40199	M1-S321
CEACAM7	1087	Q14002	M1-S243
CEACAM8	1088	P31997	M1-S327

CHL1	10752	O00533	M1-G1081
CLEC12A	160364	Q5QGZ9	K74-A265
CLEC12B	387837	Q2HXU8	L65-D276
CLEC14A	161198	Q86T13	M1-A397
CLEC1B	51266	Q9P126	S55-P229
CLMP	79827	Q9H6B4	M1-A235
CNTFR	1271	P26992	M1-S342
CNTN1	1272	Q12860	M1-S993
CNTN2	6900	Q02246	M1-N1012
CNTN3	5067	Q9P232	M1-N1008
CNTN4	152330	Q8IWV2	M1-S1000
CNTN5	53942	O94779	M1-A1073
CNTN6	27255	Q9UQ52	M1-S998
CRLF1	9244	O75462	M1-R422
CRTAM	56253	O95727	M1-R283
CSF1R	1436	P07333	M1-P517
CSF2RB	1439	P32927	M1-P441
CSF3R	1441	Q99062	M1-H627
CTLA4	1493	P16410	M1-F162
CXADR	1525	P78310	M1-G237
DAG1	1605	Q14118	M1-V749
DCC	1630	P43146	M1-N1097
DCN	1634	P07585	M1-K359
DKK3	27122	Q9UBP4	M1-I350
DLK1	8788	P80370	M1-C306
DPP4	1803	P27487	N29-P766
DSCAM	1826	O60469	M1-K1594
DSCAML1	57453	Q8TD84	M1-V1589
EDA2R	60401	Q9HAV5	M1-L139
EDAR	10913	Q9UNE0	M1-A187
EFNB1	1947	P98172	M1-K237
EFNB2	1948	P52799	M1-G230
EFNB3	1949	Q15768	M1-P226
EMB	133418	Q6PCB8	M1-P263
ENG	2022	P17813	M1-P590

EPHB6	2051	O15197	M1-L595
ERMAP	114625	Q96PL5	M1-A155
ESAM	90952	Q96AP7	M1-A248
F11R	50848	Q96AP7	M1-V238
F3	2152	Q9Y624	M1-I252
FAIM3	9214	P13726	M1-G251
FAM187A	100528020	O60667	M1-E379
FAM187B	148109	Q17R55	M1-K335
FAS	355	P25445	M1-N173
FCAMR	83953	Q8WWV6	M1-R450
FCAR	2204	P24071	M1-N227
FCER1A	2205	P12319	M1-Q205
FCGRT	2217	P55899	M1-S297
FCRL1	115350	Q96LA6	M1-G308
FCRL2	79368	Q96LA5	M1-G400
FCRL3	115352	Q96P31	M1-G576
FCRL4	83417	Q96PJ5	M1-G386
FCRL5	83416	Q96RD9	M1-G851
FCRL6	343413	Q6DN72	M1-N306
FGFR1	2260	P11362	M1-E376
FGFR2	2263	P21802	M1-E377
FGFR3	2261	P22607	M1-G375
FGFR4	2264	P22455	M1-D369
FGFRL1	53834	Q8N441	M1-P378
FLT1	2321	P17948	M1-E758
FLT3	2322	P36888	M1-S543
FLT4	2324	P35916	M1-E775
GP2	2813	P55259	M1-R502
GP5	2814	P40197	M1-G523
GP6	51206	Q9HCN6	M1-K267
GP9	2815	P14770	M1-R145
GPA33	10223	Q99795	M1-A236
GPNMB-1	10457	Q14956-1	K23-N498
GPNMB-2	10457	Q14956-2	K23-N486
GPR116	221395	Q8IZF2	M1-S1006

GPR124	25960	Q96PE1	M1-P771
GPR125	166647	Q8IWK6	M1-P761
GREM1	26585	O60565	M1-D184
HAVCR1	26762	Q96D42	M1-G290
HAVCR2	84868	Q8TDQ0	M1-G202
HEPACAM	220296	Q14CZ8	M1-R237
HEPACAM2	253012	A8MVW5	M1-P351
HFE	3077	Q30201	M1-V306
HHLA2	11148	Q9UM44	M1-G346
ICAM1	3383	P05362	M1-E480
ICAM2	3384	P13598	M1-Q223
ICAM3	3385	P32942	M1-H485
ICAM4	3386	Q14773	M1-A240
ICAM5	7087	Q9UMF0	M1-W835
ICOS	29851	Q9Y6W8	M1-F141
ICOSLG	23308	O75144	
IFNGR1	3459	P15260	M1-G245
IGDCC3	9543	Q8IVU1	M1-G640
IGDCC4	57722	Q8TDY8	M1-T957
IGFL3	388555	Q6UXB1	M1-P125
IGFLR1	79713	Q9H665	M1-P163
IGSF1	3547	Q8N6C5	E581-I1336
IGSF11	152404	Q5DX21	M1-G245
IGSF21	84966	Q96ID5	M1-A452
IGSF3	3321	O75054	M1-A1124
IGSF5	150084	Q9NSI5	M1-G270
IGSF6	10261	O95976	M1-S153
IGSF8	93185	Q969P0	M1-T579
IGSF9	57549	Q9P2J2	M1-G738
IGSF9B	22997	Q9UPX0	M1-G726
IL11RA	3590	Q14626	M1-Q365
IL18R1	8809	Q13478	M1-G330
IL18RAP	8807	O95256	M1-K355
IL1RAP	3556	Q9NPH3	M1-T367
IL1RAPL1	11141	Q9NZN1	M1-T357

IL1RAPL2	26280	Q9NP60	M1-E356
IL1RL1	9173	Q01638	M1-S328
IL1RL2	8808	Q9HB29	M1-R335
IL20RA	53832	Q9UHF4	M1-K250
IL22RA1	58985	Q8N6P7	M1-T228
IL31RA	133396	Q8NI17	M1-E519
IL6R	3570	P08887	M1-T366
IL6ST	3572	P40189	M1-A620
ILDR1	286676	Q86SU0	M1-H167
ILDR2	387597	Q71H61	M1-E186
ISLR2	57611	Q6UXK2	M1-K584
IZUMO1	284359	Q8IYV9	M1-R292
JAM2	58494	P57087	M1-S238
JAM3	83700	Q9BX67	M1-N241
KDR	3791	P35968	M1-E764
KIAA0319	9856	Q5VV43	M1-S955
KIAA1324	57535	Q6UXG2	M1-K910
KIR2DL1	3802	P43626	M1-H245
KIR2DL2	3803	P43631	M1-H245
KIR2DL3	3804	P43628	M1-H245
KIR2DL4	3805	Q99706	M1-A243
KIR2DL5A	57292	Q8N109	M1-R236
KIR2DL5B	553128	Q8NHK3	M1-R236
KIR2DS1	3806	Q14954	M1-H245
KIR2DS2	100132285	P43631	M1-H245
KIR2DS3	3808	Q14952	M1-H245
KIR2DS4	3809	P43632	M1-H245
KIR2DS5	3810	Q14953	M1-H245
KIR3DL1	3811	P43629	M1-H340
KIR3DL2	3812	P43630	M1-H340
KIR3DL3	115653	Q8N743	M1-H323
KIR3DS1	3813	Q14943	M1-H340
KIRREL	55243	Q96J84	M1-G496
KIRREL2	84063	Q6UWL6	M1-R510
KIRREL3	84623	Q8IZU9	M1-A535

KIT	3815	P10721	M1-P524
KLRK1	22914	P26718	L79-V216
L1CAM	3897	P32004	M1-G1121
LAG3	3902	P18627	M1-L450
LAIR1	3903	Q6GTX8	M1-Y165
LAMP1	3916	P11279	M1-S381
LAMP2	3920	P13473	M1-N374
LEPR	3953	P48357	M1-A840
LIFR	3977	P42702	M1-S833
LILRA1	11024	O75019	M1-N461
LILRA2	11027	Q8N149	M1-L450
LILRA3	11026	Q8N6C8	M1-E439
LILRA4	23547	P59901	M1-N446
LILRA5	353514	A6NI73	M1-N265
LILRA6	79168	Q6PI73	M1-N447
LILRB1	10859	Q8NHL6	M1-G477
LILRB2	10288	Q8N423	M1-G460
LILRB3	11025	O75022	M1-E443
LILRB4	11006	Q8NHJ6	M1-R255
LILRB5	10990	O75023	M1-G458
LINGO1	84894	Q96FE5	M1-T561
LINGO2	158038	Q7L985	M1-T545
LINGO3	645191	P0C6S8	M1-T531
LINGO4	339398	Q6UY18	M1-A533
LOC374597	391123	P0DPA2	M1-A130
LRFN1	57622	Q9P244	M1-T535
LRFN2	57497	Q9ULH4	M1-T533
LRFN3	79414	Q9BTN0	M1-T538
LRFN4	78999	Q6PJG9	M1-L518
LRFN5	145581	Q96NI6	M1-T528
LRIG1	26018	Q96JA1	M1-G794
LRIG2	9860	O94898	M1-G807
LRIG3	121227	Q6UXM1	M1-V810
LRIT1	26103	Q9P2V4	M1-Q526
LRIT2	340745	A6NDA9	M1-H462

LRIT3	345193	Q3SXY7	M1-Q580
LRRC15	131578	Q8TF66	M1-G538
LRRC19	64922	Q9H756	M1-S269
LRRC24	441381	Q50LG9	M1-T405
LRRC25	126364	Q8N386	M1-T165
LRRC4	64101	Q9HBW1	M1-K527
LRRC4B	94030	Q9NT99	M1-K527
LRRC4C	57689	Q9HCJ2	M1-K527
LRRN1	57633	Q6UXK5	M1-A631
LRRN2	10446	O75325	M1-G630
LRRN3	54674	Q9H3W5	M1-T628
LRRTM3	347731	Q86VH5	M1-K419
LSAMP	4045	Q13449	M1-S317
LTBR	4055	P36941	M1-L226
LY6G6F	259215	Q5SQ64	M1-P234
LY9	4063	Q9HBG7	M1-K454
MADCAM1	8174	Q13477	M1-L318
MAG	4099	P20916	M1-M510
MCAM	4162	P43121	M1-G559
MDGA1	266727	Q8NFP4	M1-S932
MDGA2	161357	Q7Z553	M1-A933
MERTK	10461	Q12866	M1-L503
MFAP3L	9848	O75121	M1-D148
MICA	100507436	Q29983	M1-Q308
MICB	4277	Q29980	M1-D309
MILR1	284021	Q7Z6M3	M1-K227
MOG	4340	Q16653	M1-G154
MPZ	4359	P25189	M1-G155
MPZL1	9019	O95297	M1-V165
MPZL2	10205	O60487	M1-H152
MPZL3	196264	Q6UWV2	M1-S158
MUSK	4593	O15146	M1-T495
MXRA5	25878	Q9NR99	M1-F2828
MXRA8	54587	Q9BRK3	M1-Q341
NCAM1	4684	P13591	M1-A723

NCAM2	4685	O15394	M1-N697
NCR1	9437	O76036	M1-R258
NCR2	9436	O95944	M1-A192
NCR3	259197	O14931	M1-T138
NEGR1	257194	Q7Z3B1	M1-D327
NEO1	4756	Q92859	M1-N1103
NFAM1	150372	Q8NET5	M1-G1216
NFASC	23114	O94856	M1-N250
NGFR	4804	P08138	M1-P1061
NPHS1	4868	O60500	M1-P339
NPTN	27020	Q9Y639	M1-G1168
NRCAM	4897	Q92823	M1-G1168
NRG1	3084	Q02297	M1-Q240
NRG2	9542	O14511	M1-Q403
NRP2	8828	O60462	M1-P864
NTM	50863	Q9P121	M1-N321
NTRK1	4914	P04629	M1-S419
NTRK2	4915	Q16620	M1-H430
NTRK3	4916	Q16288	M1-G431
OPCML	4978	Q14982	M1-N322
OSCAR	126014	Q8IYS5	M1-V271
OSMR	9180	Q99650	M1-S739
PCDHGB6	56100	Q9Y5F9	M1-Y692
PDCD1	5133	Q15116	M1-V170
PDCD1LG2	80380	Q9BQ51	M1-T220
PDGFRA	5156	P16234	M1-A528
PDGFRB	5159	P09619	M1-V532
PDPN	10630	Q86YL7	M1-L131
PEAR1	375033	Q5VY43	M1-A757
PECAM1	5175	P16284	M1-A639
PIGR	5284	P01833	M1-A197
PILRA	29992	Q9UKJ1	M1-R191
PILRB	29990	Q9UKJ0	M1-R191
PLXNB2	23654	O15031	M1-S1199
PRLR	5618	P16471	M1-T236

PRTG	283659	Q2VWP7	M1-G950
PTGFRN	5738	Q9P2B2	M1-P832
PTK7	5754	Q13308	M1-T704
PTPRD	5789	P23468	M1-G1266
PTPRF	5792	P10586	M1-L1262
PTPRJ	5795	Q12913	M1-G971
PTPRK	5796	Q15262	M1-K752
PTPRM	5797	P28827	M1-K742
PTPRO	5800	Q16827	M1-N819
PTPRS	5802	Q13332	M1-G1282
PTPRT	11122	O14522	M1-K746
PTPRU	10076	Q92729	M1-L749
PVR	5817	P15151	M1-N343
PVRL1	5818	Q15223	M1-A355
PVRL2	5819	Q92692	M1-G360
NECTIN3	25945	Q9NQS3	M1-D400
PVRL4	81607	Q96NY8	M1-V350
REG3A	5068	Q06141	M1-D175
REG4	83998	Q9BYZ8	D23-P158
RELT	84957	Q969Z4	M1-Q162
RNF128	79589	Q8TEB7	M1-H205
RNF13	11342	O43567	M1-Y182
RNF130	55819	Q86XS8	M1-S194
RNF133	168433	Q8WVZ7	M1-H189
RNF149	284996	Q8NC42	M1-S200
RNF150	57484	Q9ULK6	M1-S208
RNF167	26001	Q9H6Y7	M1-G171
ROBO1	6091	Q9Y6N7	M1-P897
ROBO2	6092	Q9HCK4	M1-A860
ROBO3	64221	Q96MS0	M1-P891
ROBO4	54538	Q8WZ75	M1-K466
ROR1	4919	Q01973	M1-Y406
ROR2	4920	Q01974	M1-G403
SCN1B	6324	Q07699	M1-E160
SCN2B	6327	O60939	M1-A159

SCN3B	55800	Q9NY72	M1-E159
SCN4B	6330	Q8IWT1	M1-T161
SDK1	221935	Q7Z5N4	M1-E2007
SDK2	54549	Q58EX2	M1-W1930
SEMA3A	10371	Q14563	M1-V725
SEMA4A	64218	Q9H3S1	M1-H683
SEMA4B	10509	Q9NPR2	M1-E712
SEMA4C	54910	Q9C0C4	M1-G663
SEMA4D	10507	Q92854	M1-R734
SEMA4F	10505	O95754	M1-G660
SEMA4G	57715	Q9NTN9	M1-R674
SEMA5B	54437	Q9P283	M1-H1036
SEMA6A	57556	Q9H2E6	M1-Q644
SEMA7A	8482	O75326	M1-A644
SIGIRR	59307	Q6IA17	M1-H118
SIGLEC1	6614	Q9BZZ2	M1-Q1641
SIGLEC10	89790	Q96LC7	M1-N550
SIGLEC11	114132	Q96RL6	M1-G560
SIGLEC12	89858	Q96PQ1	M1-A481
SIGLEC14	100049587	Q08ET2	M1-T359
SIGLEC15	284266	Q6ZMC9	M1-T263
SIGLEC16	400709	A6NMB1	M1-G434
SIGLEC5	8778	O15389	M1-A440
SIGLEC6	946	O43699	M1-G346
SIGLEC7	27036	Q9Y286	M1-G350
SIGLEC8	27181	Q9NYZ4	M1-A363
SIGLEC9	27180	Q9Y336	M1-G348
SIRPA	140885	P78324	M1-Y373
SIRPB1	10326	O00241	M1-P370
SIRPB2	284759	Q5JXA9	M1-G287
SIRPD	128646	Q9H106	M1-K197
SIRPG	55423	Q9P1W8	M1-G361
SIT1	27240	Q9Y3P8	M1-A41
SKINTL	391037	A8MVG2	M1-S242
SLAMF1	6504	Q13291	M1-M226

SLAMF6	114836	Q96DU3	M1-M226
SLAMF7	57823	Q9NQ25	M1-D233
SLAMF8	56833	Q9P0V8	M1-F234
SLAMF9	89886	Q96A28	M1-S210
SLITRK1	114798	Q96PX8	M1-G623
SLITRK2	84631	Q9H156	M1-V620
TAPBPL	55080	Q9BX59	M1-E403
TARM1	441864	B6A8C7	M1-R236
TGFBR1	7046	P36897	M1-A128
TGFBR2	7048	P37173	M1-G169
TGFBR3	7049	Q03167	M1-V787
THBD	7056	P07204	M1-G516
THY1	7070	P04216	M1-K129
TIE1	7075	P35590	M1-Q759
TIGIT	201633	Q495A1	M1-P141
TIMD4	91937	Q96H15	M1-Q314
TMEM123	114908	Q8N131	M1-S168
TMEM132E	124842	Q6IEE7	M1-A803
TMEM25	84866	Q86YD3	M1-G237
TMEM81	388730	Q6P7N7	M1-K221
TMIGD1	388364	Q6UXZ0	M1-P220
TMIGD2	126259	Q96BF3	M1-G150
TNFRSF10A	8797	O00220	M1-I240
TNFRSF10B	8795	O14763	M1-S210
TNFRSF10C	8794	O14798	M1-A236
TNFRSF10D	8793	Q9UBN6	M1-H211
TNFRSF11A	8792	Q9Y6Q6	M1-P212
TNFRSF11B	4982	O00300	M1-L401
TNFRSF12A	51330	Q9NP84	M1-I81
TNFRSF13B	23495	O14836	M1-S165
TNFRSF13C	115650	Q96RJ3	M1-G80
TNFRSF14	8764	Q92956	M1-V202
TNFRSF17	608	Q02223	M1-I55
TNFRSF18	8784	Q9Y5U5	M1-P162
TNFRSF19	55504	Q9NS68	M1-A172

TNFRSF1A	7132	P19438	M1-T211
TNFRSF1B	7133	P20333	M1-D257
TNFRSF21	27242	O75509	M1-H349
TNFRSF25	8718	Q93038	M1-Q199
TNFRSF4	7293	P43489	M1-A217
TNFRSF6B	8771	O95407	M1-H300
TNFRSF8	943	P28908	M1-P386
TNFRSF9	3604	Q07011	M1-Q186
TNFSF11	8600	O14788	F70-D317
TNFSF15	9966	O95150	S57-L251
TNFSF8	944	P32971	Q63-D234
TREM1	54210	Q9NP99	M1-P202
TREM2	54209	Q9NZC2	M1-S174
TREML1	340205	Q86YW5	M1-P162
TREML2	79865	Q5T2D2	M1-D265
TREML4	285852	Q6UXN2	M1-G180
TYRO3	7301	Q06418	M1-S428
UNC5A	90249	Q6ZN44	M1-Y306
UNC5B	219699	Q8IZJ1	M1-Y377
UNC5C	8633	O95185	M1-Y380
UNC5D	137970	Q6UXZ4	M1-D379
VCAM1	7412	P19320	M1-E698
VSIG1	340547	Q86XK7	M1-E232
VSIG10	54621	Q8N0Z9	M1-G413
VSIG10L	147645	Q86VR7	M1-G779
VSIG2	23584	Q96IQ7	M1-G244
VSIG4	11326	Q9Y279	M1-P283
VSIG8	391123	P0DPA2	M1-R260
VSTM1	284415	Q6UX27	M1-T135
VSTM2B	342865	A6NLU5	M1-T263
VSTM4	196740	Q8IW00	M1-L177
VTCN1	79679	Q7Z7D3	M1-S259
WISP1	8840	O95388	M1-N367
ZNRF4	148066	Q8WWF5	M1-P250

Table 2. Prey proteins.

Prey name	Prey Entrez ID	Prey Uniprot ID	Prey sequence boundaries
1110032F04RIK	NA	NA	M1-R80
A1BG	1	P04217-1	M1-S495
ABHD13	84945	Q7L211	K59-I337
ABHD14A	25864	Q9BUJ0	P56-P271
ABHD3	171586	Q8WU67	K55-S409
ABHD3	171586	Q8WU67	Y47-S409
ACE	1636	P12821	M1-Q1259
ACE2	59272	Q9BYF1	M1-S740
ACE2	59272	Q9BYF1	M1-S740
ACPP	55	P15309	M1-D386
ACPP	55	P15309	M1-D386
ACPT	93650	Q9BZG2	M1-P390
ACPT	93650	Q9BZG2	M1-P390
ACVR1	90	Q04771	M1-E123
ACVR1	90	Q04771	M1-G125
ACVR1B	91	P36896	M1-E126
ACVR1B	91	P36896	M1-E126
ACVR1C	130399	Q8NER5	M1-E113
ACVR1C	130399	Q8NER5	M1-E113
ACVR2A	92	P27037	M1-N138
ACVR2B	93	Q13705	M1-T137
ACVRL1	94	P37023	M1-Q118
ACVRL1	94	P37023	M1-Q118
ADAM10	102	O14672	M1-E672
ADAM10	102	O14672	M1-E672
ADAM11	4185	O75078	M1-N734
ADAM11	4185	O75078	M1-N734
ADAM12	8038	O43184	M1-G708
ADAM12	8038	O43184	M1-A701
ADAM15	8751	Q13444	M1-G697
ADAM15	8751	Q13444	M1-S693
ADAM17	6868	P78536	M1-N671

ADAM18	8749	Q9Y3Q7	M1-N687
ADAM18	8749	Q9Y3Q7	M1-N687
ADAM19	8728	Q9H013	M1-G701
ADAM19	8728	Q9H013	M1-P702
ADAM2	2515	Q99965	M1-R686
ADAM2	2515	Q99965	M1-R667
ADAM20	8748	O43506	M1-R692
ADAM20	8748	O43506	M1-R692
ADAM21	8747	Q9UKJ8	M1-K679
ADAM21	8747	Q9UKJ8	M1-G681
ADAM22	53616	Q9P0K1	M1-N736
ADAM23	8745	O75077	M1-N792
ADAM28	10863	Q9UKQ2	M1-S666
ADAM29	11086	Q9UKF5	M1-K669
ADAM29	11086	Q9UKF2	M1-K669
ADAM30	11085	Q9UKF2	M1-S685
ADAM30	11085	Q9UKF2	M1-S685
ADAM32	203102	Q8TC27	M1-T682
ADAM33	80332	Q9BZ11	M1-T701
ADAM7	8756	Q9H2U9	M1-N668
ADAM7	8756	Q9H2U9	M1-N668
ADAM8	101	P78325	M1-P655
ADAM8	101	P78325	M1-S653
ADAM9	8754	Q13443	M1-G698
AGER	177	Q15109-7	M1-T326
AGER	177	Q15109-6	M1-T356
AGER	177	Q15109	M1-T340
AGER	177	Q15109	M1-T340
AJAP1	55966	Q9UKB5	M1-Q282
AJAP1	55966	Q9UKB5	M1-Q282
ALCAM	214	Q13740-2	M1-K514
ALCAM	214	Q13740	M1-K527
ALCAM	214	Q13740	M1-K527
ALK	238	P36897	M1-H1030
ALPI	248	P09923	M1-A505

ALPL	249	P05186	M1-S502
ALPP	250	P05187	M1-A508
AMHR2	269	M1-I145	M1-I145
AMHR2	269	Q16671	M1-S144
AMICA1	120425	Q8WU67	M1-Q264
AMICA1	120425	Q86YT9	M1-Q274
AMIGO1	57463	Q86WK6	M1-T372
AMIGO1	57463	Q86WK6	M1-A373
AMIGO2	347902	Q86WK6	M1-T398
AMIGO2	347902	Q86SJ2	M1-T398
AMIGO3	386724	Q86WK7	M1-T383
AMIGO3	386724	Q86WK7	M1-T383
AMN	81693	Q9BXJ7	M1-G360
ANPEP	290	P15144	Y33-K967
ANTXR1	84168	Q9H6X2	M1-S321
ANTXR1	84168	Q9H6X2	M1-S321
ANTXR2	118429	P58335	M1-G318
APCDD1	147495	Q8J025	M1-H492
APCDD1L	164284	Q8NCL9	M1-G480
APLP1	333	P51693	M1-A581
APLP2	334	Q06481	M1-A694
APLP2	334	Q06481	M1-S452
APOO	79135	Q9BUR5	M1-G109
APP	351	P05067	M1-A701
APP	351	P05067	M1-G700
AQPEP	206338	Q6Q4G3	A35-T990
AQPEP	206338	Q6Q4G3	M1-T990
AQPEP	206338	Q6Q4G3	Y37-T990
AREG	374	P15514	M1-A100
AREG	374	P15514	M1-K184
ART1	417	P52961	M1-A296
ART1	417	P52961	M1-I280
ART3	419	Q13508	M1-G364
ART3	419	Q13508	M1-A361
ART4	420	Q93070	M1-K288

ART4	420	Q93070	M1-K284
ASGR1	432	P07306	G60-L291
ASGR1	432	P07306	Q62-L291
ASGR2	433	P07307	G78-A311
ASGR2	433	P07307	Q80-A311
ASPHD1	253982	Q5U4P2	R97-P390
ATP1B1	481	P050260-1	T60-F301
ATP1B1	481	P050260-2	T60-S303
ATP1B1	481	P05026	E63-S303
ATP1B2	482	P14415	Q64-T290
ATP4B	496	P51164	M63-K291
ATRAID	51374	Q6UW56	M1-S199
ATRN	8455	O75882	M1-L1279
ATRNL1	26033	Q5VV63	M1-Q1232
AXL	558	P30530-2	M1-P440
AXL	558	P30530	M1-P449
AXL	558	P30530	M1-P449
AZGP1	563	P25311-1	M1-S298
BACE1	23621	P56817	M1-T457
BACE2	25825	Q9Y5Z0	M1-Y473
BAMBI	25805	Q13145	M1-A152
BAMBI	25805	Q13145	M1-A152
BCAM	4059	P50895	M1-G548
BCAN	63827	Q96GW7-1	M1-P911
BCAN	63827	Q96GW7-2	M1-S650
BLVRB	645	P30043	M1-G161
BMP10	27302	O95393	M1-R424
BMP10	27302	O95393	M1-R424
BMP5	653	P22003	M1-H454
BMP5	653	P22003	M1-H454
BMPR1A	657	P36894	M1-R152
BMPR1A	657	P36894	M1-R152
BMPR1B	658	O00238	M1-A157
Bmpr1b	12167	O00238	M1-G121
Bmpr1b	12167	O00238	M1-G121

BMPR2	659	Q13873	M1-T150
BMPR2	659	Q13873	M1-T150
BOC	91653	Q9BWV1	M1-Y855
BSG	682	P35613-2	M1-A208
BSG	682	P35613	M1-A323
BST1	683	Q10588	M1-R291
BST1	683	Q10588	M1-Q290
BST2	684	Q10589	T45-S161
BST2	684	Q10589	T45-Q180
BTC	685	P35070	M1-Q118
BTig	NA	NA	M1-P152
BTLA	151888	Q7Z6A9	M1-P152
BTLA	151888	Q7Z6A9	M1-P152
BTLA	151888	Q7Z6A9	M1-P152
BTN1A1	696	Q13410	M1-T244
BTN1A1	696	Q13410	M1-T244
BTN2A1	11120	Q7KYR7	M1-P246
BTN2A2	10385	Q8WVV5-4	M1-P134
BTN2A2	10385	Q8WVV5-3	M1-P156
BTN2A2	10385	Q8WVV5	M1-V237
BTN2A2	10385	Q8WVV5	M1-P250
BTN2A2	10385	Q8WVV5	M1-P263
BTN2A3P	54718	Q96KV6-1	M1-P244
BTN2A3P	54718	Q96KV6	M1-P244
BTN3A1	11119	O00481-4	M1-R195
BTN3A1	11119	O00481	M1-A250
BTN3A2	11118	P78410	M1-P247
BTN3A3	10384	O00478	M1-S244
BTN3A3	10384	O00478	M1-P247
BTNL2	56244	Q9UIR0-3	M1-H270
BTNL2	56244	Q9UIR0-6	M1-P259
BTNL2	56244	Q9UIR0-4	M1-W245
BTNL2	56244	Q9UIR0	M1-W455
BTNL3	10917	Q6UXE8-2	M1-P162
BTNL3	10917	Q6UXE8	M1-S231

BTNL3	10917	Q6UXE8	M1-T226
BTNL3	10917	Q6UXE8	M1-S237
BTNL8	79908	Q6UX41-6	M1-K122
BTNL8	79908	Q6UX41	M1-V239
BTNL8	79908	Q6UXE8	M1-K238
BTNL8	79908	Q6UXE8	M1-K238
BTNL9	153579	Q6UXE8	M1-K256
BUTR1	NA	NA	M1-A255
C10orf26	NA	NA	M1-E41
C10orf35	219738	Q96D05	M1-S91
C10orf35	219738	Q96D05	M1-S91
C10orf54	64115	Q9H7M9	M1-T192
C10orf54	64115	Q9H7M9	M1-A195
C11orf24	53838	Q96F05	M1-T400
C11orf24	53838	Q96F05	M1-T400
C11orf87	399947	Q6NUJ2	M1-T61
C11orf9	NA	NA	S790-D1151
C11orf92	NA	NA	M1-S76
C12orf53	196500	Q8IYJ0	M1-Q179
C12orf53	196500	Q8IYJ0	M1-Q179
C12orf59	NA	NA	M1-V40
C12orf63	144535	Q96N23	M1-S1127
C14orf132	56967	Q9NPU4	M1-L60
C14orf180	NA	NA	M1-S103
C14orf37	145407	Q86TY3	M1-Y710
C14orf37	145407	Q86TY3	M1-M714
C15orf24	56851	Q9NPA0	M1-D159
C15orf24	56851	Q9NPA0	M1-P164
C16orf54	283897	Q96LL3	M1-C31
C16orf91	283951	Q4G0I0	M1-P75
C16orf91	283951	Q4G0I0	M1-P232
C16orf92	146378	Q96LL3	M1-G101
C16orf92	146378	Q96LL3	M1-G101
C17orf101	NA	NA	R77-P319
C17orf80	55028	Q9BSJ5	M1-R550

C17orf80	55028	Q9BSJ5	M1-S552
C17orf99	100141515	Q6UX52	M1-M265
C18orf1	753	O15165	M1-E64
C18orf1	753	O15165	M1-E64
C19orf18	147685	Q8NEA5	M1-K100
C19orf18	147685	Q8NEA5	M1-K100
C19orf24	55009	Q9BVV8	M1-S73
C19orf38	255809	A8MVS5	M1-T116
C19orf38	255809	A8MVS5	M1-T116
C19orf38	255809	A8MVS5	M1-L119
C19orf59	199675	Q8IX19	S101-Q187
C19orf59	199675	Q8IX19	K107-Q187
C19orf63	NA	NA	M1-S221
C19orf75	NA	NA	M1-A119
C1GALT1	56913	Q9NS00	L31-P363
C1GALT1C1	29071	Q96EU7	H27-D318
C1orf101	257044	Q5SY80	M1-V904
C1orf130	NA	NA	M1-A31
C1orf159	54991	Q96HA4	M1-S147
C1orf43	25912	Q9BWL3	R33-L253
C1orf43	25912	Q9BWL3	K32-L253
C1orf66	51093	Q96FB5	M1-R405
C1orf66	51093	Q96FB5	M1-R405
C1orf85	112770	Q8WWB7	M1-V370
C1orf85	112770	Q8WWB7	M1-P368
C20orf3	57136	Q9HDC9	E18-V372
C2orf82	389084	Q6UX34	M1-A92
C2orf89	129293	Q86V40	M1-M477
C3orf18	51161	Q9UK00	M1-T61
C3orf35	NA	NA	M1-S149
C3orf45	NA	NA	M1-R94
C3orf45	NA	NA	Y118-S164
C4orf32	132720	Q8N8J7	M1-V100
C4orf32	132720	Q8N8J7	M1-P99
C4orf34	201895	Q96QK8	M1-G50

C4orf34	201895	Q96QK8	M1-G50
C5orf15	56951	Q8NC54	M1-H198
C5orf15	56951	Q8NC54	M1-H198
C6orf162	57150	Q96KF7	M1-K47
C6orf25	80739	O95866	M1-147
C6orf25	80739	O95866	M1-P192
C6orf25	80739	O95866	M1-V197
C6orf25	80739	O95866	M1-V217
C6orf25	80739	O95866	M1-Q142
C6orf25	80739	O95866	M1-Q142
C6orf72	116254	Q9NU53	M1-N268
C6orf72	116254	Q9NU53	M1-P261
C6orf89	221477	Q6UWU4	Q80-L347
C9orf11	NA	NA	M1-K181
C9orf11	54586	Q9NQ60	M1-I127
C9orf57	138240	Q5W0N0	G51-F161
C9orf79	286234	Q6ZUB1	Y85-S1445
C9orf79	286234	Q6ZUB1	S88-S1445
CA12	771	O43570	M1-G303
CA12	771	O43570	M1-G299
CA14	23632	Q9ULX7	M1-E289
CA14	23632	Q9ULX7	M1-E289
CA4	762	P22748	M1-K283
CA9	768	Q16790	M1-D414
CACHD1	57685	Q5VU97	M1-P1095
CACHD1	57685	Q5VU97	M1-P799
CACNA2D3	55799	Q8IZS8	M1-A1070
CACNA2D4	93589	Q7Z3S7	M1-S1118
CADM1	23705	Q9BY67-5	M1-A347
CADM1	23705	Q9BY67-3	M1-A404
CADM1	23705	Q9BY67	M1-H374
CADM2	253559	Q8N3J6-2	M1-A337
CADM2	253559	Q8N3J6	M1-H367
CADM2	253559	Q8N3J6	M1-A368
CADM3	57863	Q8N126-3	M1-H284

CADM3	57863	Q8N126-2	M1-H364
CADM3	57863	Q8N126	M1-H330
CADM4	199731	Q8NFZ8	M1-A324
CATSPERD	257062	Q86XM0	M1-Q718
CATSPERG	57828	Q6ZRH7	M1-K1064
CCDC107	203260	Q8WV48	M1-S65
CCDC107	203260	Q8WV48	Q86-S283
CCDC47	57003	Q96A33	M1-S135
CCDC47	57003	Q96A33	M1-S135
CCPG1	9236	Q9ULG6	K249-L757
CD101	9398	Q93033	M1-P954
CD101	9398	Q93033	M1-P954
CD109	135228	Q6YHK3	M1-S1423
CD14	929	P08571	M1-N345
CD160	11126	O95971	M1-L181
CD160	11126	O95971	M1-S160
CD163	9332	Q86VB7	S42-S1050
CD164	8763	Q04900	M1-R157
CD164	8763	Q04900	M1-D162
CD164L2	388611	Q6UWJ8	M1-S141
CD177	57126	Q8N6Q3	M1-G408
CD180	4064	Q99467	M1-T628
CD180	4064	Q99467	M1-G626
CD19	930	P15391	M1-L297
CD19	930	P15391	M1-K291
CD1A	909	P06126	M1-V300
CD1B	910	P29016-2	M1-S245
CD1B	910	P29016	M1-S303
CD1C	911	P29017	M1-N303
CD1C	911	P29017	M1-N303
CD1D	912	P15813	M1-S301
CD1D	912	P15813	M1-S301
CD1E	913	P15812	M1-G303
CD2	914	P06729	M1-I216
CD2	914	P06729	M1-D209

CD200	4345	P41217	M1-G232
CD200R1	131450	Q8TD46-4	M1-K261
CD200R1	131450	Q8TD46	M1-K238
CD200R1L	344807	Q6Q8B3	M1-P234
CD200R1L	344807	Q6Q8B3	M1-S237
CD207	50489	Q9UJ71	P65-P328
CD207	50489	Q9UJ71	P65-P328
CD22	933	P20273-1	M1-R509
CD22	933	P20273-3	M1-R598
CD22	933	P20273	M1-G685
CD22	933	P20273	M1-G685
CD226	10666	Q15762	M1-L259
CD226	10666	Q15762	M1-T250
CD24	100133941	P25063	M1-A61
CD24	100133941	P25063	M1-A58
CD244	51744	Q9BZW8	M1-I231
CD244	51744	Q9BZW8-4	M1-R129
CD244	51744	Q9BZW8-2	M1-R221
CD244	51744	Q9BZW8	M1-P229
CD247	919	P20963	M1-K30
CD248	57124	Q9HCU0	M1-R685
CD248	57124	Q9HCU0	M1-R685
CD27	939	P26842	M1-R191
CD274	29126	Q9NZQ7-2	M1-H126
CD274	29126	Q9NZQ7	M1-T239
CD274	29126	Q9NZQ7	
CD274	29126	Q9NZQ7	
CD274	29126	Q9NZQ7	M1-T239
CD276	80381	Q9BY67-3	M1-P245
CD276	80381	Q5ZPR3	M1-A466
CD28	940	P10747	M1-P152
CD28	940	P10747-4	M1-P55
CD28	940	P10747-3	M1-P68
CD28	940	P10747	
CD28	940	P10747	M1-P152

CD300A	11314	Q9UGN4-2	M1-Q65
CD300A	11314	Q9UGN4	M1-P180
CD300C	10871	Q08708	M1-L185
CD300C	10871	Q08708	M1-R183
CD300E	342510	Q496F6	M1-V178
CD300E	342510	Q496F6	M1-H173
CD300E	342510	Q496F6	M1-H173
CD300LB	124599	A8K4G0	M38-H187
CD300LB	124599	A8K4G0	M1-K147
CD300LD	100131439	Q6UXZ3	M1-H165
CD300LF	146722	Q8TDQ1-5	M1-G244
CD300LF	146722	Q8TDQ1	M1-S156
CD300LG	146894	Q6UXG3-2	M1-R162
CD300LG	146894	Q6UXG3-5	M1-R213
CD300LG	146894	Q6UXG3	M1-R247
CD300LG	146894	Q6UXG3	M1-R247
CD302	9936	Q8IX05	M1-H168
CD302	9936	Q8IX05	M1-K160
CD302	9936	Q8IX05	M1-H168
CD320	51293	Q9NPF0	M1-G230
CD33	945	P20138-3	M1-A134
CD33	945	P20138	M1-I262
CD33	945	P20138	M1-G260
CD34	947	P28906	M1-T290
CD3D	915	P04234-2	M1-K127
CD3D	915	P04234	M1-A105
CD3D	915	P04234	M1-G106
CD3E	916	P07766	M1-D126
CD3E	916	P07766	M1-D126
CD3G	917	P09693	M1-N111
CD3G	917	P09693	M1-G117
CD4	920	P01730	M1-W390
CD4	920	P01730	M1-P396
CD4	920	P01730	M1-P396
CD40	958	P25942	M1-Q203

CD40	958	P25942	M1-A194
CD44	960	P16070	M1-E649
CD44	960	P16070	M1-E649
CD46	4179	P15529	M1-D343
CD46	4179	P15529	M1-D328
CD47	961	Q08722	M1-N142
CD48	962	P09326	M1-T243
CD48	962	P09326	M1-R219
CD48	962	P09326	M1-S220
CD5	921	P06127	M1-T379
CD5	921	P06127	M1-P372
CD52	1043	P31358	M1-A37
CD52	1043	P31358	M1-P35
CD55	1604	P08174	M1-G354
CD55	1604	P08174	M1-T352
CD58	965	P19256	M1-R215
CD6	923	P30203	M1-L402
CD68	968	P34810	M1-S319
CD68	968	P34810	M1-S319
CD69	969	Q07108	S62-K199
CD69	969	Q07108	S62-K199
CD7	924	P09564	M1-L179
CD7	924	P09564	M1-A182
CD72	971	P21854	R117-D359
CD79A	973	P11912-2	M1-R105
CD79A	973	P11912	M1-R143
CD79B	974	P40259-2	M1-G56
CD79B	974	P40259	M1-A43
CD79B	974	P40259	M1-G160
CD80	941	P33681-3	M1-G140
CD80	941	P33681-3	M1-V162
CD80	941	P33681	M1-N242
CD83	9308	Q01151	M1-L148
CD83	9308	Q01151	M1-E144
CD84	8832	Q9UIB8-7	M1-G111

CD84	8832	Q9UIB8-6	M1-L241
CD84	8832	Q9UIB8	M1-G225
CD86	942	P42081-5	M1-P135
CD86	942	P42081	M1-H245
CD86	942	P42081	M1-H245
CD8A	925	P01732	M1-D182
CD8A	925	P01732	M1-D182
CD8B	926	P10966	M1-T173
CD8B	926	P10966	M1-T172
CD8B	926	P10966	M1-P170
CD93	22918	Q9NPY3	M1-K580
CD93	22918	Q9NPY3	M1-K580
CD96	10225	P40200-1	M1-S504
CD96	10225	P40200-2	M1-S520
CD96	10225	P40200	M1-G518
CD96	10225	P40200	M1-G518
CD99	4267	P14209	M1-G125
CD99	4267	P14209	M1-G125
CD99L2	83692	Q8TCZ2-4	M1-F60
CD99L2	83692	Q8TCZ2-6	M1-T113
CD99L2	83692	Q8TCZ2-3	M1-T114
CD99L2	83692	Q8TCZ2-2	M1-T137
CD99L2	83692	Q8TCZ2-5	M1-T190
CD99L2	83692	Q8TCZ2	M1-T186
CD99L2	83692	Q8TCZ2	M1-T186
CDCP1	64866	Q9H5V8	M1-T667
CDCP1	64866	Q9H5V8	M1-D665
CDH1	999	P12830	M1-P708
CDH1	999	P12830	M1-R696
CDH10	1008	Q9Y6N8	M1-A613
CDH11	1009	P55287	M1-A619
CDH12	1010	P55289	M1-G615
CDH12	1010	P55289	M1-L608
CDH13	1012	P55290	M1-G693
CDH13	1012	P55290	M1-A692

CDH15	1013	P55291	M1-A606
CDH16	1014	O75309	M1-A786
CDH16	1014	O75309	M1-S785
CDH16	1014	O75309	M1-S785
CDH17	1015	Q12864	M1-G786
CDH17	1015	Q12864	M1-T784
CDH18	1016	Q13634	M1-G610
CDH18	1016	Q13634	M1-S608
CDH19	28513	Q9H159	M1-E596
CDH19	28513	Q9H159	M1-E596
CDH2	1000	P19022	M1-A724
CDH20	28316	Q9HBT6	M1-G620
CDH20	28316	Q9HBT6	M1-G620
CDH22	64405	Q9UJ99	M1-A626
CDH24	64403	Q86UP0	M1-A641
CDH24	64403	Q86UP0	M1-T601
CDH26	60437	Q8IXH8	M1-A617
CDH26	60437	Q8IXH8	M1-E610
CDH3	1001	P22223	M1-G654
CDH3	1001	P22223	M1-G654
CDH4	1002	P55283	M1-A734
CDH4	1002	P55283	M1-T721
CDH5	1003	P33151	M1-Q484
CDH5	1003	P33151	M1-Q599
CDH6	1004	P55285	M1-A615
CDH6	1004	P55285	M1-T609
CDH7	1005	Q9ULB5	M1-A609
CDH7	1005	Q9ULB5	M1-S606
CDH8	1006	P55286	M1-A623
CDH8	1006	P55286	M1-A612
CDH9	1007	Q9ULB4	M1-A615
CDH9	1007	Q9ULB4	M1-A604
CDHR1	92211	Q96JP9	M1-N697
CDHR2	54825	Q9BYE9	M1-S1154
CDHR3	222256	Q6ZTQ4	M1-R701

CDHR3	222256	Q6ZTQ4	M1-V712
CDHR5	53841	Q9HBB8	M1-A670
CDON	50937	Q4KMG0	M1-D963
CDON	50937	Q4KMG0	M1-D963
CEACAM1	634	P13688-7	M1-A157
CEACAM1	634	P13688-5	M1-G367
CEACAM1	634	P13688	M1-G367
CEACAM1	634	P13688-5	M1-G367
CEACAM1	634	P13688	M1-G367
CEACAM1	634	P13688-3	M1-K321
CEACAM1	634	P13688	M1-L425
CEACAM1	634	P13688-4	M1-V351
CEACAM1	634	P13688	M1-A429
CEACAM16	388551	Q2WEN9	M1-G363
CEACAM16	388551	Q2WEN9	M1-G425
CEACAM18	729767	A8MTB9-1	M1-R380
CEACAM19	56971	Q7Z692	M1-A160
CEACAM20	125931	Q6UY09	M1-G446
CEACAM20	125931	Q6UY09	M1-G446
CEACAM20	125931	Q6UY09	M1-A447
CEACAM21	90273	Q3KPI0	M1-G239
CEACAM21	90273	Q3KPI0	M1-G240
CEACAM3	1084	P40198	M1-A154
CEACAM3	1084	P40198	M1-G155
CEACAM4	1089	O75871	M1-G151
CEACAM4	1089	O75871	M1-G155
CEACAM5	1048	P06731	M1-A685
CEACAM6	4680	P40199	M1-S321
CEACAM7	1087	Q14002	M1-A241
CEACAM7	1087	Q14002	M1-A241
CEACAM7	1087	Q14002	M1-S243
CEACAM8	1088	P31997	M1-I349
CEACAM8	1088	P31997	M1-S327
CHL1	10752	O00533-2	M1-G1097
CHL1	10752	O00533	M1-G1081

CHL1	10752	O00533	M1-G1081
CHODL	140578	Q9H9P2	M1-N216
CILP	8483	O75339-1	M1-N1184
CILP2	148113	Q8IUL8-1	M1-Q1156
CLCA2	9635	Q9UQC9	M1-Y900
CLCA2	9635	Q9UQC9	M1-A680
CLCA2	9635	Q9UQC9	A681-D899
CLCA4	22802	Q14CN2	M1-G894
CLEC10A	10462	Q8IUN9	Q61-H316
CLEC10A	10462	Q8IUN9	Q61-H316
CLEC12A	160364	Q5QGZ9-3	A61-I81
CLEC12A	160364	Q5QGZ9-5	K74-A213
CLEC12A	160364	Q5QGZ9	K69-A265
CLEC12B	387837	Q2HXU8	L65-Y232
CLEC12B	387837	Q2HXU8	S68-D276
CLEC14A	161198	Q86T13	M1-A397
CLEC17A	388512	Q6ZS10	K194-C378
CLEC17A	388512	Q6ZS10	K194-C378
CLEC2A	387836	Q6UVW9	S50-L174
CLEC2B	9976	Q92478	K26-H149
CLEC2B	9976	Q92478	K26-H149
CLEC2L	154790	P0C7M8	A89-T214
CLEC2L	154790	P0C7M8	S90-T214
CLEC4A	50856	Q9UMR7	K67-L204
CLEC4A	50856	Q9UMR7	Q70-L237
CLEC4A	50856	Q9UMR7	Q70-L237
CLEC4D	338339	Q8WXI8	V41-N215
CLEC4D	338339	Q8WXI8	T42-N215
CLEC4E	26253	Q9ULY5	T45-L219
CLEC4E	26253	Q9ULY5	Q50-L219
CLEC4F	165530	Q8N1N0	Q61-N589
CLEC4G	339390	Q6UXB4	S54-C293
CLEC4G	339390	Q6UXB4	S54-C293
CLEC5A	23601	Q9NY25	P28-K188
CLEC5A	23601	Q9NY25	P28-K188

CLEC6A	93978	Q6EIG7	T41-L209
CLEC6A	93978	Q6EIG7	T46-L209
CLEC7A	64581	Q9BXN2-4	G65-E192
CLEC7A	64581	Q9BXN2-10	G65-L116
CLEC7A	64581	Q9BXN2-7	G65-L143
CLEC7A	64581	Q9BXN2-3	G65-L189
CLEC7A	64581	Q9BXN2-2	G65-M201
CLEC7A	64581	Q9BXN2	G65-M247
CLEC7A	64581	Q9BXN2-6	G65-S132
CLEC7A	64581	Q9BXN2	S71-M201
CLEC9A	283420	Q6UXN8	G55-V241
CLEC9A	283420	Q6UXN8	K57-V241
CLECL1	160365	Q8IZS7	A86-I167
CLECL1	160365	Q8IZS7	A86-I167
CLECSF13	10462	Q8IUN9	Q61-N589
CLECSF13	10462	Q8IUN9	Q61-N589
CLMP	79827	Q9H6B4	M1-A235
CLSTN1	22883	O94985	M1-A860
CLSTN2	64084	Q9H4D0	M1-S827
CLSTN2	64084	Q9H4D0	M1-S831
CLSTN3	9746	Q9BQT9	M1-A848
CNST	163882	Q6PJW8	M1-R616
CNTFR	1271	P26992	M1-S342
CNTN1	1272	Q12860	M1-S993
CNTN2	6900	Q02246	M1-S1007
CNTN2	6900	Q02246	M1-N1012
CNTN3	5067	Q9P232	M1-N1008
CNTN4	152330	Q8IWV2-2	M1-T260
CNTN4	152330	Q8IWV2	M1-S1000
CNTN5	53942	O94779	M1-I1070
CNTN5	53942	O94779	M1-A1073
CNTN6	27255	Q9UQ52	M1-S998
CNTN6	27255	Q9UQ52	M1-S998
CNTNAP1	8506	P78357	M1-A1283
CNTNAP1	8506	P78357	M1-G1280

CNTNAP2	26047	Q9UHC6	M1-A1262
CNTNAP2	26047	Q9UHC6	M1-S1261
CNTNAP3	79937	Q9BZ76	M1-R1241
CNTNAP3	79937	Q9BZ76	M1-R1241
CNTNAP4	85445	Q9C0A0	M1-A1241
CNTNAP5	129684	Q8WYK1	M1-S1237
CNTNAP5	129684	Q8WYK1	M1-S1237
CORIN	10699	Q9Y5Q5	S67-N1042
CORIN	10699	Q9Y5Q5	G70-N1042
CPM	1368	P14384	M1-A425
CPM	1368	P14384	M1-S406
CR1	1378	P17927	M1-A1972
CR2	1380	P20023	M1-P975
CR2	1380	P20023	M1-S1031
CRB1	23418	P82279	M1-T1347
CRB1	23418	P82279	M1-T1346
CRB2	286204	Q5IJ48	M1-A1226
CRB3	92359	Q9BUF7	M1-A59
CRB3	92359	Q9BUF7	M1-E55
CREB3L2	64764	Q70SY1	G399-F520
CRIM1	51232	Q9NZV1	M1-S939
CRLF1	9244	O75462	M1-R422
CRLF2	64109	Q9HC73	M1-K231
CRTAM	56253	O95727-2	M1-G88
CRTAM	56253	O95727	M1-L289
CRTAM	56253	O95727	M1-R283
CSF1	1435	P09603	M1-S496
CSF1	1435	P09603	M1-S496
CSF1R	1436	P07333-2	M1-A306
CSF1R	1436	P07333	M1-F513
CSF1R	1436	P07333	M1-P517
CSF2RA	1438	P15509	M1-S324
CSF2RA	1438	P15509	M1-N321
CSF2RB	1439	P32927	M1-P447
CSF2RB	1439	P32927	M1-P441

CSF2RB	1439	P32927	M1-P441
CSF3R	1441	Q99062-2	M1-W771
CSF3R	1441	Q99062	M1-E625
CSF3R	1441	Q99062	M1-H627
CSPG5	10675	O95196	M1-Q420
CSPG5	10675	O95196	M1-Q420
CTLA4	1493	P16410	M1-F162
CTLA4	1493	P16410	M1-F162
CUZD1	50624	Q86UP6	M1-H570
CX3CL1	6376	P78423	M1-R339
CX3CL1	6376	P15509	M1-Q341
CXADR	1525	P78310-7	M1-G196
CXADR	1525	P78310	M1-G237
CXCL16	58191	Q9H2A7	M1-T205
CXCL16	58191	Q9H2A7	M20-A223
CXorf59	286464	Q6ZTR5	M1-A457
CXorf61	203413	Q5H943	R23-T113
CXorf61	203413	Q5H943	F24-T113
CXorf68	NA	NA	M1-A73
CYYR1	116159	Q96J86	M1-G65
CYYR1	116159	Q96J86	M1-T61
DAG1	1605	Q14118	M1-G653
DAG1	1605	Q14118	I655-D748
DAG1	1605	Q14118	M1-V749
DCBLD1	285761	Q8N8Z6	M1-A460
DCBLD2	131566	Q96PD2	M1-A530
DCC	1630	P43146	M1-N1097
DCC	1630	P43146	M1-N1097
DCT	1638	P40126	M1-G468
DDOST	1650	P39656	M1-P427
DDR1	780	Q08345	M1-A417
DDR2	4921	P51511	M1-R399
DDR2	4921	Q16832	M1-R399
DGCR2	9993	P98153	M1-R349
DGCR2	9993	P98153	M1-G347

DLK1	8788	P80370	M1-Q304
DLK1	8788	P80370	M1-Q304
DLK1	8788	P80370	M1-C306
DLK2	65989	Q6UY11	M1-S306
DLK2	65989	Q6UY11	M1-S306
DLL1	28514	O00548	M1-P544
DLL3	10683	Q9NYJ7	M1-Y491
DLL4	54567	Q9NR61	M1-P528
DLL4	54567	Q9NR61	M1-S526
DNER	92737	Q8NFT8	M1-Y640
DPCR1	135656	Q3MIW9	M1-A448
DPEP1	1800	P16444	M1-G386
DPEP2	64174	Q9H4A9	M1-E464
DPEP2	64174	Q9H4A9	M1-V462
DPEP3	64180	Q9H4B8	M1-A466
DPEP3	64180	Q9H4B8	M26-R486
DPP4	1803	P27487	N29-P766
DPP4	1803	P27487	M1-P766
DPP4	1803	P27487	N29-P766
DPP6	1804	O14944	K130-D865
DPP6	1804	P42658	T118-D865
DSC1	1823	Q08554	M1-R691
DSC2	1824	Q02487	M1-K694
DSC2	1824	Q02487	M1-K694
DSC3	1825	Q14574	M1-K690
DSC3	1825	Q14574	M1-K690
DSCAM	1826	O60469	M1-K1594
DSCAM	1826	O60469	M1-K1594
DSCAML1	57453	Q8TD84-2	M1-K1379
DSCAML1	57453	Q8TD84	M1-V1589
DSE	29940	Q9UL01	M1-R902
DSG1	1828	Q02413	M1-G550
DSG1	1828	Q02413	M1-H545
DSG2	1829	Q14126	M1-S606
DSG2	1829	Q14126	M1-A614

DSG3	1830	P32926	M1-G617
DSG4	147409	Q86SJ6	M1-G632
DSG4	147409	Q86SJ6	M1-G632
DTPQ5903	147645	Q86VR7	M1-G779
ECSM2	NA	NA	M1-A124
EDA	1896	Q92838	A179-S391
EDA	1896	Q92838	S165-S396
EDA2R	60401	Q9HAV5	M1-L139
EDAR	10913	Q9UNE0	M1-A187
EDAR	10913	Q9UNE0	M1-A187
EDAR	10913	Q9UNE0	M1-H183
EFNA3	1944	P52797	M1-G214
EFNA3	1944	P52797	M1-S213
EFNA5	1946	P52803	M1-A205
EFNA5	1946	P52803	M1-E202
EFNB1	1947	P98172	M1-K237
EFNB2	1948	P52799	M1-G230
EFNB3	1949	Q15768	M1-P226
EGF	1950	P01133	M1-K1032
EGF	1950	P01133	M1-K1032
EGFR	1956	P00533	M1-S645
EGFR	1956	P00533	M1-S645
ELFN1	392617	P0C7U0	M1-Y418
ELFN2	114794	Q5R3F8	M1-Y397
EMB	133418	Q6PCB8	M1-P263
EMCN	51705	Q9ULC0	M1-S190
EMCN	51705	Q9ULC0	M1-S190
ENG	2022	P17813	M1-P590
ENPEP	2028	Q07075	T40-G957
ENPEP	2028	Q07075	T40-G957
ENPP5	59084	Q9UJA9	M1-Y431
EPCAM	4072	P16422	M1-G267
EPCAM	4072	P16422	M1-K265
EPGN	255324	Q6UW88	M1-Y111
EPHA1	2041	P21709	M1-E547

EPHA1	2041	P21709	M1-E547
EPHA10	284656	Q5JZY3	M1-A565
EPHA2	1969	P29317	M1-A536
EPHA2	1969	P29317	M1-G531
EPHA3	2042	P29320	M1-Q541
EPHA3	2042	P29320	M1-Q541
EPHA3	2042	P29320	M1-Q541
EPHA4	2043	P54764	M1-T547
EPHA4	2043	P54764	M1-T547
EPHA5	2044	P54756	M1-P573
EphA5/Ehk1	2044	P54756	M1-I572
EPHA6	285220	Q9UF33	M1-Q547
EPHA7	2045	Q15375	M1-V555
EPHA8	2046	P29322	M1-T542
EPHB1	2047	P54762	M1-P540
EPHB1	2047	P54762	M1-P540
EPHB2	2048	P29323	M1-P542
EPHB2	2048	P29323	M1-P542
EPHB3	2049	P54753	M1-P558
EPHB3	2049	P54753	M1-P558
EPHB4	2050	P54760	M1-A539
EPHB4	2050	P54760	M1-Q537
EPHB6	2051	O15197	M1-L595
EPOR	2057	P19235	M1-P250
ERBB2	2064	P04626	
ERBB2	2064	P04626	M1-S653
ERBB3	2065	P21860	M1-T643
ERBB4	2066	Q15303	M1-P651
EREG	2069	O14944	M1-A120
EREG	2069	O14944	M1-L108
ERMAP	114625	Q96PL5	M1-I161
ERMAP	114625	Q96PL5	M1-A155
ERN2	10595	Q76MJ5	M1-D432
ESAM	90952	Q96AP7-2	M1-A69
ESAM	90952	Q96AP7	M1-A248

EVA1C	59271	P58658	M1-A323
EVC2	132884	Q86UK5	M1-A300
EVI2A	2123	P22794	M1-M135
EVI2B	2124	P34910	M1-S202
F11R	50848	Q9Y624-2	M1-G188
F11R	50848	Q9Y624	M1-V238
F3	2152	P13726	M1-I252
FAIM3	9214	O60667	M1-I256
FAIM3	9214	O60667	M1-G251
FAM171A1	221061	Q5VUB5	M1-T303
FAM171A1	221061	Q5VUB5	M1-T303
FAM171B	165215	Q6P995	M1-T353
FAM171B	165215	Q6P995	M1-T355
FAM173A	65990	Q9BQD7	R48-S235
FAM174A	345757	Q8TBP5	M1-A124
FAM174B	400451	Q3ZCQ3	M1-K92
FAM187A	100528020	A6NFU0	M1-E379
FAM187B	148109	O60667	M1-G333
FAM187B	148109	Q17R55	M1-K335
FAM187B	148109	Q17R55	M1-K335
FAM189A2	9413	Q15884	M1-K84
FAM189A2	9413	Q15884	M1-A89
FAM200A	221786	Q8TCP9	M1-R511
FAM200A	221786	Q8TCP9	M1-S513
FAM209A	200232	Q5JX71	M1-G54
FAM209A	200232	Q5JX71	M1-G54
FAM209B	388799	Q5JX69	M1-G54
FAM210A	125228	Q96ND0	K158-E272
FAM62C	84258	Q9BQG1	M1-Y50
FAM62C	84258	Q9BQG1	M1-Y50
FAM69A	388650	Q5T7M9	S48-S428
FAM69B	138311	Q5VUD6	S51-S431
FAM73A	374986	Q8NAN2	G102-Q632
FAM75A1	647060	Q5TZJ5	M76-I1347
FAM75A3	727830	Q5VYP0	

FAM75A5	727905	Q5VU36	S47-I1347
FAM75A5	727905	Q5VU36	M1-I1347
FAM75A7	727905	Q5VU36	P44-I1347
FAM75A7	727905	Q5VU36	Y48-I1347
FAM75D1	NA	NA	S51-K1576
FAP	2191	Q12884	L26-D760
FAS	355	P25445-5	M1-A129
FAS	355	P25445-3	M1-A83
FAS	355	P25445-2	M1-H103
FAS	355	P25445-4	M1-H149
FAS	355	P25445-6	M1-N173
FAS	355	P25445-1	M1-V314
FAS	355	P25445	M1-N173
FASLG	356	P48023	Q103-L281
FASLG	356	P48023	H106-L281
FCAMR	83953	Q8WWV6	M1-P577
FCAMR	83953	Q8WWV6	M1-R450
FCAMR	83953	Q8WWV6	M1-R450
FCAR	2204	P24071-3	M1-N131
FCAR	2204	P24071-2	M1-N205
FCAR	2204	P24071-6	M1-N231
FCAR	2204	P24071	M1-N227
FCER1A	2205	P12319	M1-Q205
FCER2	2208	P06734	D48-S321
FCER2	2208	P06734	D48-S321
FCER2	2208	P06734	M150-S321
FCGR1A	2209	P12314	M1-P288
FCGR1A	2209	P12314	M1-H292
FCGR1B	2210	Q92637-3	M1-V103
FCGR1B	2210	Q92637	M1-H198
FCGR1C	100132417	A6NKC4-1	M1-V195
FCGR2A	2212	P12318	M1-G217
FCGR2A	2212	P12318	M1-G217
FCGR2B	2213	P31994-3	M1-G216
FCGR2B	2213	P31994	M1-P221

FCGR2B	2213	P31994	M1-G223
FCGR2C	9103	P31995	M1-P221
FCGR2C	9103	P31995	M1-G223
FCGR3A	2214	P08637	M1-Q208
FCGR3B	2215	O75015	M1-Q208
FCGR3B	2215	O75015	M1-G206
FCGR3B	2215	O75015	M1-Q208
FCGR3B	2215	O75015	M1-Q208
FCGRT	2217	P55899	M1-S297
FCGRT	2217	P55899	M1-S297
FCRL1	115350	Q96LA6-3	M1-P366
FCRL1	115350	Q96LA6	M1-G308
FCRL2	79368	Q96LA5	M1-G388
FCRL2	79368	Q96LA5-5	M1-R109
FCRL2	79368	Q96LA5	M1-G400
FCRL3	115352	Q96P31-2	M1-G476
FCRL3	115352	Q96P31-3	M1-G577
FCRL3	115352	Q96P31	M1-I161
FCRL3	115352	Q96P31-5	M1-R199
FCRL3	115352	Q96P31	M1-G571
FCRL3	115352	Q96P31	M1-G576
FCRL4	83417	Q96PJ5	M1-G386
FCRL4	83417	Q96PJ5	M1-G386
FCRL4	83417	Q96PJ5	M1-G386
FCRL5	83416	Q96RD9-3	M1-N759
FCRL5	83416	Q96RD9-4	M1-P592
FCRL5	83416	Q96RD9-5	M1-Q152
FCRL5	83416	Q96RD9-2	M1-T124
FCRL5	83416	Q96RD9	M1-G851
FCRL6	343413	Q6DN72	M1-L332
FCRL6	343413	Q6DN72-4	M1-N211
FCRL6	343413	Q6DN72	M1-N306
FCRL6	343413	Q6DN72	M1-N306
FCRLA	84824	Q7L513-1	M1-E359
FCRLA	84824	Q7L513	A28-E359

FCRLB	127943	Q6BAA4-1	M1-S426
FGFR1	2260	P11362	M1-E374
FGFR1	2260	P11362	M1-E376
FGFR2	2263	P21802	M20-E396
FGFR2	2263	P21802	M1-E377
FGFR3	2261	P22607-2	M1-V374
FGFR3	2261	P22607	M1-S371
FGFR3	2261	P22607	M1-G375
FGFR4	2264	P22455	M1-D369
FGFRL1	53834	Q8N441	M1-P378
FIBCD1	84929	Q8N539	N55-R461
FIBCD1	84929	Q8N539	N55-R461
FKTN	2218	O75072	K29-Y461
FLJ40235	284369	Q8N7X8	M1-G118
FLJ40235	284369	Q8N7X8	M1-G118
FLRT1	23769	Q9NZU1	M1-P524
FLRT2	23768	O43155	M1-P540
FLRT2	23768	O43155	M1-P540
FLRT2	23768	O43155	M1-P540
FLRT3	23767	Q9NZU0	M1-P528
FLT1	2321	P17948	M1-H687
FLT1	2321	P17948	M1-E758
FLT3	2322	P36888	M1-N541
FLT3	2322	P36888	M1-S543
FLT3LG	2323	P49771	M1-P185
FLT3LG	2323	P49771	M1-Q159
FLT4	2324	P35916	M1-Y830
FLT4	2324	P35916	M1-E775
FLT4	2324	P35916	M1-E775
FNDC3A	22862	Q9Y2H6	M1-R1165
FNDC3B	64778	Q53EP0	M1-D67
FNDC3B	64778	Q53EP0	M1-Q1178
FNDC4	64838	Q9H6D8	M1-E169
FNDC4	64838	Q9H6D8	M1-E169
FNDC9	408263	Q8TBE3	M1-S112

FNDC9	408263	Q8TBE3	M1-Q110
FOLR1	2348	P15328	M1-G237
FOLR1	2348	P15328	M1-M233
FOLR2	2350	P14207	M1-G232
FOLR2	2350	P14207	M1-V229
FRMD3	257019	A2A2Y4	E551-S597
FRMD3	257019	A2A2Y4	M1-R530
FRMD5	84978	Q7Z6J6	T523-T570
FRMD5	84978	Q7Z6J6	M1-K496
FRRS1L	23732	Q9P0K9	M1-T322
FSTL4	23105	Q6MZW2	M1-V842
FSTL5	56884	Q8N475-1	M1-A847
FURIN	5045	P09958	M1-E715
FUT1	2523	P19526	H26-P365
FXYD4	53828	P59646	M1-Q38
FXYD5	53827	Q96DB9	M1-R143
FXYD5	53827	Q96DB9	M1-R145
GAS1	2619	P54826	M1-R316
GFRA1	2674	P56159	M1-S435
GFRA1	2674	P56159	M1-T428
GFRA2	2675	O00451	M1-S444
GFRA2	2675	O00451	M1-P443
GFRA3	2676	O60609	M1-N374
GFRA4	64096	Q9GZZ7	M1-G278
GFRAL	389400	Q6UXV0	M1-E351
GFRAL	389400	Q6UXV0	M1-E351
GGT1	2678	P19440	P27-Y569
GGT1	2678	P19440	P27-Y569
GGT5	2687	P36269	S30-Y586
GGT7	2686	Q9UJ14-5	Q128-C251
GGT7	2686	Q9UJ14	Q128-L662
GGT7	2686	Q9UJ14-4	Q52-G213
GGTA1P	2681	Q4G0N0	N26-T100
GHR	2690	P10912	M1-Y264
GLDN	342035	Q6ZMI3	Q40-Q551

GLG1	2734	Q92896	M1-N1145
GLIPR1	11010	P48060	M1-S235
GLIPR1	11010	P48060	M1-N231
GLIPR1L2	144321	Q4G1C9	M1-P251
GLIPR1L2	144321	Q4G1C9	M1-C253
GLT8D1	55830	Q68CQ7	S30-K371
GLT8D2	83468	Q9H1C3	K26-S349
GLT8D2	83468	Q9H1C3	V27-S349
GML	2765	Q99445	M1-G140
GML	2765	Q99445	M1-K143
GNA13	10672	Q14344	M1-Q377
GOLM1	51280	Q8NBJ4	S36-L401
GP1BA	2811	P07359	M1-G532
GP1BA	2811	P07359	M1-D498
GP1BB	2812	P13224	M1-A150
GP2	2813	P55259	M1-R502
GP5	2814	P40197	M1-G523
GP6	51206	Q9HCN6-2	M1-N251
GP6	51206	Q9HCN6	M1-K267
GP9	2815	P14770	M1-G147
GP9	2815	P14770	M1-R145
GPA33	10223	Q99795	M1-M233
GPA33	10223	Q99795	M1-A236
GPC1	2817	P35052	M1-S530
GPC2	221914	Q8N158	M1-A556
GPC3	2719	P51654	M1-S560
GPC3	2719	P51654	M1-P561
GPC4	2239	O75487	M1-G531
GPC4	2239	O75487	M1-D528
GPC6	10082	Q9Y625	M1-R524
GPC6	10082	Q9Y625	M1-D528
GPIHBP1	338328	Q8IV16	M1-S160
GPIHBP1	338328	Q8IV16	M1-A167
GPNMB	10457	Q14956	M1-A500
GPR116	221395	Q8IZF2	M1-S1006

GPR124	25960	Q96PE1	M1-P771
GPR125	166647	Q8IWK6	M1-P761
GUCY2C	2984	P25092	M1-L432
GUCY2D	3000	Q02846	G57-P463
GUCY2F	2986	P51841	M1-A467
GUCY2F	2986	P51841	M1-A467
GYPA	2993	P02724	M1-E91
GYPA	2993	P02724	M1-E91
GYPB	2994	P06028	M1-P60
GYPC	2995	P04921	M1-D58
GYPC	2995	P04921	M1-D58
HAPLN2	60484	Q9GZV7-1	M1-N340
HAPLN3	145864	Q96S86-1	M1-H360
HAPLN4	404037	Q86UW8-1	M1-V402
HAVCR1	26762	Q14CZ8	M1-V300
HAVCR1	26762	Q96D42	M1-G295
HAVCR1	26762	Q96D42	M1-G290
HAVCR2	84868	Q8TDQ0-2	M1-E142
HAVCR2	84868	Q8TDQ0	M1-G202
HBEGF	1839	Q99075	M1-T161
HBEGF	1839	Q99075	M1-T161
HCST	10870	Q9UBK5	M1-L49
HEG1	57493	Q9ULI3	M1-L1248
HEPACAM	220296	Q14CZ8	M1-G248
HEPACAM	220296	Q14CZ8	M1-Y236
HEPACAM	220296	Q14CZ8	M1-R237
HEPACAM2	253012	A8MVW5-2	M1-A341
HEPACAM2	253012	A8MVW5	M1-L441
HEPACAM2	253012	A8MVW5	M1-P351
HEPACAM2	253012	A8MVW5	M1-P351
HEPH	9843	Q9BQS7	M1-E1106
HEPH	9843	Q9BQS7	M1-E1108
HEPHL1	341208	Q6MZM0	M1-A1115
HFE	3077	Q30201	M1-W297
HFE	3077	Q30201	M1-V306

HFE2	148738	Q6ZVN8	M1-G402
HHLA2	11148	Q9UM44-2	M1-G282
HHLA2	11148	Q9UM44	M1-N344
HHLA2	11148	Q9UM44	M1-G346
HMP19	NA	NA	K93-H171
HPN	3249	P05981	R45-L417
HPN	3249	P05981	R45-L417
HYAL2	8692	Q12891	M1-S450
HYAL2	8692	Q12891	M1-G447
HYAL4	23553	Q2M3T9	K30-G454
ICAM1	3383	P05362	M1-L333
ICAM1	3383	P05362	M1-E480
ICAM2	3384	P13598	M1-Y216
ICAM2	3384	P13598	M1-Q223
ICAM3	3385	P32942	M1-H485
ICAM3	3385	P32942	M1-H485
ICAM4	3386	Q14773	M1-A240
ICAM5	7087	Q9UMF0	M1-W835
ICOS	29851	Q9Y6W8	M1-I145
ICOS	29851	Q9Y6W8	M1-F141
ICOSLG	23308	O75144-3	M1-T139
ICOSLG	23308	O75144	M1-N253
ICOSLG	23308	O75144	M1-S258
IFNAR1	3454	P17181	M1-K436
IFNAR1	3454	P17181	M1-K436
IFNAR2	3455	P48551	M1-G246
IFNAR2	3455	P48551	M1-A242
IFNGR1	3459	P15260	M1-G245
IFNGR2	3460	P38484	M1-Q247
IFNGR2	3460	P38484	M1-Q247
IFNLR1	163702	Q8IU57	M1-A228
IGDCC3	9543	Q8IVU1	M1-G640
IGDCC4	57722	Q8TDY8	M1-T957
IGF1R	3480	P08069	M1-H935
IGF2R	3482	P11717	M1-A2305

IGFBP7	3490	Q16270-1	M1-L282
IGFBPL1	347252	Q8WX77-1	M1-M278
IGFLR1	79713	Q9H665-2	M1-A167
IGFLR1	79713	Q9H665-1	M1-P163
IGFLR1	79713	Q9H665	M1-N160
IGLON5	402665	A6NGN9-1	M1-A316
IGSF1	3547	Q8N6C5	M1-A520
IGSF1	3547	Q8N6C5	E581-I1336
IGSF11	152404	Q5DX21-3	M1-N214
IGSF11	152404	Q5DX21	M1-G245
IGSF21	84966	Q96ID5	M1-A452
IGSF21	84966	Q96ID5	M1-A452
IGSF3	3321	O75054-2	M1-A1144
IGSF3	3321	O75054	M1-D1123
IGSF3	3321	O75054	M1-A1124
IGSF5	150084	Q9NSI5	M1-V267
IGSF5	150084	Q9NSI5	M1-G270
IGSF6	10261	O95976	M1-V159
IGSF6	10261	O95976	M1-S153
IGSF8	93185	Q969P0-3	M1-T492
IGSF8	93185	Q969P0	M1-T579
IGSF8	93185	Q969P0	M1-T579
IGSF9	57549	Q9P2J2-2	M1-G722
IGSF9	57549	Q9P2J2	M1-G738
IGSF9B	22997	Q9UPX0	M1-P722
IGSF9B	22997	Q9UPX0	M1-G726
IL10RA	3587	Q13651	M1-N235
IL10RA	3587	Q13651	M1-N235
IL10RB	3588	Q08334	M1-S220
IL11RA	3590	Q14626	M1-Q365
IL11RA	3590	Q14626	M1-Q365
IL12B	3593	P29460-1	M1-S328
IL12RB1	3594	P42701	M1-D545
IL12RB1	3594	P42701	M1-D545
IL12RB2	3595	Q99665-3	M1-N536

IL12RB2	3595	Q99665	M1-N622
IL13RA1	3597	P78552	M1-K338
IL13RA1	3597	P78552	M1-S342
IL13RA2	3598	Q14627	M1-K338
IL13RA2	3598	Q14627	M1-R343
IL15RA	3601	Q13261	M1-T205
IL15RA	3601	Q13261	M1-T205
IL17RA	23765	Q96F46	M1-Y322
IL17RB	55540	Q9NRM6	M1-G289
IL17RB	55540	Q9NRM6	M1-G289
IL17RC	84818	Q8NAC3	M1-K537
IL17RD	54756	Q8NFM7	M1-A300
IL17RD	54756	Q8NFM7	M1-R299
IL17RE	132014	Q8NFR9	M1-H454
IL18BP	10068	O95998-2	M1-G194
IL18R1	8809	Q13478	M1-G330
IL18R1	8809	Q13478	M1-G330
IL18RAP	8807	O95256	M1-K355
IL18RAP	8807	O95256	M1-K355
IL1R1	3554	P14778	M1-K336
IL1R1	3554	P14778	M1-H337
IL1R2	7850	P27930	M1-E343
IL1RAP	3556	Q9NPH3-2	M1-Q356
IL1RAP	3556	Q9NPH3-3	M1-R346
IL1RAP	3556	Q9NPH3	M1-C362
IL1RAP	3556	Q9NPH3	M1-T367
IL1RAPL1	11141	Q9NZN1	M1-G341
IL1RAPL1	11141	Q9NZN1	M1-T357
IL1RAPL2	26280	Q9NP60	M1-E356
IL1RL1	9173	Q01638	M1-S328
IL1RL2	8808	Q9HB29-2	M1-Y219
IL1RL2	8808	Q9HB29	M1-R335
IL20RA	53832	Q9UHF4	M1-K250
IL20RB	53833	Q6UXL0	M1-L233
IL21R	50615	Q9HBE5	M1-H237

IL22RA1	58985	Q8N6P7	M1-T228
IL23R	149233	Q5VWK5	M1-G355
IL27RA	9466	Q6UWB1	M1-G520
IL2RA	3559	P01589	M1-Q240
IL2RB	3560	P14784	M1-P242
IL2RG	3561	P31785	M1-A262
IL31RA	133396	Q8NI17	M1-E519
IL3RA	3563	P26951	M1-R305
IL4R	3566	P24394	M1-L233
IL4R	3566	P24394	M1-C227
IL5RA	3568	Q01344	M1-E341
IL6R	3570	P08887	M1-T366
IL6ST	3572	P40189-2	M1-F329
IL6ST	3572	P40189-3	M1-I560
IL6ST	3572	P40189	M1-A620
IL7R	3575	P16871	M1-P240
IL9R	3581	Q01113	M1-G250
IL9R	3581	Q01113	M1-G271
ILDR1	286676	Q86SU0	M1-K162
ILDR1	286676	Q86SU0	M1-V161
ILDR1	286676	Q86SU0	M1-H167
ILDR2	387597	Q71H61	M1-E186
ILDR2	387597	Q71H61	M1-E186
IMPG2	50939	Q9BZV3	M1-V1100
INSR	3643	P06213	M1-K956
INSRR	3645	P14616	M1-H921
INSRR	3645	P14616	A747-H921
ISLR	3671	O14498-1	M1-E402
ISLR2	57611	Q6UXK2	M1-S589
ISLR2	57611	Q6UXK2	M1-K584
ITFG1	81533	Q8TB96	M1-N565
ITFG1	81533	Q8TB96	M1-N565
ITFG3	83986	Q9H0X4	P73-A552
ITGA1	3672	P56199	M1-P1141
ITGA1	3672	P56199	M1-P1141

ITGA10	8515	O75578	M1-S1122
ITGA11	22801	Q9UKX5	M1-P1141
ITGA2	3673	P17301	M1-T1132
ITGA2B	3674	P08514	M1-R993
ITGA2B	3674	P08514	M1-P996
ITGA2B	3674	P08514	M1-K886
ITGA3	3675	P26006	F33-E991
ITGA4	3676	P13612	N35-K973
ITGA5	3678	P08648	M1-P998
ITGA5	3678	P08648	M1-P998
ITGA6	3655	P23229	M1-S1050
ITGA7	3679	Q13683	F34-P1081
ITGA8	8516	P53708	M1-P1011
ITGA9	3680	Q13797	M1-G980
ITGAD	3681	Q13349	F18-N1099
ITGAE	3682	P38570	M1-S1124
ITGAL	3683	P20701	Y26-L1090
ITGAM	3684	P11215	M1-N1104
ITGAV	3685	P06756	M1-P991
ITGAX	3687	P20702	M1-P1107
ITGB6	3694	P18564	M1-P709
ITGB6	3694	P18564	M1-I708
ITLN1	55600	Q8WWA0	M1-S300
ITLN1	55600	Q8WWA0	M1-R313
ITM2A	9452	O43736	Y75-E263
ITM2A	9452	O43736	M79-E263
ITM2B	9445	Q9Y287	Y76-S266
ITM2B	9445	Q9Y287	K77-K242
ITM2B	9445	Q9Y287	K77-S266
ITM2C	81618	Q9NQX7	A75-V267
ITM2C	81618	Q9NQX7	R81-V267
ITM2C	81618	Q9NQX7	R81-K241
IYD	389434	Q6PHW0	M1-N213
IZUMO1	284359	Q8IYV9	M1-R292
IZUMO2	126123	Q6UXV1	M1-A187

JAG1	182	P78504	M1-R1059
JAG1	182	P78504	M1-D1067
JAG2	3714	Q9Y219	M1-G1081
JAM2	58494	P57087-2	M1-N200
JAM2	58494	P57087	M1-S238
JAM3	83700	Q9BX67-2	M1-N190
JAM3	83700	Q9BX67	M1-N241
JTB	10899	O76095	M1-R104
KAZALD1	81621	Q96I82-1	M1-Y304
KCNE4	23704	P51787	M1-E86
KDR	3791	P35968	M1-E764
KDR	3791	P35968	M1-E764
KEL	3792	P23276	N68-W732
KIAA0090	23065	Q8N766	M1-D961
KIAA0090	23065	Q8N766	M1-D958
KIAA0319	9856	Q5VV43	M1-S955
KIAA0319	9856	Q5VV43	M1-S955
KIAA0319L	79932	Q8IZA0	S46-V930
KIAA0319L	79932	Q8IZA0	M1-L931
KIAA1024	23251	Q9UPX6	M1-K878
KIAA1324	57535	Q6UXG2	M1-K823
KIAA1324	57535	Q6UXG2	M1-K910
KIAA1324L	222223	A8MWY0	M1-K929
KIAA1467	57613	A2RU67	P126-I622
KIAA1467	57613	A2RU67	P128-I622
KIAA1644	85352	Q3SXP7	M1-L100
KIAA1944	121256	Q14C87	M1-E917
KIAA1944	121256	Q14C87	M1-E917
KIR2DL1	3802	P43626-2	M1-H269
KIR2DL1	3802	P43626	M1-R242
KIR2DL1	3802	P43626	M1-H245
KIR2DL2	3803	P43627	M1-H245
KIR2DL3	3804	P43628-2	M1-H147
KIR2DL3	3804	P43631	M1-I248
KIR2DL3	3804	P43628	M1-R242

KIR2DL3	3804	P43628	M1-H245
KIR2DL4	3805	Q99706-2	M1-A226
KIR2DL4	3805	Q99706-6	M1-I230
KIR2DL4	3805	Q99706-5	M1-I307
KIR2DL4	3805	Q99706-4	M1-I325
KIR2DL4	3805	Q99706-3	M1-I342
KIR2DL4	3805	Q99706	M1-A243
KIR2DL4	3805	Q99706	M1-A243
KIR2DL5A	57292	Q8N109	M1-I235
KIR2DL5A	57292	Q8N109	M1-R236
KIR2DL5B	553128	Q8NHK3	M1-H238
KIR2DL5B	553128	Q8NHK3	M1-R236
KIR2DS1	3806	Q14954	M1-H243
KIR2DS1	3806	Q14954	M1-H245
KIR2DS2	100132285	P43631	M1-Y226
KIR2DS2	100132285	P43631	M1-H245
KIR2DS3	3808	Q14952	M1-H243
KIR2DS3	3808	Q14952	M1-H245
KIR2DS4	3809	P43632	M1-R242
KIR2DS4	3809	P43632	M1-H245
KIR2DS5	3810	Q14953	M1-H243
KIR2DS5	3810	Q14953	M1-H245
KIR3DL1	3811	P43626-1	M1-H245
KIR3DL1	3811	P43629	M1-I343
KIR3DL1	3811	P43629	M1-H340
KIR3DL2	3812	P43630-2	M1-H323
KIR3DL2	3812	P43630	M1-H338
KIR3DL2	3812	P43630	M1-H340
KIR3DL3	115653	Q8N743	M1-H321
KIR3DL3	115653	Q8N743	M1-V410
KIR3DL3	115653	Q8N743	M1-H323
KIR3DP1	548594	A8MWS1-1	M1-L328
KIR3DS1	3813	O43469	M1-H340
KIR3DX1	90011	Q9H7L2-1	M1-Q352
KIRREL	55243	Q96J84-3	M1-G393

KIRREL	55243	Q96J84-2	M1-G512
KIRREL	55243	Q96J84	M1-G496
KIRREL	55243	Q96J84	M1-G496
KIRREL2	84063	Q6UWL6-3	M1-R460
KIRREL2	84063	Q6UWL6	M1-R510
KIRREL2	84063	Q6UWL6	M1-R510
KIRREL3	84623	Q8IZU9	M1-S531
KIRREL3	84623	Q8IZU9	M1-A535
KIT	3815	P10721	M1-T520
KIT	3815	P10721	M1-P524
KITLG	4254	P21583	M1-H214
KITLG	4254	P21583	M1-S212
KL	9365	Q9UEF7	M1-R979
KLB	152831	Q86Z14	M1-Q993
KLB	152831	Q86Z14	T51-K994
KLRAP1	10748	O75889	M1-E164
KLRAP1	10748	O75889	I69-Y215
KLRAP1	10748	O75889	I69-E194
KLRB1	3820	Q12918	Q67-S225
KLRB1	3820	Q12918	Q67-S225
KLRC1	3821	P26715-2	P94-L215
KLRC1	3821	P26715-1	P94-L216
KLRC1	3821	P26715	P94-L233
KLRC1	3821	P26715	S95-L233
KLRC2	3822	P26717	P95-L231
KLRC2	3822	P26717	E98-L231
KLRC4	8302	O43908	I97-L158
KLRD1	3824	Q13241	K32-I179
KLRD1	3824	Q13241	K32-I179
KLRF1	51348	Q9NZS2	S63-Y232
KLRF1	51348	Q9NZS2	S63-T124
KLRF1	51348	Q9NZS2	S63-Y231
KLRG1	10219	Q96E93	L60-F195
KLRG1	10219	Q96E93-2	L60-L189
KLRG1	10219	Q96E93	L60-F195

KLRG2	346689	A4D1S0	A283-Q409
KLRK1	22914	P26718	N80-V216
KREMEN1	83999	Q96MU8	M1-T392
KREMEN2	79412	Q8NCW0	M1-A364
L1CAM	3897	P32004	M1-E1120
L1CAM	3897	P32004	M1-G1121
LAG3	3902	P18627	M1-L450
LAIR1	3903	Q6GTX8-3	M1-H145
LAIR1	3903	Q6GTX8-2	M1-H146
LAIR1	3903	Q6GTX8	M1-Y165
LAIR1	3903	Q6GTX8	M1-Y165
LAIR2	3904	Q6ISS4-1	M1-P152
LAMP1	3916	P11279	M1-S381
LAMP2	3920	P13473	M1-N374
LAMP3	27074	Q9UQV4	M1-T381
LAMP3	27074	Q9UQV4	M1-T381
LAMP5	24141	Q9UJQ1	M1-T236
LAMP5	24141	Q9UJQ1	M1-E235
LAX1	54900	Q8IWV1	M1-I22
LAX1	54900	Q8IWV1	M1-I38
LAYN	143903	Q6UX15	M1-A234
LAYN	143903	Q6UX15	M1-N232
LCTL	197021	Q6UWM7	M1-E541
LCTL	197021	Q6UWM7	M1-E541
LDLR	3949	P01130	M1-K782
LDLR	3949	P01130	M1-R788
LDLRAD1	388633	Q5T700	G61-P205
LDLRAD1	388633	Q5T700	P63-P205
LDLRAD2	401944	Q5SZI1	M1-S233
LDLRAD3	143458	Q86YD5	M1-T173
LDLRAD3	143458	Q86YD5	M1-S171
LECT1	11061	O75829	K66-V334
LECT1	11061	O75829	E215-V334
LEPR	3953	P48357	M1-D839
LEPR	3953	P48357	M1-A840

LIFR	3977	P42702	M1-S833
LILRA1	11024	O75019-2	M1-N261
LILRA1	11024	O75019	M1-N461
LILRA1	11024	O75019	M1-N461
LILRA2	11027	Q8N149	M1-N432
LILRA2	11027	Q8N149	M1-L450
LILRA3	11026	Q8N6C8-2	M1-E375
LILRA3	11026	Q8N6C8	M1-E439
LILRA4	23547	P59901	M1-N446
LILRA4	23547	P59901	M1-N446
LILRA5	353514	A6NI73-2	M1-N253
LILRA5	353514	A6NI73	M1-N265
LILRA5	353514	A6NI73	M1-N265
LILRA6	79168	Q6PI73	M1-R191
LILRA6	79168	Q6PI73	M1-N447
LILRA6	79168	Q6PI73	M1-N447
LILRB1	10859	Q8NHL6	M1-H458
LILRB1	10859	Q8NHL6	M1-H458
LILRB2	10288	Q8N423	M1-I479
LILRB2	10288	Q8N423	M1-G460
LILRB3	11025	O75022-2	M1-E460
LILRB3	11025	O75022	M1-E443
LILRB4	11006	Q8NHJ6	M1-V186
LILRB4	11006	Q8NHJ6	M1-E259
LILRB4	11006	Q8NHJ6	M1-R255
LILRB5	10990	O75023-2	M1-G359
LILRB5	10990	O75023	M1-R455
LILRB5	10990	O75023	M1-G458
LINGO1	84894	Q96FE5	M1-T556
LINGO1	84894	Q96FE5	M1-T561
LINGO2	158038	Q7L985	M1-T540
LINGO2	158038	Q7L985	M1-T545
LINGO3	645191	P0C6S8	M1-T531
LINGO4	339398	Q6UY18	M1-G531
LINGO4	339398	Q6UY18	M1-A533

LMLN	89782	Q96KR4	M1-L624
LMLN	89782	Q96KR4	M1-H655
LNPEP	4012	Q9UIQ6	K144-L1025
LOC160348	NA	NA	M1-E924
LOC256223	256223	A8MXV6	M1-A211
LOC256223	256223	A8MXV6	M1-A211
LOC374383	374383	Q68D85	M1-H264
LOC374597	391123	Q5VU13	M1-A130
LOC376666	391123	Q5VU13	M1-R260
LOC652900	NA	NA	M1-N844
LRCH1	23143	Q9Y2L9	M1-K690
LRCH4	4034	O75427	M1-G661
LRFN1	57622	Q9P244	M1-T535
LRFN2	57497	Q9ULH4	M1-Q528
LRFN2	57497	Q9ULH4	M1-T533
LRFN3	79414	Q9BTN0	M1-G535
LRFN3	79414	Q9BTN0	M1-T538
LRFN4	78999	Q6PJG9	M1-L518
LRFN5	145581	Q96NI6	M1-Q523
LRFN5	145581	Q96NI6	M1-T528
LRIG1	26018	Q96JA1-2	M1-G762
LRIG1	26018	Q96JA1	M1-T792
LRIG1	26018	Q96JA1	M1-G794
LRIG2	9860	O94898	M1-G807
LRIG3	121227	Q6UXM1-2	M1-T747
LRIG3	121227	Q6UXM1	M1-V810
LRIT1	26103	Q9P2V4	M1-Q526
LRIT1	26103	Q9P2V4	M1-Q526
LRIT2	340745	A6NDA9	M1-H462
LRIT2	340745	A6NDA9	M1-H462
LRIT3	345193	Q3SXY7	M1-W536
LRIT3	345193	Q3SXY7	M1-Q580
LRP10	26020	Q7Z4F1	M1-R439
LRP11	84918	Q86VZ4	M1-G450
LRP12	29967	Q9Y561	M1-R492

LRP12	29967	Q9Y561	M1-R492
LRP3	4037	O75074	M1-R495
LRP4	4038	O75096	M1-S1725
LRP4	4038	O75096	M1-H1723
LRP5	4041	O75197	M1-A1386
LRP6	4040	O75581	M1-T1373
LRP8	7804	Q14114	M1-A826
LRPAP1	4043	P30533	M1-L357
LRPAP1	4043	P30533	M1-L357
LRRC15	131578	Q8TF66	M1-A540
LRRC15	131578	Q8TF66	M1-G538
LRRC19	64922	Q9H756	M1-S269
LRRC19	64922	Q9H756	M1-S269
LRRC24	441381	Q50LG9	M1-T405
LRRC25	126364	Q8N386	M1-T165
LRRC25	126364	Q8N386	M1-T165
LRRC26	389816	Q2I0M4	M1-A263
LRRC3	81543	Q9BY71	M1-D204
LRRC3	81543	Q9BY71	M1-D204
LRRC32	2615	Q14392	M1-N627
LRRC32	2615	Q14392	M1-N627
LRRC33	375387	Q86YC3	M1-G649
LRRC33	375387	Q86YC3	M1-G649
LRRC37A	9884	A6NMS7-1	M1-K1570
LRRC37A2	474170	A6NM11	M1-K1570
LRRC37A3	374819	O60309	M1-K1580
LRRC37B	114659	Q96QE4	M1-K905
LRRC37B	114659	Q96QE4	M1-K905
LRRC38	126755	Q5VT99	M1-I250
LRRC3B	116135	Q96PB8	M1-K199
LRRC4	64101	Q9HBW1	M1-T526
LRRC4	64101	Q9HBW1	M1-K527
LRRC4B	94030	Q9NT99	M1-K576
LRRC4C	57689	Q9HCJ2	M1-K527
LRRC4C	57689	Q9HCJ2	M1-K527

LRRC52	440699	Q8N7C0	M1-D244
LRRC52	440699	Q8N7C0	M1-D244
LRRC55	219527	Q6ZSA7	M1-D270
LRRC55	219527	Q6ZSA7	M1-D300
LRRC66	339977	Q68CR7	M1-D374
LRRC66	339977	Q68CR7	M1-L375
LRRN1	57633	Q6UXK5	M1-A631
LRRN2	10446	O75325	M1-P629
LRRN2	10446	O75325	M1-G630
LRRN3	54674	Q9H3W5	M1-T627
LRRN3	54674	Q9H3W5	M1-T628
LRRN4	164312	Q8WUT4	M1-A681
LRRN4CL	221091	Q8ND94	M1-L195
LRRTM1	347730	Q86UE6	M1-K427
LRRTM2	26045	O43300	M1-R422
LRRTM2	26045	O43300	M1-R422
LRRTM3	347731	Q86VH5	M1-F417
LRRTM3	347731	Q86VH5	M1-K419
LRRTM4	80059	Q86VH4	M1-K424
LRRTM4	80059	Q86VH4	M1-K424
LRTM1	57408	Q9HBL6-1	M1-T287
LRTM1	57408	Q9HBL6	M1-H284
LRTM2	654429	Q8N967	M1-R305
LRTM2	654429	Q8N967	M1-R306
LSAMP	4045	P55082	M1-L320
LSAMP	4045	Q13449	M1-S317
LSR	51599	Q86X29-2	M1-D222
LSR	51599	Q86X29-4	M1-D240
LSR	51599	Q86X29-6	M1-V492
LSR	51599	Q86X29-5	M1-V581
LSR	51599	Q86X29	M1-D259
LSR	51599	Q86X29	M1-D259
LTBR	4055	P36941-1	M1-L226
LTBR	4055	P36941	M1-T224
LTK	4058	P29376	M1-P424

LY6D	8581	Q14210	M1-A105
LY6E	4061	Q16553	M1-A103
LY6E	4061	Q16553	M1-F100
LY6G5C	80741	Q5SRR4	G41-P150
LY6G6C	80740	O95867	M1-A100
LY6G6D	58530	O95868	M1-A105
LY6G6F	259215	Q5SQ64	M1-W235
LY6G6F	259215	Q5SQ64	M1-P234
LY6H	4062	O94772	M1-A116
LY6K	54742	Q17RY6	M1-S139
LY6K	54742	Q17RY6	M59-E200
LY75	4065	O60449	M1-A1669
LY9	4063	Q9HBG7-3	M1-K364
LY9	4063	Q9HBG7-4	M1-K454
LY9	4063	Q9HBG7	M1-K454
LY9	4063	Q9HBG7	M1-K454
LYPD1	116372	Q8N2G4	M1-A120
LYPD3	27076	O95274	M1-G325
LYPD5	284348	Q6UWN5	M1-S226
LYPD6	130574	Q86Y78	M1-G151
LYPD6B	130576	Q8NI32	M1-A166
LYPD6B	130576	Q8NI32	M1-G163
LYSMD3	116068	Q7Z3D4	M1-G217
LYSMD3	116068	Q7Z3D4	M1-G215
LYSMD4	145748	Q5XG99	M1-D213
LYSMD4	145748	Q5XG99	M1-Q218
LYVE1	10894	Q9Y5Y7	M1-A239
LYVE1	10894	Q9Y5Y7	M1-T238
M6PR	4074	P20645	M1-S190
MADCAM1	8174	Q13477-4	M1-A139
MADCAM1	8174	Q13477-3	M1-A234
MADCAM1	8174	Q13477	M1-L318
MAG	4099	P20916	M1-H507
MAG	4099	P20916	M1-M510
MAMDC4	158056	Q6UXC1	M1-A1154

MANSC1	54682	Q9H8J5	M1-K383
MANSC1	54682	Q9H8J5	M1-K383
MCAM	4162	P43121	M1-G559
MCAM	4162	P43121	M1-G559
MDGA1	266727	Q8NFP4	M1-S932
MDGA2	161357	Q7Z553	M1-V930
MDGA2	161357	Q7Z553	M1-A933
MEGF10	84466	Q96KG7	M1-A858
MEGF10	84466	Q96KG7	M1-I856
MEGF11	84465	A6BM72	M1-S848
MEGF8	1954	Q7Z7M0	M1-D2647
MEGF9	1955	Q9H1U4	M1-N514
MEP1A	4224	Q16819	M1-S717
MEP1A	4224	Q16819	M1-V712
MEP1B	4225	Q16820	M1-K645
MEP1B	4225	Q16820	M1-T652
MERTK	10461	Q12866	M1-L503
MEST	4232	Q5EB52	P32-F335
MET	4233	P08581	M1-G933
MFAP3	4238	P55082	M1-Y150
MFAP3	4238	P55082	M1-S148
MFAP3	4238	P55082	M1-S148
MFAP3L	9848	O75121	M1-D148
MFI2	4241	P08582	M1-G711
MFI2	4241	P08582	M1-Q708
MFRP	83552	Q9BY79	Q91-P579
MFRP	83552	Q9BY79	Q91-P579
MGC39681	283197	Q8NCQ3	K48-A95
MICA	100507436	Q29983-2	M1-T213
MICA	100507436	Q29983	M1-Q308
MICB	4277	Q29980-2	M1-D266
MICB	4277	Q29980-3	M1-S41
MICB	4277	Q29980	M1-D266
MICB	4277	Q29980	M1-D309
MILR1	284021	Q7Z6M3	M1-L133

MILR1	284021	Q7Z6M3	M1-L138
MILR1	284021	Q7Z6M3	M1-K227
MILR1	284021	Q7Z6M3	M1-K227
MME	4311	P08473	T51-W750
MME	4311	P08473	D53-W750
MMEL1	79258	Q495T6	R51-W779
MMGT1	93380	Q8N4V1	M1-D44
MMP14	4323	P50281	M1-A541
MMP14	4323	P50281	M1-S538
MMP15	4324	P51511	M1-N625
MMP15	4324	P51511	M1-N625
MMP16	4325	P51512	M1-A564
MMP23B	8510	O75900	R39-G390
MMP24	10893	Q9Y5R2	M1-A602
MOG	4340	Q9HD47	M1-S152
MOG	4340	Q16653	M1-G154
MOG	4340	Q16653	M1-G154
MPEG1	219972	Q2M385	M1-A656
MPEG1	219972	Q2M385	M1-G655
MPL	4352	P40238	M1-A490
MPL	4352	P40238	M1-T489
MPZ	4359	P25189	M1-V166
MPZ	4359	P25189	M1-G155
MPZL1	9019	O95297	M1-R117
MPZL1	9019	O95297	M1-V165
MPZL2	10205	O60487	M1-H152
MPZL3	196264	Q6UWV2-2	M1-S145
MPZL3	196264	Q6UWV2	M1-S158
MR1	3140	Q95460-3	M1-L208
MR1	3140	Q95460-2	M1-L255
MR1	3140	Q95460-1	M1-L300
MRC1	4360	P22897	M1-R1377
MRC1	4360	P22897	M1-R1377
MRC2	9902	Q9UBG0	M1-A1414
MSLN	10232	Q13421	M1-T608

MSLN	10232	Q13421	M1-A621
MSR1	4481	P21757	A72-L451
MST1R	4486	Q04912	M1-G960
MUC1	4582	P15941	M1-G1158
MUC13	56667	Q9H3R2	M1-L421
MUC15	143662	Q8N387	M1-G237
MUC15	143662	Q8N387	M28-T263
MUC21	394263	Q5SSG8	M1-E479
MUSK	4593	O15146-3	M1-Y396
MUSK	4593	O15146-2	M1-Y406
MUSK	4593	O15146	M1-T495
MXRA5	25878	Q9NR99	M1-F2828
MXRA7	439921	P84157	M1-M204
MXRA8	54587	Q9BRK3-4	M1-Q240
MXRA8	54587	Q9BRK3	M1-Q341
MYEOV	26579	Q96EZ4	M1-P296
MYEOV	26579	Q96EZ4	M1-G293
NAALAD2	10003	Q9Y3Q0	K32-L740
NAALAD2	10003	Q9Y3Q0	E36-L740
NAALADL1	10004	Q9UQQ1	K31-L740
NAALADL1	10004	Q9UQQ1	K31-L791
NAGPA	51172	Q9UK23	M1-A449
NAGPA	51172	Q9UK23	M1-T448
NCAM1	4684	P13591-4	M1-A708
NCAM1	4684	P13591-2	M1-A711
NCAM1	4684	P13591-3	M1-A743
NCAM1	4684	P13591	M1-L719
NCAM1	4684	P13591	M1-A723
NCAM2	4685	O15394	M1-T694
NCAM2	4685	O15394	M1-N697
NCAN	1463	O14594-1	M1-C1321
NCLN	56926	Q969V3	M1-A522
NCR1	9437	O76036-4	M1-L144
NCR1	9437	O76036-3	M1-L161
NCR1	9437	O76036-2	M1-L239

NCR1	9437	O76036	M1-R258
NCR1	9437	O76036	M1-N255
NCR1	9437	O76036	M1-R258
NCR2	9436	O95944-2	M1-A204
NCR2	9436	O95944	M1-P190
NCR2	9436	O95944	M1-A192
NCR3	259197	Q68D85-1	M1-A111
NCR3	259197	O14931	M1-R143
NCR3	259197	O14931	M1-T138
NCSTN	23385	Q92542	M1-E669
NCSTN	23385	Q92542	M1-E669
NEGR1	257194	Q7Z3B1	M1-S331
NEGR1	257194	Q7Z3B1	M1-D327
NEO1	4756	Q92859-4	M1-N1092
NEO1	4756	Q92859	M1-N1103
NEO1	4756	Q92859	M1-N1103
NETO1	81832	Q8TDF5	M1-K329
NETO1	81832	Q8TDF5	M1-T344
NETO2	81831	Q8NC67	M1-K334
NETO2	81831	Q8NC67	M1-E333
NFAM1	150372	Q8NET5	M1-L165
NFAM1	150372	Q8NET5	M1-K163
NFASC	23114	O94856-3	M1-G1038
NFASC	23114	O94856-5	M1-G1201
NFASC	23114	O94856-4	M1-G935
NFASC	23114	O94856	M1-G1216
NFASC	23114	O94856	M1-G1216
NGFR	4804	P08138-2	M1-L157
NGFR	4804	P08138-1	M1-N250
NGFR	4804	P08138	M1-N250
NLGN1	22871	Q8N2Q7	M1-S694
NLGN1	22871	Q8N2Q7	M1-V678
NLGN2	57555	Q8NFZ4	M1-S677
NLGN3	54413	Q9NZ94	M1-S709
NLGN4X	57502	Q8N0W4	M1-K668

NLGN4Y	22829	Q8NFZ3	M1-K668
NOMO1	23420	Q15155	M1-S1160
NOMO3	408050	P69849	M1-R1149
NOTCH1	4851	P46531	M1-H1735
NOTCH2	4853	Q04721	M1-Q1677
NOTCH3	4854	Q9UM47	M1-L1643
NOTCH4	4855	Q99466	M1-V1449
NPDC1	56654	Q9NQX5	M1-G182
NPDC1	56654	Q9NQX5	M1-G182
NPHS1	4868	O60500	M1-S1055
NPHS1	4868	O60500	M1-P1061
NPHS2	7827	Q9NP85	V125-L383
NPR1	4881	P16066	M1-E473
NPR2	4882	P20594	M1-T455
NPR2	4882	P20594	M1-T455
NPR3	4883	P17342	M1-E481
NPTN	27020	Q9Y639-3	M1-L224
NPTN	27020	Q9Y639	M1-R216
NPTN	27020	Q9Y639	M1-P339
NRCAM	4897	Q92823-3	M1-G1044
NRCAM	4897	Q92823-4	M1-G1047
NRCAM	4897	Q92823	M1-G1168
NRCAM	4897	Q92823	M1-G1168
NRG1	3084	Q02297	M1-Q240
NRG2	9542	O14511	M1-Q403
NRG4	145957	Q8WWG1	M1-A64
NRG4	145957	Q8WWG1	M1-E63
NRN1	51299	Q9NPD7	M1-A118
NRN1L	123904	Q496H8	M1-P140
NRP1	8829	O14786	M1-R845
NRP2	8828	O60462	M1-P864
NRP2	8828	O60462	M1-P864
NRXN1	9378	Q9ULB1	M1-G1402
NRXN1	9378	Q9ULB1	M1-T1401
NRXN2	9379	Q9P2S2	M1-G1637

NRXN3	9369	Q9Y4C0	M1-G1569
NT5E	4907	P21589	M1-T550
NT5E	4907	P21589	M1-F548
NTM	50863	Q9P121-4	M1-T334
NTM	50863	Q9P121	M1-N321
NTNG1	22854	Q9Y2I2	M1-G513
NTNG1	22854	Q9Y2I2	M1-F438
NTRK1	4914	P04629-4	M1-S321
NTRK1	4914	P04629-3	M1-S383
NTRK1	4914	P04629-2	M1-S413
NTRK1	4914	P04629	M1-S419
NTRK1	4914	P04629	M1-S419
NTRK2	4915	Q16620	M1-H430
NTRK2	4915	Q16620	M1-H430
NTRK3	4916	Q16288	M1-G423
NTRK3	4916	Q16288	M1-T429
NTRK3	4916	Q16288	M1-G431
OLR1	4973	P78380	G57-Q273
OLR1	4973	P78380	G57-Q273
OMG	4974	P23515	M1-S417
OPCML	4978	Q14982	M1-V321
OPCML	4978	Q14982	M1-N322
OSCAR	126014	Q8IYS5-6	M1-N218
OSCAR	126014	Q8IYS5-4	M1-V271
OSCAR	126014	Q8IYS5-1	M1-V282
OSMR	9180	Q99650	M1-S739
OSMR	9180	Q99650	M1-S739
OSTM1	28962	Q86WC4	M1-P284
OTOA	146183	Q7RTW8	M1-A1130
P2RX2	22953	Q9UBL9	Q64-S337
PAPLN	89932	O95428-1	M1-Q1278
PARM1	25849	Q6UWI2	M1-S258
PBOV1	59351	Q9GZY1	M1-I135
PCDH10	57575	Q9P2E7	M1-D713
PCDH11X	27328	Q9BZA7	M1-K812

PCDH11Y	83259	Q9BZA8	M1-K844
PCDH12	51294	Q9NPG4	M1-S715
PCDH17	27253	O14917	M1-D703
PCDH18	54510	Q9HCL0	M1-S699
PCDH19	57526	Q8TAB3	M1-S678
PCDH20	64881	Q8N6Y1	M1-T862
PCDH9	5101	Q9HC56	M1-T814
PCDHA13	56136	Q9Y5I0	M1-N697
PCDHA7	56141	Q9UN72	M1-N697
PCDHA8	56140	Q9Y5H6	M1-N697
PCDHAC1	56135	Q9H158	M1-Y683
PCDHB1	29930	Q9Y5F3	M1-K689
PCDHB10	56126	Q9UN67	M1-L692
PCDHB11	56125	Q9Y5F2	M1-T687
PCDHB13	56123	Q9Y5F0	M1-T687
PCDHB3	56132	Q9Y5E6	M1-T687
PCDHB4	56131	Q9Y5E5	M1-T686
PCDHB5	26167	Q9Y5E4	M1-T686
PCDHB6	56130	Q9Y5E3	M1-T685
PCDHB7	56129	Q9Y5E2	M1-S683
PCDHB9	56127	Q9Y5E1	M1-T687
PCDHGA11	56105	Q9Y5H2	M1-D689
PCDHGA2	56113	Q9Y5H1	M1-Y692
PCDHGA4	56111	Q9Y5G9	M1-Y692
PCDHGA7	56108	Q9Y5G6	M1-Y692
PCDHGA8	9708	Q9Y5G5	M1-Y692
PCDHGA9	56107	Q9Y5G4	M1-D688
PCDHGB4	8641	Q9UN71	M1-Y689
PCDHGB5	56101	Q9Y5G0	M1-Q685
PCDHGB6	56100	Q9Y5F9	M1-Q689
PCDHGC3	5098	Q9UN70	M1-K687
PCDHGC4	56098	Q9Y5F7	M1-Y693
PCDHGC5	56097	Q9Y5F6-1	M1-T691
PCSK4	54760	Q6UW60	M1-A709
PCSK7	9159	Q16549	M1-T667

PDCD1	5133	Q15116	
PDCD1	5133	Q15116	M1-V170
PDCD1LG2	80380	Q9BQ51-3	M1-L182
PDCD1LG2	80380	Q9BQ51-2	M1-T130
PDCD1LG2	80380	Q9BQ51	M1-T220
PDCD1LG2	80380	Q9BQ51	M1-T220
PDCD1LG2	80380	Q9BQ51	M1-T220
PDGFRA	5156	P16234-2	M1-L218
PDGFRA	5156	P16234	M1-A528
PDGFRB	5159	P09619-2	M1-R336
PDGFRB	5159	P09619	M1-V532
PDGFRL	5157	PDGFRL	M1-S375
PDPN	10630	Q86YL7	M1-L131
PEAR1	375033	Q5VY43	M1-A757
PECAM1	5175	P16284	M1-G602
PECAM1	5175	P16284	M1-K600
PGBD5	79605	Q8N414	M1-Q404
PHEX	5251	P78562	Q42-W749
Phospholipase_In	NA	NA	M1-N215
PI16	221476	Q6UXB8	M1-H443
PIGR	5284	P01833	M1-L640
PIGR	5284	P01833	M1-R638
PIGR	5284	P01833	M1-A639
PIK3IP1	113791	Q96FE7	M1-L173
PILRA	29992	Q9UKJ1-3	M1-A230
PILRA	29992	Q9UKJ1-4	M1-S175
PILRA	29992	Q9UKJ1	M1-V198
PILRA	29992	Q9UKJ1	M1-A197
PILRB	29990	Q9UKJ0-2	M1-R149
PILRB	29990	Q9UKJ0	M1-V192
PILRB	29990	Q9UKJ0	M1-R191
PILRB	29990	Q9UKJ0	M1-R191
PLA2R1	22925	Q13018	M1-P1400
PLB1	151056	Q6P1J6	M1-E1414
PLB1	151056	Q6P1J6	M1-E1414

PLD3	23646	Q8IV08	E61-L490
PLSCR4	57088	Q9NRQ2	M1-D301
PLVAP	83483	Q9BX97	G50-G442
PLVAP	83483	Q9BX97	G50-G442
PLXDC1	57125	Q9Y4D7	M1-T426
PLXDC1	57125	Q9BX97	M1-P409
PLXDC2	84898	Q6UX71	M1-K447
PLXDC2	84898	Q6UX71	M1-G455
PLXNA1	5361	Q9UIW2	M1-A1245
PLXNA2	5362	O75051	M1-P1237
PLXNA3	55558	P51805	M1-A1220
PLXNA4	91584	Q9HCM2	M1-A1238
PLXNB1	5364	O43157	M1-Q1307
PLXNB1	5364	O43157	M1-Q1490
PLXNB2	23654	O15031	M1-P1197
PLXNB2	23654	O15031	M1-S1199
PLXNB3	5365	Q9ULL4	M1-Q1255
PLXNC1	10154	O60486	M1-T944
PLXND1	23129	Q9Y4D7	M1-A1271
PMEL	6490	P40967	M1-Q595
PMEL	6490	P40967	M1-Q595
PMEPA1	56937	Q969W9	M1-F41
PODXL	5420	O00592	M1-P461
PODXL	5420	O00592	M1-M460
PODXL2	50512	Q9NZ53	M1-T500
POMGNT1	55624	Q8WZA1	R63-T660
PRIMA1	145270	Q86XR5	M1-G92
PRLR	5618	P16471	M1-T135
PRLR	5618	P16471	M1-T235
PRLR	5618	P16471	M1-T236
PRND	23627	Q9UKY0	M1-G154
PRND	23627	Q9UKY0	M1-R151
PRNP	5621	P04156	M1-S231
PRNP	5621	P04156	M1-G229
PROCR	10544	Q9UNN8	M1-S210

PROCR	10544	Q9UNN8	M1-S210
PRR24	NA	NA	P57-G142
PRRG1	5638	O14668	M1-L83
PRRG2	5639	O14669	M1-S109
PRRG2	5639	O14669	M1-D106
PRRG3	79057	Q9BZD7	M1-A79
PRRG3	79057	Q9BZD7	M1-D78
PRRG4	79056	Q9BZD6	M1-G116
PRRG4	79056	Q9BZD6	M1-D113
PRSS21	10942	Q9Y6M0	M1-G289
PRSS21	10942	Q9Y6M0	M1-Q287
PRSS41	NA	NA	M1-R293
PRSS55	203074	Q6UWB4	M1-K310
PRSS55	203074	Q6UWB4	M1-G326
PRSS8	5652	Q16651	M1-G319
PRSS8	5652	Q16651	M1-G319
PRTG	283659	Q2VWP7	M1-G950
PSG1	5669	P11464	M1-P419
PSG1	5669	P11464	M1-P419
PSG2	5670	P11465-1	M1-T335
PSG3	5671	Q16557-1	M1-L428
PSG4	5672	Q00888-1	M1-P419
PSG4	5672	P11464	M1-P419
PSG4	5672	Q00888-1	M1-P419
PSG4	5672	P11464	M1-P419
PSG5	5673	Q15238-1	M1-I335
PSG6	5675	Q00889	M1-T335
PSG6	5675	Q00889	M1-L257
PSG6	5675	Q00889	M1-L435
PSG7	5676	Q13046-1	M1-P419
PSG8	440533	Q9UQ74-1	M1-I426
PSG9	5678	Q00887-1	M1-S426
PTCRA	171558	Q6ISU1	M1-A147
PTCRA	171558	Q6ISU1	M1-A147
PTGFRN	5738	Q9P2B2	M1-K830

PTGFRN	5738	Q9P2B2	M1-P832
PTK7	5754	Q13308-3	M1-T574
PTK7	5754	Q13308-4	M1-T648
PTK7	5754	Q13308-2	M1-T664
PTK7	5754	Q13308	M1-T704
PTK7	5754	Q13308	M1-T704
PTPRA	5786	P18433	M1-P142
PTPRA	5786	P18433	M1-P142
PTPRB	5787	P23467-2	M1-G1532
PTPRB	5787	P23467-4	M1-G1532
PTPRB	5787	P23467-2	M1-G1532
PTPRB	5787	P23467-4	M1-G1532
PTPRB	5787	P23467-3	M1-G1840
PTPRB	5787	P23467	M1-G1622
PTPRC	5788	P08575	D193-A576
PTPRC	5788	P08575	M1-A576
PTPRCAP	5790	Q14761	M1-V34
PTPRD	5789	P23468-2	M1-G1244
PTPRD	5789	P23468-3	M1-G737
PTPRD	5789	P23468-4	M1-G845
PTPRD	5789	P23468-7	M1-G852
PTPRD	5789	P23468	M1-G1266
PTPRE	5791	P23469	M1-L47
PTPRF	5792	P10586-2	M1-E1251
PTPRF	5792	P10586	M1-L1262
PTPRG	5793	P23470	M1-E736
PTPRG	5793	P23470	M1-E736
PTPRH	5794	Q9HD43-2	M1-G575
PTPRH	5794	Q9HD43-3	M1-G575
PTPRH	5794	Q9HD43-2	M1-G575
PTPRH	5794	Q9HD43-3	M1-G575
PTPRH	5794	Q9HD43-1	M1-G753
PTPRH	5794	Q9HD43	M1-S751
PTPRJ	5795	Q12913	M1-G971
PTPRK	5796	Q15262	M1-K753

PTPRK	5796	Q15262	M1-K752
PTPRK	5796	Q15262	M1-K752
PTPRM	5797	P28827	M1-K742
PTPRM	5797	P28827	M1-K742
PTPRN	5798	Q16849	M1-S576
PTPRN	5798	Q16849	M1-S576
PTPRN	5798	Q16849	M1-E446
PTPRN2	5799	Q92932	M1-K614
PTPRO	5800	Q16827	M1-V820
PTPRO	5800	Q16827	M1-N819
PTPRR	5801	Q15256	M1-G227
PTPRR	5801	Q15256	M1-G227
PTPRS	5802	Q13332-6	M1-G1260
PTPRS	5802	Q13332-7	M1-G851
PTPRS	5802	Q13332	M1-G1282
PTPRT	11122	O14522	M1-M766
PTPRT	11122	O14522	M1-K746
PTPRU	10076	Q92729	M1-L749
PTPRZ1	5803	P23471	M1-K775
PTPRZ1	5803	P23471	M1-K1635
PVR	5817	P15151	
PVR	5817	P15151	M1-N343
PVRL1	5818	Q15223	A1-S244
PVRL1	5818	Q15223-3	M1-F352
PVRL1	5818	Q15223-2	M1-R348
PVRL1	5818	Q15223	M1-A355
PVRL2	5819	Q92692-2	M1-V361
PVRL2	5819	Q92692	M1-G360
NECTIN3	25945	Q9NQS3-2	M1-C366
NECTIN3	25945	Q9NQS3-3	M1-G347
NECTIN3	25945	Q9NQS3	M1-G411
NECTIN3	25945	Q9NQS3	M1-D400
PVRL4	81607	Q96NY8	M1-S349
PVRL4	81607	Q96NY8	M1-V350
PXDN	7837	A1KZ92-1	M1-P1479

PXDNL	137902	A1KZ92-1	M1-K1462
QSOX1	5768	O00391	M1-D709
QSOX2	169714	Q6ZRP7	M1-S662
RAET1E	135250	Q8TD07	M1-R226
RAET1E	135250	Q8TD07	M1-T212
RAET1G	353091	Q6H3X3	M1-A226
RAET1G	353091	Q6H3X3	M1-V213
RAET1L	154064	Q5VY80	M1-T220
RAET1L	154064	Q5VY80	M1-S217
RAMP1	10267	O60894	M1-S117
RAMP2	10266	O60895	M1-D144
RAMP3	10268	O60896	M1-V118
RARRES1	5918	P49788	A38-F294
RECK	8434	Q13634	M1-G944
RECK	8434	O95980	M1-P941
REKL31489	284274	Q3B7S5	M1-E47
REKL31489	284274	Q3B7S5	M1-E47
RELL1	768211	Q8IUW5	M1-Y58
RELT	84957	Q969Z4	M1-Q162
RELT	84957	Q969Z4	M1-Q162
RET	5979	P07949	M1-R635
RET	5979	P07949	M1-T636
RGMA	56963	Q96B86	M1-G427
RGMB	285704	Q6NW40	M1-T415
RGMB	285704	Q6NW40	M1-G412
RNF128	NA	NA	M1-H205
RNF13	NA	NA	M1-Y182
RNF130	NA	NA	M1-S194
RNF133	NA	NA	M1-H189
RNF149	NA	NA	M1-S200
RNF150	NA	NA	M1-S208
RNF167	NA	NA	M1-G171
ROBO1	6091	Q9Y6N7-4	M1-A859
ROBO1	6091	Q9Y6N7-3	M1-A862
ROBO1	6091	Q9Y6N7-2	M1-A902

ROBO1	6091	Q9Y6N7	M1-P897
ROBO1	6091	Q9Y6N7	M1-P897
ROBO2	6092	Q9HCK4	M1-A860
ROBO2	268902	Q9HCK4	M1-P859
ROBO3	64221	Q96MS0	M1-P891
ROBO4	54538	Q8WZ75	M1-K356
ROBO4	54538	Q8WZ75	M1-K466
ROBO4	54538	Q8WZ75	M1-K466
ROR1	4919	Q01973	M1-Y406
ROR1	4919	Q01973	M1-Y406
ROR2	4920	Q01974	M1-M402
ROR2	4920	Q01974	M1-G403
ROS1	6098	P08922	M1-S1861
RPN1	6184	P04843	M1-P439
RPRML	388394	Q8N4K4	M1-Q69
RTN4R	65078	Q9BZR6	M1-S447
RTN4RL1	146760	Q86UN2	M1-A422
RTP3	83597	Q9BQQ7	M1-N210
RTP4	64108	Q96DX8	M1-D224
RYK	6259	P34925	M1-R224
SARAF	51669	Q96BY9	M1-N172
SAYSD1	55776	Q9NPB0	M1-K105
SCARB1	949	Q8WTV0	K37-H442
SCARF1	8578	Q14162	M1-A422
SCARF2	91179	Q96GP6	M1-R440
SCN1B	6324	Q07699	M1-E160
SCN2B	6327	O60939	M1-G163
SCN2B	6327	O60939	M1-A159
SCN3B	55800	Q9NY72	M1-E159
SCN3B	55800	Q9NY72	M1-E159
SCN4B	6330	Q8IWT1	M1-T161
SCN4B	6330	Q8IWT1	M1-T161
SDC1	6382	P18827	M1-R249
SDC1	6382	P18827	M1-E251
SDC2	6383	P34741	M1-K141

SDC2	6383	P34741	M1-E144
SDC3	9672	O75056	M1-R382
SDC4	6385	P31431	M1-E145
SDC4	6385	P31431	M1-E145
SDK1	221935	Q7Z5N4	M1-E2007
SDK2	54549	Q58EX2	M1-W1930
SECTM1	6398	Q8WVN6	M1-G145
SECTM1	6398	Q8WVN6	M1-G145
SEL1L3	23231	Q68CR1	M1-R1051
SELE	6401	P16581	M1-P556
SELE	6401	P16581	M1-N554
SELL	6402	P14151	M1-P333
SELL	6402	P14151	M1-P333
SELP	6403	P16109	M1-A771
SELP	6403	P16109	M1-E769
SELPLG	6404	Q14242	M1-Q319
SELPLG	6404	Q14242	M1-C310
SEMA3A	10371	Q14563-1	M1-V725
SEMA3B	7869	Q13214-1	M1-S723
SEMA3C	10512	Q99985-1	M1-R739
SEMA3D	223117	O95025-1	M1-E738
SEMA3E	9723	O15041-1	M1-R737
SEMA3F	6405	Q13275	M1-K773
SEMA3G	56920	Q9NS98	M1-K762
SEMA4A	64218	Q9H3S1	M1-S679
SEMA4A	64218	Q9H3S1	M1-H683
SEMA4B	10509	Q9NPR2	M1-D711
SEMA4B	10509	Q9NPR2	M1-E712
SEMA4C	54910	Q9C0C4	M1-G663
SEMA4C	54910	Q9C0C4	M1-G663
SEMA4D	10507	Q92854-2	M1-L738
SEMA4D	10507	Q92854	M1-R734
SEMA4D	10507	Q92854	M1-R734
SEMA4F	10505	O95754-2	M1-T503
SEMA4F	10505	O95754	M1-T658

SEMA4F	10505	O95754	M1-G660
SEMA4G	57715	Q9NTN9-2	M1-L680
SEMA4G	57715	Q9NTN9-3	M1-V702
SEMA4G	57715	Q9NTN9	M1-R674
SEMA4G	57715	Q9NTN9	M1-R674
SEMA5A	9037	Q13591	M1-K961
SEMA5A	9037	Q9P283	M1-N967
SEMA5B	54437	Q9P283	M1-H1036
SEMA6A	57556	Q9H2E6-2	M1-T666
SEMA6A	57556	Q9H2E6	M1-Q644
SEMA6A	57556	Q9H2E6	M1-Q644
SEMA6B	10501	Q9H3T3	M1-S603
SEMA6B	10501	Q9H3T3	M1-S603
SEMA6C	10500	Q9H3T2	M1-P604
SEMA6C	10500	Q9H3T2	M1-P604
SEMA6D	80031	Q8NFY4	M1-N662
SEMA6D	80031	Q8NFY4	M1-N662
SEMA7A	8482	O75326	M1-L647
SEMA7A	8482	O75326	M1-A644
SERPINB7	8710	O75635	Q47-P380
SERTM1	400120	A2A2V5	M1-V41
SEZ6	124925	Q53EL9	M1-A928
SEZ6L	23544	Q9BYH1	M1-A958
SEZ6L2	26470	Q6UXD5	M1-N844
SGCA	6442	Q16586	M1-A290
SGCA	6442	Q16586	M1-D285
SGCB	6443	Q16585	A88-H318
SGCB	6443	Q16585	R91-H318
SGCD	6444	Q92629	K57-L289
SGCD	6444	Q92629	K58-L290
SGCE	8910	O43556	M1-F317
SGCG	6445	Q13326	K59-L291
SGCG	6445	Q13326	K59-L291
SGCZ	137868	Q96LD1	K59-S299
SGCZ	137868	Q96LD1	K72-S312

SHISA2	387914	Q6UWI4	M1-V116
SHISA3	152573	A0PJX4	M1-P98
SHISA3	152573	A0PJX4	M1-P94
SHISA4	149345	Q96DD7	M1-A92
SHISA4	149345	Q96DD7	M1-G88
SHISA5	51246	Q8N114	M1-T109
SIGIRR	59307	Q6IA17	M1-H118
SIGIRR	59307	Q6IA17	M1-H118
SIGLEC1	6614	Q9BZZ2	M1-Q1641
SIGLEC1	6614	Q9BZZ2	M1-Q1641
SIGLEC10	89790	Q96LC7	M1-A494
SIGLEC10	89790	Q96LC7-7	M1-A309
SIGLEC10	89790	Q96LC7-9	M1-A374
SIGLEC10	89790	Q96LC7-6	M1-A399
SIGLEC10	89790	Q96LC7-7	M1-A409
SIGLEC10	89790	Q96LC7-2	M1-A457
SIGLEC10	89790	Q96LC7-4	M1-A462
SIGLEC10	89790	Q96LC7-5	M1-P185
SIGLEC10	89790	Q96LC7	M1-N550
SIGLEC10	89790	Q96LC7	M1-N550
SIGLEC11	114132	Q96RL6-2	M1-G466
SIGLEC11	114132	Q96RL6	M1-G558
SIGLEC11	114132	Q96RL6	M1-G560
SIGLEC12	89858	Q96PQ1	M1-T478
SIGLEC12	89858	Q96PQ1	M1-A481
SIGLEC14	100049587	Q08ET2-1	M1-L356
SIGLEC15	284266	Q6ZMC9	M1-T263
SIGLEC15	284266	Q6ZMC9	M1-T263
SIGLEC16	400709	A6NMB1	M1-G434
SIGLEC5	8778	O15389-1	M1-A440
SIGLEC5	8778	O15389	M1-S353
SIGLEC5	8778	O15389	M1-T359
SIGLEC5	8778	O15389	M1-A440
SIGLEC6	946	O43699-6	M1-G294
SIGLEC6	946	O43699-3	M1-G330

SIGLEC6	946	O43699-5	M1-G357
SIGLEC6	946	O43699-4	M1-P341
SIGLEC6	946	O43699-2	M1-P352
SIGLEC6	946	O43699	M1-V299
SIGLEC6	946	O43699	M1-G346
SIGLEC6	946	O43699	M1-G346
SIGLEC7	27036	Q9Y286-3	M1-E145
SIGLEC7	27036	Q9Y286-2	M1-V258
SIGLEC7	27036	Q9Y286	M1-G350
SIGLEC7	27036	Q9Y286	M1-G350
SIGLEC8	27181	Q9NYZ4-2	M1-T267
SIGLEC8	27181	Q9NYZ4	M1-A363
SIGLEC9	27180	Q9Y336	M1-G348
SIGLECP16	400709	A6NMB1	M1-T433
SIRPA	140885	P78324	M1-Y373
SIRPB1	10326	O00241-2	M1-P153
SIRPB1	10326	O00241	M1-P370
SIRPB2	284759	Q5JXA9-3	M1-L190
SIRPB2	284759	Q5JXA9	M1-G287
SIRPD	128646	Q9H106	M1-K197
SIRPD	128646	Q9H106	H31-K197
SIRPD	128646	Q9H106	M1-Q181
SIRPD	128646	Q9H106	M1-K197
SIRPG	55423	Q9P1W8-3	M1-A146
SIRPG	55423	Q9P1W8-4	M1-A252
SIRPG	55423	Q9P1W8	M1-T359
SIRPG	55423	Q9P1W8	M1-G361
SIT1	27240	Q9Y3P8	M1-A41
SKINTL	391037	A8MVG2	M1-S242
SLAMF1	6504	Q13291	M1-S305
SLAMF1	6504	Q13291	M1-P237
SLAMF6	114836	Q96DU3-3	M1-K114
SLAMF6	114836	Q96DU3	M1-M226
SLAMF7	57823	Q9NQ25-7	M1-I188
SLAMF7	57823	Q9NQ25-6	M1-I204

SLAMF7	57823	Q9NQ25-4	M1-L165
SLAMF7	57823	Q9NQ25-2	M1-S118
SLAMF7	57823	Q9NQ25	M1-M226
SLAMF8	56833	Q9P0V8	M1-D233
SLAMF9	89886	SLAMF9	M1-A142
SLAMF9	89886	Q96A28	M1-C235
SLAMF9	89886	Q96A28	M1-S210
SLAMF9	89886	Q96A28	M1-F234
SLITRK1	114798	Q96PX8	M1-G623
SLITRK2	84631	Q9H156	M1-P617
SLITRK2	84631	Q9H156	M1-V620
SLITRK3	22865	O94933	M1-S654
SLITRK3	22865	O94933	M1-S654
SLITRK4	139065	Q8IW52	M1-S618
SLITRK4	139065	Q8IW52	M1-P616
SLITRK5	26050	O94991	M1-S664
SLITRK5	26050	O94991	M1-S664
SLITRK6	84189	Q9H5Y7	M1-S608
SLITRK6	84189	Q9H5Y7	M1-P606
SMAGP	57228	Q0VAQ4	M1-L36
SMCR7	125170	Q96C03	K48-L454
SMCR7L	54471	Q9NQG6	K47-T463
SNPH	9751	O15079	M1-R423
SOGA3	387104	Q5TF21	M1-Q914
SORCS1	114815	Q8WY21	M1-A1102
SORCS2	57537	Q96PQ0	M1-G1079
SORCS3	22986	Q9UPU3	M1-A1126
SORL1	6653	Q92673	M1-A2138
SORT1	6272	Q99523	M1-S756
SPACA1	81833	Q9HBV2	M1-I220
SPACA1	81833	Q9HBV2	M1-D216
SPACA4	171169	Q8TDM5	M1-T104
SPACA4	171169	Q8TDM5	M1-T104
SPATA9	83890	Q9BWV2	M1-S146
SPATA9	83890	Q9BWV2	M1-S146

SPEM1	374768	Q8N4L4	S51-R309
SPINT1	6692	O43278	M1-K446
SPINT2	10653	O43291	M1-K197
SPINT2	10653	O43291	M1-N189
SPN	6693	P16150	M1-G254
SPN	6693	P16150	M1-R253
SPRN	503542	Q5BIV9	M1-G128
ST14	6768	Q9Y5Y6	H78-V855
ST14	6768	Q9Y5Y6	Q80-V855
ST6GAL1	6480	P15907	K31-C406
STAB1	23166	Q9NY15	M1-G2479
STAB2	55576	Q8WWQ8	M1-G2463
STIM1	6786	Q13586	M1-D213
SUSD1	64420	Q6UWL2	M1-Q724
SUSD2	56241	Q9UGT4	M1-A785
SUSD2	56241	Q9UGT4	M1-A785
SUSD3	203328	Q96L08	M1-K103
SUSD3	203328	Q96L08	M1-K103
SUSD4	55061	Q5VX71	M1-K321
SUSD4	55061	Q5VX71	M1-T321
SUSD5	26032	O60279	M1-G573
TACSTD2	4070	P09758	M1-K271
TAPBP	6892	O15533-4	M1-G328
TAPBP	6892	O15533-1	M1-G415
TAPBPL	55080	Q9BX59	M1-E403
TARM1	441864	B6A8C7	M1-N233
TARM1	441864	B6A8C7	M1-R236
TCP11	6954	Q8WWU5	M1-Q329
TCP11	6954	Q8WWU5	M1-Q266
TCTN2	79867	Q96GX1	M1-Q667
TCTN2	79867	Q96GX1	M1-K671
TCTN3	26123	Q6NUS6	M1-K585
TCTN3	26123	Q6NUS6	M1-C586
TDGF1	6997	P13385	M1-A170
TDGF1	6997	P13385	H33-Y188

TDGF1	6997	P13385	M1-P168
TECTA	7007	O75443	M1-R2081
TECTB	6975	Q96PL2	M1-G305
TECTB	6975	Q96PL2	M1-L301
TEK	7010	Q02763-3	M1-K598
TEK	7010	Q02763-2	M1-K702
TEK	7010	Q02763	M1-K745
TEX101	83639	Q9BY14	M1-R218
TEX101	83639	Q9BY14	M1-E221
TEX29	121793	Q8N6K0	M1-P56
TEX29	121793	Q8N6K0	M1-V55
TFR2	7036	Q9UP52	R104-F801
TFR2	7036	Q9UP52	R105-F801
TGFA	7039	P01135	M1-K96
TGFA	7039	P01135	M1-A89
TGFBR1	7046	P36897-1	M1-A128
TGFBR1	7046	P36897-2	M1-A132
TGFBR1	7046	P36897	M1-E125
TGFBR2	7048	P37173	M1-G169
TGFBR3	7049	Q03167	M1-V787
TGFBR3	7049	Q03167	M1-T784
TGOLN2	10618	O43493	M1-H384
TGOLN2	10618	O43493	M1-H384
THBD	7056	P07204	M1-G516
THBD	7056	P07204	M1-G516
THSD1	55901	Q9NS62	M1-N413
THSD7A	221981	Q9UPZ6	M1-T1606
THSD7B	80731	Q9C0I4	M1-K1557
THSD7B	80731	Q9C0I4	M1-K1558
THY1	7070	P04216	M1-L161
THY1	7070	P04216	M1-L161
THY1	7070	P04216	M1-K129
TIE1	7075	P35590-2	M1-G379
TIE1	7075	P35590-3	M1-S317
TIE1	7075	P35590	M1-Q759

TIGIT	201633	Q495A1	
TIGIT	201633	Q495A1	M1-P141
TIMD4	91937	Q96H15	M1-I319
TIMD4	91937	Q96H15-2	M1-Q286
TIMD4	91937	Q96H15	M1-Q314
TIMD4	91937	Q96H15	M1-Q314
TLR1	7096	Q15399	M1-T580
TLR1	7096	Q15399	M1-T580
TLR10	81793	Q9BXR5	M1-A577
TLR10	81793	Q9BXR5	M1-T576
TLR2	7097	O60603	M1-T588
TLR3	7098	O15455	M1-L704
TLR4	7099	O00206	M1-K631
TLR5	7100	O60602	M1-K639
TLR6	10333	Q9Y2C9	M1-T585
TLR6	10333	Q9Y2C9	M1-T585
TLR7	51284	Q9NYK1	M1-L840
TLR8	51311	Q9NR97	M1-A828
TLR8	51311	Q9NR97	M1-D825
TLR9	54106	Q9NR96	M1-A820
TMEFF1	8577	O95980	M1-H329
TMEFF1	8577	Q8IYR6	M1-H329
TMEFF2	23671	Q9UIK5	M1-V320
TMEM106A	113277	Q96A25	P116-P262
TMEM106A	113277	Q96A25	P116-P262
TMEM108	66000	Q6UXF1	M1-D468
TMEM108	66000	Q6UXF1	M1-D468
TMEM119	338773	Q4V9L6	M1-M96
TMEM123	114908	Q8N131	M1-S149
TMEM123	114908	Q8N131	M1-T166
TMEM123	114908	Q8N131	M1-S168
TMEM130	222865	Q8N3G9	M1-A340
TMEM130	222865	Q8N3G9	M1-P339
TMEM132A	54972	Q24JP5	M1-A852
TMEM132B	114795	Q14DG7	M1-A903

TMEM132B	114795	Q14DG7	M1-Y902
TMEM132C	92293	Q8N3T6	M1-E924
TMEM132C	92293	Q8N3T6	M1-E924
TMEM132D	121256	Q14C87	M1-G919
TMEM132E	124842	Q6IEE7	M1-A803
TMEM154	201799	Q6P9G4	M1-E75
TMEM154	201799	Q6P9G4	M1-E75
TMEM156	80008	Q8N614	M1-K213
TMEM156	80008	Q8N614	M1-K213
TMEM158	25907	Q8WZ71	M1-A226
TMEM167A	153339	Q8TBQ9	M1-R52
TMEM167A	153339	Q8TBQ9	M1-K53
TMEM167B	56900	Q9NRX6-1	M1-R54
TMEM183A	92703	Q8IXX5	M1-N301
TMEM183A	92703	Q8IXX5	M1-T299
TMEM183B	653659	Q1AE95	M1-N301
TMEM183B	653659	Q1AE95	T171-N301
TMEM190	147744	Q8WZ59	M1-R77
TMEM190	147744	Q8WZ59	M1-H80
TMEM2	23670	Q9UHN6	S104-H1383
TMEM207	131920	Q6UWW9	M1-Y51
TMEM207	131920	Q6UWW9	M1-G49
TMEM213	155006	A2RRL7	M1-G71
TMEM24	9854	O14523	Q32-L706
TMEM24	9854	O14523	Q32-L706
TMEM240	339453	Q5SV17-1	M1-L90
TMEM25	84866	Q86YD3-3	M1-L218
TMEM25	84866	Q86YD3-2	M1-L322
TMEM25	84866	Q86YD3	M1-G237
TMEM27	57393	Q9HBJ8	M1-P141
TMEM27	57393	Q9HBJ8	M1-P141
TMEM27	57393	Q9HBJ8	L163-L222
TMEM52	339456	Q8NDY8	M1-H55
TMEM52	339456	Q8NDY8	M1-L43
TMEM53	79639	Q6P2H8	H196-C277

TMEM59	9528	Q9BXS4	M1-G239
TMEM59	9528	Q9BXS4	M1-G239
TMEM59L	25789	Q9UK28	M1-R261
TMEM59L	25789	Q9UK28	M1-R267
TMEM81	388730	Q6P7N7	M1-K221
TMEM92	162461	Q6UXU6	M1-R57
TMEM95	339168	Q3KNT9	M1-K145
TMEM95	339168	Q3KNT9	M1-K145
TMEM98	26022	Q9NQ34	Q29-I226
TMEM9B	56674	Q9NQ34	M1-T104
TMIE	259236	Q8NEW7	M1-L56
TMIE	259236	Q8NEW7	M1-R55
TMIGD1	388364	Q6UXZ0	M1-A226
TMIGD1	388364	Q6UXZ0	M1-P220
TMIGD2	126259	Q96BF3	M1-F153
TMIGD2	126259	Q96BF3	M1-G150
TMPRSS11A	339967	Q6ZMR5	K48-I421
TMPRSS11B	132724	Q86T26	E42-L416
TMPRSS11D	9407	O60235	A42-I418
TMPRSS11D	9407	O60235	F43-I418
TMPRSS11E	28983	Q9UL52	H41-I423
TMPRSS11E	28983	Q9UL52	I192-I423
TMPRSS11E	28983	Q9UL52	K49-I423
TMPRSS11F	389208	Q6ZWK6	E54-M438
TMPRSS11F	389208	Q6ZWK6	E54-M438
TMPRSS12	283471	Q86WS5	M1-G324
TMPRSS12	283471	Q86WS5	M1-Q323
TMPRSS13	84000	Q9BYE2	Q187-V586
TMPRSS13	84000	Q9BYE2	Q182-V581
TMPRSS15	9966	O95150	T42-H1019
TMPRSS2	7113	O15393	K107-G492
TMPRSS4	56649	Q9NRS4	K54-L437
TMPRSS4	56649	Q9NRS4	D58-L437
TMPRSS5	80975	Q9H3S3	P74-L457
TMPRSS5	80975	Q9H3S3	Y71-L457

TMPRSS7	344805	Q7RTY8	S100-L843
TMPRSS7	344805	Q7RTY8	M1-L717
TMPRSS9	360200	Q7Z410	S51-E1059
TMX4	56255	Q9H1E5	M1-A185
TMX4	56255	Q9H1E5	2.M1-S188
TNF	7124	P01375	G57-L233
TNF	7124	P01375	I56-L233
TNFRSF10A	8797	O00220-1	M1-I240
TNFRSF10A	8797	O00220	M1-N239
TNFRSF10A	8797	O00220	M1-N239
TNFRSF10B	8795	O14763-2	M1-G184
TNFRSF10B	8795	O14763-3	M1-R118
TNFRSF10B	8795	O14763	M1-S210
TNFRSF10C	8794	O14798	M1-A236
TNFRSF10C	8794	O14798	M41-S278
TNFRSF10D	8793	Q9UBN6-1	M1-H211
TNFRSF10D	8793	Q9UBN6	M1-P209
TNFRSF11A	8792	Q9Y6Q6-6	M1-H194
TNFRSF11A	8792	Q9Y6Q6-1	M1-P212
TNFRSF11A	8792	Q9Y6Q6	M1-H208
TNFRSF11B	4982	O00300-1	M1-L401
TNFRSF12A	51330	Q9NP84	M1-I81
TNFRSF13B	23495	O14836-2	M1-A115
TNFRSF13B	23495	O14836-3	M1-G176
TNFRSF13B	23495	O14836-1	M1-S165
TNFRSF13B	23495	O14836	M1-V160
TNFRSF13C	115650	Q96RJ3	M1-G80
TNFRSF14	8764	Q92956	M1-H116
TNFRSF14	8764	Q92956-2	M1-H116
TNFRSF14	8764	Q92956	M1-V202
TNFRSF14	8764	Q92956	
TNFRSF17	608	Q02223-1	M1-I55
TNFRSF17	608	Q02223-2	M1-R135
TNFRSF17	608	Q02223	M1-G51
TNFRSF18	8784	Q9Y5U5	M1-S255

TNFRSF18	8784	Q9Y5U5	M1-P162
TNFRSF19	55504	Q9NS68	M1-A172
TNFRSF1A	7132	P19438-5	M1-K218
TNFRSF1A	7132	P19438-1	M1-T211
TNFRSF1A	7132	P19438-4	M1-T228
TNFRSF1A	7132	P19438	M1-N201
TNFRSF1B	7133	P20333	M1-D257
TNFRSF21	27242	O75509-1	M1-H349
TNFRSF21	27242	O75509	M1-H349
TNFRSF25	8718	Q93038-11	M1-G208
TNFRSF25	8718	Q93038-8	M1-P234
TNFRSF25	8718	Q93038-9	M1-Q154
TNFRSF25	8718	Q93038-3	M1-R218
TNFRSF25	8718	Q93038-12	M1-R277
TNFRSF25	8718	Q93038-7	M1-S126
TNFRSF25	8718	Q93038-6	M1-T136
TNFRSF25	8718	Q93038-5	M1-T181
TNFRSF25	8718	Q93038	M1-Q199
TNFRSF4	7293	P43489	M1-A217
TNFRSF6B	8771	O95407	M1-H300
TNFRSF8	943	P28908	M1-P386
TNFRSF9	3604	Q07011-1	M1-Q186
TNFRSF9	3604	Q12933	M1-Q186
TNFSF10	8743	P50591	T39-G281
TNFSF10	8743	P50591	T39-G299
TNFSF11	NA	NA	F70-D317
TNFSF11	8600	O14788	I140-D317
TNFSF13	8741	O75888	A105-L250
TNFSF14	8740	O43557	Q60-V240
TNFSF15	NA	NA	S57-L251
TNFSF15	9966	O95150-3	M1-L174
TNFSF15	9966	O95150	M1-L192
TNFSF15	9966	O95150	Q27-L174
TNFSF15	9966	O95150	S57-L250
TNFSF15	9966	O95150	L72-L251

TNFSF18	8995	Q9UNG2	Q50-S177
TNFSF4	7292	P23510	H46-L183
TNFSF4	7292	P23510	Q51-L183
TNFSF8	944	P32971	Q63-D234
TNFSF8	944	P32971	Q63-D234
TNFSF8	944	P32971	Q63-D234
TNFSF9	8744	P41273	R71-E254
TNFSF9	8744	P41273	S56-E254
TNMD	64102	Q9H2S6	K60-V317
TNMD	64102	Q9H2S6	K51-V317
TP53I13	90313	Q8NBR0	M1-A311
TPBG	7162	Q13641	M1-S355
TPO	7173	P23467	M1-T848
TPSG1	25823	Q9NRR2	M1-P283
TPSG1	25823	Q9NRR2	M1-R281
TPSG1	25823	Q9NRR2	I38-R281
TREH	11181	O43280	M1-A558
TREM1	54210	Q9NP99-3	M1-M225
TREM1	54210	Q9NP99-2	M1-S150
TREM1	54210	Q9NP99	M1-P202
TREM1	54210	Q9NP99	M1-P202
TREM2	54209	Q9NZC2-2	M1-G219
TREM2	54209	Q9NZC2-2	M1-G219
TREM2	54209	Q9NZC2-3	M1-Q222
TREM2	54209	Q9NZC2	M1-S174
TREML1	340205	Q86YW5	M1-G166
TREML1	340205	Q86YW5-3	M1-P51
TREML1	340205	Q86YW5	M1-P162
TREML2	79865	Q5T2D2	M1-D265
TREML2	79865	Q5T2D2	M1-D265
TREML4	285852	Q6UXN2	M1-R183
TREML4	285852	Q6UXN2	M1-G180
TRHDE	29953	TRHDE	S62-H1024
TRHDE	29953	Q9UKU6	R64-H1024
TRIL	9865	Q7L0X0	M1-Q696

TXNDC15	79770	Q96J42	M1-D323
TYRO3	7301	Q06418	M1-S428
TYROBP	7305	O43914-3	M1-V31
TYROBP	7305	O43914-1	M1-V42
TYRP1	7306	P17643	M1-E477
ULBP1	80329	Q9BZM6	M1-A222
ULBP1	80329	Q9BZM6	M1-A214
ULBP2	80328	Q9BZM5	M1-G218
ULBP3	79465	Q9BZM4	M1-P216
ULBP3	79465	Q9BZM4	M1-A215
UMOD	7369	P07911	M1-R606
UMOD	7369	P07911	M1-V613
UMODL1	NA	NA	M1-E1388
UMODL1	89766	Q5DID0	M1-G1271
UNC5A	90249	Q6UXZ4	M1-P301
UNC5A	90249	Q6ZN44	M1-P301
UNC5A	90249	Q6ZN44	M1-Y306
UNC5B	219699	Q8IZJ1-2	M1-A364
UNC5B	219699	Q8IZJ1	M1-Y377
UNC5C	8633	O95185-2	M1-D395
UNC5C	8633	O95185	M1-D376
UNC5C	8633	O95185	M1-Y380
UNC5D	137970	Q6UXZ4	M1-D379
UNC5D	137970	Q6UXZ4	M1-D379
UPK3BL	100134938	B0FP48	M1-T202
UPK3BL	100134938	B0FP48	M1-T202
UXS1	80146	Q8NBZ7	R41-S420
UXS1	80146	Q8NBZ7	E85-Q402
VASN	114990	Q6EMK4	M1-P575
VCAM1	7412	P19320-3	M1-E606
VCAM1	7412	P19320-2	M1-E636
VCAM1	7412	P19320	M1-E698
VLDLR	7436	P98155	M1-A799
VLDLR	7436	P98155	M1-S797
VNN1	8876	O95497	M1-G491

VNN2	8875	O95498	M1-S492
VNN3	55350	Q9NY84	M1-A472
VPREB1	7441	P12018-1	M1-P145
VPREB3	29802	Q9UKI3-1	M1-P123
VSIG1	340547	Q86XK7-2	M1-G270
VSIG1	340547	Q86XK7	M1-E232
VSIG1	340547	Q86XK7	M1-E232
VSIG10	54621	Q8N0Z9	M1-N410
VSIG10	54621	Q8N0Z9	M1-G413
VSIG2	23584	Q96IQ7	M1-G244
VSIG4	11326	Q9Y279-3	M1-P189
VSIG4	11326	Q9Y279	M1-P283
VSTM1	284415	Q6UX27-2	M1-V205
VSTM1	284415	Q6UX27	M1-T135
VSTM1	284415	Q6UX27	M1-T135
VSTM2A	222008	Q8TAG5-1	M1-G220
VSTM2B	342865	A6NLU5	M1-T263
VSTM2L	128434	Q96N03-1	M1-L192
VSTM2L	128434	Q96N03-1	M1-L204
VSTM4	196740	Q8IW00-2	M1-S191
VSTM4	196740	Q8IW00	M1-Y180
VSTM4	196740	Q8IW00	M1-L177
VSTM5	387804	A8MXK1-1	M1-H147
VTCN1	79679	Q7Z7D3-3	M1-F87
VTCN1	79679	Q7Z7D3-2	M1-K130
VTCN1	79679	Q7Z7D3-2	M1-S143
VTCN1	79679	Q7Z7D3	M1-L260
VTCN1	79679	Q7Z7D3	M1-S259
VTCN1	79679	Q7Z7D3	M1-K246
WBP1	23559	Q96G27	M1-L56
WBP1	23559	Q96G27	R76-P269
WDR11	55717	Q9BZH6	M1-K1126
WFIKKN1	117166	Q96NZ8-1	M1-D548
WFIKKN2	124857	Q8TEU8-1	M1-H576
XG	7499	P55808	M1-K142

XPNPEP2	7512	O43895	M1-A650
XXYLT1	152002	Q8NBI6	R54-D393
ZAN	7455	Q9Y493	M1-R2753
ZNRF4	NA	NA	M1-P250
ZP1	22917	P60852	M1-P601
ZP1	22917	P60852	M1-P601
ZP2	7783	Q05996	M1-A716
ZP3	7784	P21754	M1-V387
ZP4	57829	Q12836	M1-K505
ZPBP	11055	Q9BS86-1	M1-L351
ZPBP2	124626	Q6X784-2	M1-D316
ZPBP2	124626	Q6X784-1	M1-D338
ZPLD1	131368	Q8TCW7	M1-A373
ZPLD1	131368	Q8TCW7	M1-S372

Table 3. Proteins predicted to interact

Gene A Gene Symbol	Gene B Gene Symbol	Gene A EntrezID	Gene B EntrezID
ACE2	TIGIT	59272	201633
ACPT	VSTM2B	93650	342865
ACVR1	EGF	90	1950
ADAM12	RNF13	8038	11342
ADAM17	CLEC1B	6868	51266
ADAM20	IL1RAPL1	8748	11141
ADAM20	IL1RAPL2	8748	26280
ADAM21	CLEC12B	8747	387837
ADAM21	CRTAM	8747	56253
ADAM21	IGSF21	8747	84966
ADAM7	BAMBI	8756	25805
ADAM9	RNF13	8754	11342
ADAM9	RNF167	8754	26001
AGER	CLEC14A	177	161198
AJAP1	CD177	55966	57126
ALCAM	ALCAM	214	214
APLP1	CNTN3	333	5067

APLP1	CNTN4	333	152330
APLP2	CLEC1B	334	51266
APLP2	FLT1	334	2321
APLP2	GREM1	334	26585
APLP2	LILRB5	334	10990
APP	CLEC1B	351	51266
APP	CNTN3	351	5067
APP	CNTN4	351	152330
APP	FLT1	351	2321
AQPEP	VSIG8	206338	391123
ASGR1	RNF128	432	79589
ATP1B1	BCAM	481	4059
AXL	IL1RL1	558	9173
AXL	VSIG10L	558	147645
BCAM	ROBO4	4059	54538
BMP5	PTPRD	653	5789
BMP5	WISP1	653	8840
BSG	NCAM1	682	4684
BTN1A1	DPP4	696	1803
BTN1A1	RNF167	696	26001
BTN2A1	FAM187B	11120	148109
BTN3A1	LRRC4B	11119	94030
BTN3A1	VSIG8	11119	391123
BTN3A2	LRRC4B	11118	94030
BTN3A3	LRRC4B	10384	94030
C10orf54	IGSF11	64115	152404
C10orf54	VSIG8	64115	391123
C11orf24	CD177	53838	57126
C6orf25	LRRTM1	80739	347730
CA12	SIGLEC6	771	946
CA9	CLEC1B	768	51266
CADM1	CRTAM	23705	56253
CADM3	C12orf63	57863	144535
CADM3	CADM2	57863	253559
CADM3	CADM3	57863	57863

CADM3	CADM4	57863	199731
CADM3	PEAR1	57863	375033
CADM4	CADM2	199731	253559
CD14	PLXND1	929	23129
CD177	C2orf82	57126	389084
CD177	CACHD1	57126	57685
CD177	CADM2	57126	253559
CD177	CD300LG	57126	146894
CD177	FCRL6	57126	343413
CD177	HEG1	57126	57493
CD177	LRP11	57126	84918
CD177	LRRC15	57126	131578
CD177	RNF150	57126	57484
CD177	TEX101	57126	83639
CD1B	IL6ST	910	3572
CD2	CD177	914	57126
CD2	NLGN3	914	54413
CD22	IGSF21	933	84966
CD244	IYD	51744	389434
CD244	MUC15	51744	143662
CD248	CD177	57124	57126
CD28	TMEM95	940	339168
CD300A	CLEC1B	11314	51266
CD300A	IGSF5	11314	150084
CD300C	IGSF5	10871	150084
CD300C	NTNG1	10871	22854
CD300LB	LRRC52	124599	440699
CD300LF	IGSF5	146722	150084
CD320	AMICA1	51293	120425
CD320	IGSF5	51293	150084
CD320	TMEM167A	51293	153339
CD33	KIRREL3	945	84623
CD34	NECTIN3	947	25945
CD34	NECTIN4	947	81607
CD3G	RNF13	917	11342

CD4	MOG	920	4340
CD4	NCR1	920	9437
CD4	SIGLEC6	920	946
CD40	IL11RA	958	3590
CD47	PCSK4	961	54760
CD47	SCN1B	961	6324
CD47	SIGLEC1	961	6614
CD48	CD177	962	57126
CD48	PDCD1	962	5133
CD5	TNFRSF25	921	8718
CD59	SIGLEC1	966	6614
CD59	STAB1	966	23166
CD59	TNFSF15	966	9966
CD6	DAG1	923	1605
CD6	HBEGF	923	1839
CD6	PILRA	923	29992
CD6	SIGLEC10	923	89790
CD6	SIGLEC8	923	27181
CD69	MXRA5	969	25878
CD69	SIRPA	969	140885
CD7	ADAM15	924	8751
CD7	FRMD3	924	257019
CD7	KIAA0319L	924	79932
CD79A	VSIG8	973	391123
CD79B	CD244	974	51744
CD79B	IGSF21	974	84966
CD79B	KREMEN1	974	83999
CD79B	NTM	974	50863
CD80	LSAMP	941	4045
CD99	SIRPA	4267	140885
CDH11	GLIPR1	1009	11010
CDH11	PLXDC1	1009	57125
CDH11	VSTM2L	1009	128434
CDH13	NCAM2	1012	4685
CDH6	CNTN1	1004	1272

CDH6	PTGFRN	1004	5738
CDH9	BTN3A1	1007	11119
CDH9	CD177	1007	57126
CEACAM1	CEACAM1	634	634
CEACAM1	ITGA1	634	3672
CEACAM19	CD177	56971	57126
CEACAM20	VSIG8	125931	391123
CEACAM3	CEACAM7	1084	1087
CEACAM3	PTPRD	1084	5789
CEACAM4	FLT4	1089	2324
CEACAM4	PDCD1LG2	1089	80380
CEACAM5	CEACAM3	1048	1084
CEACAM5	CEACAM5	1048	1048
CEACAM5	CEACAM7	1048	1087
CEACAM5	CEACAM8	1048	1088
CEACAM5	LRP8	1048	7804
CEACAM6	STAB1	4680	23166
CEACAM6	UXS1	4680	80146
CEACAM8	BTN2A2	1088	10385
CEACAM8	PTPRO	1088	5800
CEACAM8	TECTB	1088	6975
CHL1	CNTN5	10752	53942
CHL1	SIRPA	10752	140885
CHL1	TMEM132A	10752	54972
CLEC10A	CD177	10462	57126
CLEC10A	LILRA1	10462	11024
CLEC10A	LILRA3	10462	11026
CLEC10A	LILRB5	10462	10990
CLEC10A	RNF128	10462	79589
CLEC1B	AQPEP	51266	206338
CLEC1B	CCDC47	51266	57003
CLEC1B	LRRC15	51266	131578
CLEC1B	LVRN	51266	206338
CLEC1B	MDGA2	51266	161357
CLEC1B	PRRG4	51266	79056

CLECSF13	CD177	10462	57126
CLECSF13	LILRA1	10462	11024
CLECSF13	LILRA3	10462	11026
CLECSF13	LILRB5	10462	10990
CLECSF13	RNF128	10462	79589
CLMP	AMICA1	79827	120425
CNTFR	LILRB4	1271	11006
CNTN1	CHL1	1272	10752
CNTN1	FCGRT	1272	2217
CNTN1	PCDHB7	1272	56129
CNTN1	SGCG	1272	6445
CNTN2	CNTN2	6900	6900
CNTN2	KREMEN1	6900	83999
CNTN4	AQPEP	152330	206338
CNTN4	LVRN	152330	206338
CORIN	KIRREL	10699	55243
CORIN	LRRC4C	10699	57689
CR2	CD177	1380	57126
CR2	ILDR1	1380	286676
CR2	RNF130	1380	55819
CRTAM	ILDR2	56253	387597
CRTAM	MUC15	56253	143662
CSF1R	LY6G6F	1436	259215
CSF1R	MGC39681	1436	283197
CSF1R	PRTG	1436	283659
CSF1R	TEK	1436	7010
CSF3R	CD244	1441	51744
CSF3R	IGSF21	1441	84966
CSPG5	CLEC1B	10675	51266
CTLA4	FAM200A	1493	221786
CTLA4	PCDHGB4	1493	8641
CTLA4	WBP1	1493	23559
CXADR	KLRAP1	1525	10748
CXADR	LILRB1	1525	10859
CXADR	TNFRSF10A	1525	8797

DAG1	EFNB1	1605	1947
DAG1	SARAF	1605	51669
DDR1	LY6G6F	780	259215
DPP4	CADM3	1803	57863
DPP4	CUZD1	1803	50624
DPP4	EMC1	1803	23065
DPP4	IGFLR1	1803	79713
DPP4	IMPG2	1803	50939
DPP4	KIAA0090	1803	23065
DPP4	NOTCH2	1803	4853
DPP4	SLITRK3	1803	22865
DSC1	CD177	1823	57126
DSC3	CRTAM	1825	56253
DSCAM	DSCAM	1826	1826
DSCAM	PTPRT	1826	11122
DSCAML1	DSCAML1	57453	57453
DSG1	FLT4	1828	2324
EDA	IL1RL1	1896	9173
EDA2R	KIR3DL3	60401	115653
EDAR	REG4	10913	83998
EFNB1	AQPEP	1947	206338
EFNB1	DSG4	1947	147409
EFNB1	EVC2	1947	132884
EFNB1	FAM187B	1947	148109
EFNB1	ITLN1	1947	55600
EFNB1	LAIR1	1947	3903
EFNB1	LVRN	1947	206338
EFNB1	NAALAD2	1947	10003
EFNB1	SLAMF9	1947	89886
EFNB1	TRHDE	1947	29953
EFNB2	C19orf38	1948	255809
EFNB2	FCRL1	1948	115350
EFNB2	KIR2DS3	1948	3808
EFNB2	KLRAP1	1948	10748
EFNB2	MGC39681	1948	283197

EFNB2	TCTN2	1948	79867
EFNB3	C19orf38	1949	255809
EFNB3	FAM200A	1949	221786
EFNB3	MGC39681	1949	283197
EFNB3	PTPRN	1949	5798
EFNB3	TCTN3	1949	26123
EGF	TNFRSF11B	1950	4982
ENPEP	SLITRK1	2028	114798
EPHA3	CD274	2042	29126
EPHA3	LILRA3	2042	11026
EPHA7	PILRB	2045	29990
EPHB6	FLT1	2051	2321
ERBB4	DLK1	2066	8788
F11R	ULBP3	50848	79465
F3	ULBP3	50848	79465
FCAR	TNFRSF14	2204	8764
FCAR	VSIG8	2204	391123
FCER1A	PEAR1	2205	375033
FCGR2A	PDCD1	2212	5133
FCGR3B	EDA2R	2215	60401
FCGRT	CD300E	2217	342510
FCGRT	IGFLR1	2217	79713
FCGRT	SHISA4	2217	149345
FCRL1	VSIG8	115350	391123
FCRL4	AMICA1	83417	120425
FGFR2	RAMP1	2263	10267
FGFR3	IL1RAPL2	2261	26280
FGFR3	KL	2261	9365
FGFR4	BCAM	2264	4059
FGFR4	GPC3	2264	2719
FGFR4	GPC6	2264	10082
FGFR4	MCAM	2264	4162
FGFR4	NRXN2	2264	9379
FGFR4	NRXN3	2264	9369
FGFR4	SIGLEC15	2264	284266

FGFR4	TGFBR3	2264	7049
FGFRL1	PLVAP	53834	83483
FLRT1	UNC5A	23769	90249
FLRT1	UNC5B	23769	219699
FLRT1	UNC5D	23769	137970
FLRT2	PILRA	23768	29992
FLRT2	UNC5A	23768	90249
FLRT2	UNC5B	23768	219699
FLRT3	UNC5A	23767	90249
FLRT3	UNC5B	23767	219699
FLRT3	UNC5D	23767	137970
FLT1	C14orf37	2321	145407
FLT1	CCDC47	2321	57003
FLT1	CD300LB	2321	124599
FLT1	CD300LF	2321	146722
FLT1	CLEC10A	2321	10462
FLT1	CLECSF13	2321	10462
FLT1	CSPG5	2321	10675
FLT1	ELFN1	2321	392617
FLT1	ELFN2	2321	114794
FLT1	GPC3	2321	2719
FLT1	GPIHBP1	2321	338328
FLT1	TGFBR3	2321	7049
FLT1	TMEFF1	2321	8577
FLT1	TREM2	2321	54209
FLT1	UNC5B	2321	219699
FLT1	VLDLR	2321	7436
FLT4	ADAM21	2324	8747
FLT4	FCRL1	2324	115350
FLT4	FLRT2	2324	23768
FLT4	KIR2DS5	2324	3810
FLT4	LILRB1	2324	10859
FLT4	MUC15	2324	143662
G6B	LRRTM1	80739	347730
GFRA1	CD177	2674	57126

GFRA1	TREM2	2674	54209
GFRA2	CD177	2675	57126
GFRA2	CLEC1B	2675	51266
GLG1	CD177	2734	57126
GLG1	MOG	2734	4340
GLG1	UNC5B	2734	219699
GP2	P2RX2	2813	22953
GP2	PIGR	2813	5284
GP2	SEMA3A	2813	10371
GP5	LAIR1	2814	3903
GP5	LAYN	2814	143903
GPC1	GREM1	2817	26585
GPC1	TNFRSF11B	2817	4982
GPC3	GREM1	2719	26585
GPC3	TNFRSF11B	2719	4982
GPC3	UNC5C	2719	8633
GPC3	UNC5D	2719	137970
GPC3	VSIG10L	2719	147645
GPC4	FGFR4	2239	2264
GPC4	FGFRL1	2239	53834
GPC4	FLT1	2239	2321
GPC4	GREM1	2239	26585
GPC4	NECTIN4	2239	81607
GPC4	TNFRSF11B	2239	4982
GPC6	FGFRL1	10082	53834
GPC6	GREM1	10082	26585
GREM1	C14orf37	26585	145407
GREM1	CCDC47	26585	57003
GREM1	GPIHBP1	26585	338328
GREM1	PCDHB9	26585	56127
GUCY2D	NECTIN3	3000	25945
GUCY2D	NECTIN4	3000	81607
HAVCR1	CLEC1B	26762	51266
HAVCR1	IGSF21	26762	84966
HBEGF	MOG	1839	4340

HBEGF	PILRA	1839	29992
HHLA2	KIR3DL3	11148	115653
HHLA2	TMIGD2	11148	126259
HHLA2	VSIG8	11148	391123
HHLA2	VSTM2B	11148	342865
ICAM5	CLEC10A	7087	10462
ICAM5	CLECSF13	7087	10462
ICAM5	CSPG5	7087	10675
ICAM5	PDCD1LG2	7087	80380
ICOSLG	NTM	23308	50863
IFNAR2	CLEC1B	3455	51266
IGDCC3	IL22RA1	9543	58985
IGDCC4	PLB1	57722	151056
IGSF11	CLEC2L	152404	154790
IGSF11	EPGN	152404	255324
IGSF21	ILDR2	84966	387597
IGSF21	IYD	84966	389434
IGSF21	MUC15	84966	143662
IGSF3	HAVCR1	3321	26762
IGSF3	MRC1	3321	4360
IGSF3	PTGFRN	3321	5738
IGSF3	TIMD4	3321	91937
IGSF9B	NEGR1	22997	257194
IL15RA	CD177	3601	57126
IL15RA	IL22RA1	3601	58985
IL17RC	IGSF8	84818	93185
IL18R1	NETO2	8809	81831
IL1RAP	PTPRD	3556	5789
IL1RAP	PTPRF	3556	5792
IL1RAP	PTPRS	3556	5802
IL1RAPL1	APOO	11141	79135
IL1RAPL1	CNTN5	11141	53942
IL1RAPL1	MILR1	11141	284021
IL1RAPL1	SIGLEC12	11141	89858
IL1RAPL2	APOO	26280	79135

IL1RAPL2	CNTN5	26280	53942
IL1RAPL2	MILR1	26280	284021
IL20RA	CD276	53832	80381
IL20RA	CLEC14A	53832	161198
IL20RA	LYPD6	53832	130574
IL20RA	PCDHAC1	53832	56135
IL2RA	CD177	3559	57126
IL2RG	CADM3	3561	57863
IL4R	PCDHGB6	3566	56100
IL4R	SIGLEC8	3566	27181
IL6R	BTNL9	3570	153579
IL6R	LILRB1	3570	10859
IL6R	LRTM2	3570	654429
IL6ST	VSIG10	3572	54621
IL7R	GREM1	3575	26585
IL7R	TNFRSF11B	3575	4982
IMPG2	CADM3	50939	57863
IMPG2	CD177	50939	57126
ITGA1	CEACAM6	3672	4680
IZUMO1	LILRA5	284359	353514
KIAA0319L	CD300LF	79932	146722
KIR2DL4	MOG	3805	4340
KIR2DL5A	KIAA0319L	57292	79932
KIR2DL5A	TMEM167A	57292	153339
KIR2DS3	NEGR1	3808	257194
KIR2DS5	IGSF21	3810	84966
KIR3DL1	TREML1	3811	340205
KIR3DL1	VSIG8	3811	391123
KIR3DL2	LILRA1	3812	11024
KIRREL	KIRREL	55243	55243
KITLG	LRRN3	4254	54674
KLRAP1	PILRA	10748	29992
L1CAM	AQPEP	3897	206338
L1CAM	CHL1	3897	10752
L1CAM	L1CAM	3897	3897

L1CAM	LVRN	3897	206338
LAYN	LY6G6F	143903	259215
LDLR	IL20RA	3949	53832
LDLR	LILRA1	3949	11024
LDLR	LILRB5	3949	10990
LDLR	LRRC4C	3949	57689
LEPR	KIR2DL5A	3953	57292
LILRA1	EPHA6	11024	285220
LILRA1	JAM3	11024	83700
LILRA1	LILRA1	11024	11024
LILRA1	NETO2	11024	81831
LILRA1	SEMA6A	11024	57556
LILRA1	TMEM183B	11024	653659
LILRA3	IGSF9B	11026	22997
LILRA3	NETO2	11026	81831
LILRA6	CD300E	79168	342510
LILRA6	LCTL	79168	197021
LILRA6	LY6G6F	79168	259215
LILRA6	SLITRK4	79168	139065
LILRB1	CLEC6A	10859	93978
LILRB1	EDAR	10859	10913
LILRB1	ILDR1	10859	286676
LILRB1	LILRA5	10859	353514
LILRB2	IGSF8	10288	93185
LILRB3	LRRC15	11025	131578
LILRB3	LY6G6F	11025	259215
LILRB5	CD177	10990	57126
LILRB5	PILRA	10990	29992
LRCH4	CADM3	4034	57863
LRFN3	FCRL1	79414	115350
LRIT1	FCRL1	26103	115350
LRPAP1	CD320	4043	51293
LRPAP1	SIRPA	4043	140885
LRRC3	SIRPA	81543	140885
LRRC4	NETO2	64101	81831

LRRC4	PRSS55	64101	203074
LRRC4B	UNC5D	94030	137970
LRRC4C	SIGLEC15	57689	284266
LRRC4C	TMEM53	57689	79639
LRRN1	LRRC4	57633	64101
LRRN1	LRRC4C	57633	57689
LRRN2	TMEM123	10446	114908
LSAMP	OPCML	4045	4978
LVRN	VSIG8	206338	391123
LY6D	TNFRSF10B	8581	8795
LY6G6F	LILRA5	259215	353514
LY9	LILRA1	4063	11024
MANSC1	CD177	54682	57126
MCAM	CD226	4162	10666
MCAM	TMEM132A	4162	54972
MERTK	IGSF5	10461	150084
MFAP3L	PI16	9848	221476
MOG	APCDD1	4340	147495
MOG	C6orf25	4340	80739
MOG	G6B	4340	80739
MOG	IL20RA	4340	53832
MOG	LILRA1	4340	11024
MOG	LILRB2	4340	10288
MOG	LRIG1	4340	26018
MOG	LRIG3	4340	121227
MOG	LRRTM2	4340	26045
MOG	LRRTM3	4340	347731
MOG	NRG2	4340	9542
MOG	VSTM4	4340	196740
MRC1	IL20RA	4360	53832
MRC1	RNF149	4360	284996
MUSK	DLL1	4593	28514
MUSK	LDLRAD2	4593	401944
MUSK	PTPRO	4593	5800
MXRA5	SIGLEC7	25878	27036

MXRA8	JAM3	54587	83700
NAALADL1	CD96	10004	10225
NCAM1	CLEC14A	4684	161198
NCAM1	CLEC2L	4684	154790
NCAM1	ISLR2	4684	57611
NCAM1	LILRA1	4684	11024
NCAM1	NCAM1	4684	4684
NCAM1	NPTN	4684	27020
NCAM1	PTPRS	4684	5802
NCAM2	NCAM2	4685	4685
NCR1	SIGLEC7	9437	27036
NCR1	SIGLEC8	9437	27181
NECTIN1	NECTIN1	5818	5818
NECTIN2	NECTIN2	5819	5819
NECTIN3	CD177	25945	57126
NECTIN3	KIR3DP1	25945	548594
NECTIN3	NECTIN3	25945	25945
NECTIN3	PDCD1LG2	25945	80380
NEGR1	NEGR1	257194	257194
NETO2	FCRL1	81831	115350
NFASC	LINGO4	23114	339398
NGFR	LRRTM3	4804	347731
NLGN3	MDGA1	54413	266727
NLGN4X	MDGA1	57502	266727
NOTCH4	UNC5B	4855	219699
NRCAM	LCTL	4897	197021
NRG2	CD177	9542	57126
NRG2	RNF13	9542	11342
NRP2	FCRL6	8828	343413
NRP2	IL20RA	8828	53832
NRP2	NRG2	8828	9542
NRXN1	VSTM2B	9378	342865
NRXN2	FGFRL1	9379	53834
NRXN2	IGSF21	9379	84966
NRXN2	SIGLEC8	9379	27181

NRXN2	VSTM2B	9379	342865
NRXN3	CD177	9369	57126
NRXN3	FGFRL1	9369	53834
NRXN3	GREM1	9369	26585
NT5E	FCRL1	4907	115350
NTM	AMIGO2	50863	347902
NTM	LRRC4C	50863	57689
NTM	LRRN3	50863	54674
NTM	THSD7A	50863	221981
NTM	VSIG8	50863	391123
NTNG1	SIGLEC8	22854	27181
NTRK1	TIE1	4914	7075
NTRK3	CRTAM	4916	56253
OLR1	IGSF8	4973	93185
OPCML	NEGR1	4978	257194
OPCML	OPCML	4978	4978
PCDH12	CD177	51294	57126
PCDH17	CD177	27253	57126
PCDHAC1	MICA	56135	100507436
PCDHB3	IGSF11	56132	152404
PCDHGA11	CD177	56105	57126
PCDHGA9	CD177	56107	57126
PCDHGB5	CD177	56101	57126
PCDHGB6	PLXDC1	56100	57125
PCDHGC4	CD177	56098	57126
PDGFRB	IL20RA	5159	53832
PDPN	CD177	10630	57126
PECAM1	CLEC6A	5175	93978
PECAM1	PECAM1	5175	5175
PIGR	RNF130	5284	55819
PIGR	TNFRSF10B	5284	8795
PILRA	C12orf53	29992	196500
PILRA	CD300E	29992	342510
PILRA	CNTNAP5	29992	129684
PILRA	EVA1C	29992	59271

PILRA	PIANP	29992	196500
PILRA	PRRG4	29992	79056
PILRA	PRSS55	29992	203074
PILRB	CD177	29990	57126
PILRB	EPHA10	29990	284656
PLA2R1	CLEC1B	22925	51266
PLXND1	GP6	23129	51206
PMEL	PILRA	6490	29992
PODXL	CD177	5420	57126
PRLR	CADM3	5618	57863
PRLR	EMC1	5618	23065
PRLR	IMPG2	5618	50939
PRLR	KIAA0090	5618	23065
PRLR	NCR2	5618	9436
PRNP	TNFRSF10B	5621	8795
PRNP	TNFRSF25	5621	8718
PRRG2	CLEC1B	5639	51266
PRRG4	CADM4	79056	199731
PSG9	PDCD1LG2	5678	80380
PTGFRN	SGCG	5738	6445
PTGFRN	TMEM59L	5738	25789
PTPRCAP	TGFBR3	5790	7049
PTPRD	IL1RAPL2	5789	26280
PTPRD	LECT1	5789	11061
PTPRD	LRFN5	5789	145581
PTPRD	SIRPG	5789	55423
PTPRD	SLITRK3	5789	22865
PTPRD	SLITRK4	5789	139065
PTPRD	SLITRK6	5789	84189
PTPRD	TGFA	5789	7039
PTPRF	CD177	5792	57126
PTPRF	LRFN5	5792	145581
PTPRG	IL1RAPL1	5793	11141
PTPRM	PTPRM	5797	5797
PTPRM	SIGLEC10	5797	89790

PTPRO	CD300C	5800	10871
PTPRO	SIGLEC7	5800	27036
PTPRO	SIGLEC8	5800	27181
PTPRS	IL1RAPL1	5802	11141
PTPRS	IL1RAPL2	5802	26280
PTPRS	LRFN1	5802	57622
PTPRS	LRFN5	5802	145581
PTPRS	LRRC4B	5802	94030
PTPRS	SLITRK1	5802	114798
PTPRS	SLITRK2	5802	84631
PTPRS	SLITRK3	5802	22865
PTPRS	SLITRK4	5802	139065
PTPRS	SLITRK6	5802	84189
PTPRT	PTPRT	11122	11122
PVR	C6orf25	5817	80739
PVR	G6B	5817	80739
PVR	KIR2DL5A	5817	57292
PVR	NECTIN4	5817	81607
RARRES1	GP6	5918	51206
RARRES1	NRP2	5918	8828
RECK	TIGIT	8434	201633
REG3A	SDK2	5068	54549
RNF13	LRRTM2	11342	26045
RNF13	LRRTM4	11342	80059
RNF13	SIGLEC12	11342	89858
RNF13	SIRPD	11342	128646
RNF13	TMEM95	11342	339168
RNF13	TNFRSF13B	11342	23495
RNF167	CLEC4D	26001	338339
RNF167	SPEM1	26001	374768
ROBO3	ESAM	64221	90952
ROBO3	F11R	64221	90952
ROBO3	LY6G6F	64221	259215
ROBO4	UNC5B	54538	219699
ROR2	CD320	4920	51293

SDC2	CD177	6383	57126
SDC3	CD177	9672	57126
SDK2	CADM4	54549	199731
SELL	IGDCC3	6402	9543
SELL	UNC5D	6402	137970
SELPLG	CD177	6404	57126
SEMA3C	RNF13	10512	11342
SEMA4F	C10orf54	10505	64115
SEMA5A	RNF167	9037	26001
SEMA7A	UNC5D	8482	137970
SIGLEC5	CD300LB	8778	124599
SIGLEC6	KIR2DL4	946	3805
SIGLEC6	NCR1	946	9437
SIGLEC7	LRP12	27036	29967
SIGLEC7	PCDHAC1	27036	56135
SIGLEC7	TIMD4	27036	91937
SIGLEC8	LRRC4C	27181	57689
SIGLEC8	PCDHGA7	27181	56108
SIGLEC8	SIGLEC8	27181	27181
SIGLEC8	TEX101	27181	83639
SIGLEC8	TREML4	27181	285852
SIRPA	TIGIT	140885	201633
SIRPB1	PILRB	10326	29990
SLAMF6	SLAMF6	114836	114836
SLAMF7	SLAMF7	57823	57823
SLITRK3	CD177	22865	57126
SNPH	CD177	9751	57126
SPN	CD177	6693	57126
ST14	BTN3A1	6768	11119
STAB1	NTM	23166	50863
SUSD5	CD177	26032	57126
SUSD5	CLEC1B	26032	51266
TAPBP	LILRA1	6892	11024
TCTN3	FCRL1	26123	115350
TGFBR3	GPR124	7049	25960

TGFBR3	LRIG3	7049	121227
TGOLN2	BTN3A1	10618	11119
TGOLN2	LILRA1	10618	11024
TIE1	LRFN5	7075	145581
TMEFF1	GREM1	8577	26585
TMEM167A	RNF149	153339	284996
TMEM190	IGSF11	147744	152404
TNFRSF10B	LILRA3	8795	11026
TNFRSF10C	PILRA	8794	29992
TNFRSF11A	ACE2	8792	59272
TNFRSF11A	MYEOV	8792	26579
TNFRSF11A	PDCD1LG2	8792	80380
TNFRSF11B	ACE2	4982	59272
TNFRSF11B	C14orf37	4982	145407
TNFRSF11B	GPC6	4982	10082
TNFRSF11B	NRP1	4982	8829
TNFRSF11B	NRXN2	4982	9379
TNFRSF11B	NRXN3	4982	9369
TNFRSF11B	PCDHAC1	4982	56135
TNFRSF11B	SLITRK1	4982	114798
TNFRSF11B	TGFBR3	4982	7049
TNFRSF14	LRFN5	8764	145581
TNFRSF17	CD300E	608	342510
TNFRSF17	LY9	608	4063
TNFRSF17	NEGR1	608	257194
TNFRSF17	NTM	608	50863
TNFRSF18	LILRA5	8784	353514
TNFRSF21	PI16	27242	221476
TNFSF9	FCRL1	8744	115350
TPSG1	SIRPA	25823	140885
TREM1	NECTIN4	54210	81607
TREM1	VSIG8	54210	391123
TREM1	VSTM2B	54210	342865
TREM2	HAPLN4	54209	404037
TREM2	LRRC52	54209	440699

TREML2	ANTXR1	79865	84168
TREML2	GPR116	79865	221395
UNC5C	FLRT1	8633	23769
UNC5C	FLRT2	8633	23768
UNC5C	FLRT3	8633	23767
UNC5C	LILRB5	8633	10990
UNC5D	SIGLEC15	137970	284266
VLDLR	BTN3A2	7436	11118
VLDLR	CD177	7436	57126
VLDLR	NECTIN4	7436	81607
VSIG4	KIR2DL5A	11326	57292
WISP1	PILRA	8840	29992

Table 4. IgSF queries

IgSF query name	IgSF query Entrez ID	IgSF query Uniprot ID	IgSF query sequence boundaries
ACVR1B	91	P36896	M1-E126
ADAM17	6868	P78536	M1-N671
AGER	177	Q15109	M1-T340
ALCAM	214	Q13740	M1-K527
AMICA1	120425	Q86YT9	M1-Q274
AMIGO1	57463	Q86WK6	M1-A373
AMIGO2	347902	Q86SJ2	M1-T398
AMIGO3	386724	Q86WK7	M1-T383
AXL	558	P30530	M1-P449
BOC	91653	Q9BWV1	M1-Y855
BTLA	151888	Q7Z6A9	M1-P152
BTN1A1	696	Q13410	M1-T244
BTN2A1	11120	Q7KYR7	M1-P246
BTN2A3P	54718	Q96KV6	M1-P244
BTN3A1	11119	O00481	M1-A250
BTN3A2	11118	P78410	M1-P247
BTN3A3	10384	O00478	M1-P247
BTNL2	56244	Q9UIR0	M1-W455
BTNL3	10917	Q6UXE8	M1-S237
BTNL8	79908	Q6UX41	M1-K238
BTNL9	153579	Q6UXG8	M1-K256
BUTR1	100129094	A8MVZ5	M1-A255
C10orf54	64115	Q9H7M9	M1-A195
C19orf38	255809	A8MVS5	M1-L119

CADM1	23705	Q9BY67	M1-H374
CADM2	253559	Q8N3J6	M1-A368
CADM3	57863	Q8N126	M1-H330
CADM4	199731	Q8NFZ8	M1-A324
CD101	9398	Q93033	M1-P954
CD109	135228	Q6YHK3	M1-S1423
CD14	929	P08571	M1-N345
CD160	11126	O95971	M1-S160
CD163	9332	Q86VB7	S42-S1050
CD164	8763	Q04900	M1-D162
CD164L2	388611	Q6UWJ8	M1-S141
CD19	930	P15391	M1-K291
CD1A	909	P06126	M1-V300
CD1B	910	P29016	M1-S303
CD1C	911	P29017	M1-N303
CD1D	912	P15813	M1-S301
CD1E	913	P15812	M1-G303
CD2	914	P06729	M1-D209
CD200	4345	P41217	M1-G232
CD200R1	131450	Q8TD46	M1-K238
CD200R1L	344807	Q6Q8B3	M1-S237
CD22	933	P20273	M1-G685
CD226	10666	Q15762	M1-T250
CD244	51744	Q9BZW8	M1-P229
CD27	939	P26842	M1-R191
CD274	29126	Q9NZQ7	M1-R191
CD276	80381	Q5ZPR3	M1-A466
CD28	940	P10747	M1-P152
CD300A	11314	Q9UGN4	M1-P180
CD300C	10871	Q08708	M1-R183
CD300E	342510	Q496F6	M1-H173
CD300LB	124599	A8K4G0	M1-K147
CD300LD	100131439	Q6UXZ3	M1-H165
CD300LF	146722	Q8TDQ1	M1-S156
CD300LG	146894	Q6UXG3	M1-R247
CD320	51293	Q9NPF0	M1-G230
CD33	945	P20138	M1-G260
CD34	947	P28906	M1-T290
CD3D	915	P04234	M1-G106
CD3E	916	P07766	M1-D126
CD3G	917	P09693	M1-G117
CD4	920	P01730	M1-P396
CD40	958	P25942	M1-A194

CD47	961	Q08722	M1-N142
CD48	962	P09326	M1-S220
CD5	921	P06127	M1-T379
CD55	1604	P08174	M1-T352
CD58	965	P19256	M1-R215
CD59	966	P13987	M1-P128
CD6	923	P30203	M1-L402
CD7	924	P09564	M1-R143
CD79A	973	P11912	M1-G160
CD79B	974	P40259	M1-N242
CD80	941	P33681	M1-N242
CD83	9308	Q01151	M1-E144
CD84	8832	Q9UIB8	M1-G225
CD86	942	P42081	M1-P135
CD8A	925	P01732	M1-D182
CD8B	926	P10966	M1-P170
CD96-1	10225	P40200-1	M1-G518
CD96-2	10225	P40200-2	M1-G502
CDON	50937	Q4KMG0	M1-D963
CEACAM16	388551	Q2WEN9	M1-G425
CEACAM19	56971	Q7Z692	M1-A160
CEACAM20	125931	Q6UY09	M1-A447
CEACAM21	90273	Q3KPI0	M1-G240
CEACAM3	1084	P40198	M1-G155
CEACAM4	1089	O75871	M1-G155
CEACAM5	1048	P06731	M1-A685
CEACAM6	4680	P40199	M1-S321
CEACAM7	1087	Q14002	M1-S243
CEACAM8	1088	P31997	M1-S327
CHL1	10752	O00533	M1-G1081
CLEC12A	160364	Q5QGZ9	K74-A265
CLEC12B	387837	Q2HXU8	L65-D276
CLEC14A	161198	Q86T13	M1-A397
CLMP	79827	Q9H6B4	M1-A235
CNTFR	1271	P26992	M1-S342
CNTN1	1272	Q12860	M1-S993
CNTN2	6900	Q02246	M1-N1012
CNTN3	5067	Q9P232	M1-N1008
CNTN4	152330	Q8IWV2	M1-S1000
CNTN5	53942	O94779	M1-A1073
CNTN6	27255	Q9UQ52	M1-S998
CRLF1	9244	O75462	M1-R422
CRTAM	56253	O95727	M1-R283

CSF1R	1436	P07333	M1-P517
CSF2RB	1439	P32927	M1-P441
CSF3R	1441	Q99062	M1-H627
CTLA4	1493	P16410	M1-F162
CXADR	1525	P78310	M1-G237
DAG1	1605	Q14118	M1-V749
DCC	1630	P43146	M1-N1097
DCN	1634	P07585	M1-K359
DLK1	8788	P80370	M1-C306
DSCAM	1826	O60469	M1-K1594
DSCAML1	57453	Q8TD84	M1-V1589
EDA2R	60401	Q9HAV5	M1-L139
EDAR	10913	Q9UNE0	M1-A187
EFNB1	1947	P98172	M1-K237
EFNB2	1948	P52799	M1-G230
EFNB3	1949	Q15768	M1-P226
EMB	133418	Q6PCB8	M1-P263
ENG	2022	P17813	M1-P590
EPHB6	2051	O15197	M1-L595
ERMAP	114625	Q96PL5	M1-A155
ESAM	90952	Q96AP7	M1-A248
F11R	50848	Q96AP7	M1-V238
F3	2152	Q9Y624	M1-I252
FAIM3	9214	P13726	M1-G251
FAM187A	100528020	O60667	M1-E379
FAM187B	148109	Q17R55	M1-K335
FAS	355	P25445	M1-N173
FCAMR	83953	Q8WWV6	M1-R450
FCAR	2204	P24071	M1-N227
FCER1A	2205	P12319	M1-Q205
FCGRT	2217	P55899	M1-S297
FCRL1	115350	Q96LA6	M1-G308
FCRL2	79368	Q96LA5	M1-G400
FCRL3	115352	Q96P31	M1-G576
FCRL4	83417	Q96PJ5	M1-G386
FCRL5	83416	Q96RD9	M1-G851
FCRL6	343413	Q6DN72	M1-N306
FGFR1	2260	P11362	M1-E376
FGFR2	2263	P21802	M1-E377
FGFR3	2261	P22607	M1-G375
FGFR4	2264	P22455	M1-D369
FGFRL1	53834	Q8N441	M1-P378
FLT1	2321	P17948	M1-E758

FLT3	2322	P36888	M1-S543
FLT4	2324	P35916	M1-E775
GP5	2814	P40197	M1-G523
GP9	2815	P14770	M1-R145
GPA33	10223	Q99795	M1-A236
GPNMB-1	10457	Q14956-1	K23-N498
GPNMB-2	10457	Q14956-2	K23-N486
GPR116	221395	Q8IZF2	M1-S1006
GPR124	25960	Q96PE1	M1-P771
GPR125	166647	Q8IWK6	M1-P761
HAVCR1	26762	Q96D42	M1-G290
HAVCR2	84868	Q8TDQ0	M1-G202
HEPACAM	220296	Q14CZ8	M1-R237
HEPACAM2	253012	A8MVW5	M1-P351
HFE	3077	Q30201	M1-V306
HHLA2	11148	Q9UM44	M1-G346
ICAM1	3383	P05362	M1-E480
ICAM2	3384	P13598	M1-Q223
ICAM3	3385	P32942	M1-H485
ICAM4	3386	Q14773	M1-A240
ICAM5	7087	Q9UMF0	M1-W835
ICOS	29851	Q9Y6W8	M1-F141
ICOSLG	23308	O75144	
IFNGR1	3459	P15260	M1-G245
IGDCC4	57722	Q8TDY8	M1-T957
IGFL3	388555	Q6UXB1	M1-P125
IGFLR1	79713	Q9H665	M1-P163
IGSF1	3547	Q8N6C5	E581-I1336
IGSF11	152404	Q5DX21	M1-G245
IGSF21	84966	Q96ID5	M1-A452
IGSF3	3321	O75054	M1-A1124
IGSF5	150084	Q9NSI5	M1-G270
IGSF6	10261	O95976	M1-S153
IGSF8	93185	Q969P0	M1-T579
IGSF9	57549	Q9P2J2	M1-G738
IGSF9B	22997	Q9UPX0	M1-G726
IL11RA	3590	Q14626	M1-Q365
IL18R1	8809	Q13478	M1-G330
IL18RAP	8807	O95256	M1-K355
IL1RAP	3556	Q9NPH3	M1-T367
IL1RAPL1	11141	Q9NZN1	M1-T357
IL1RAPL2	26280	Q9NP60	M1-E356
IL1RL1	9173	Q01638	M1-S328

IL1RL2	8808	Q9HB29	M1-R335
IL20RA	53832	Q9UHF4	M1-K250
IL31RA	133396	Q8NI17	M1-E519
IL6R	3570	P08887	M1-T366
IL6ST	3572	P40189	M1-A620
ILDR1	286676	Q86SU0	M1-H167
ILDR2	387597	Q71H61	M1-E186
ISLR2	57611	Q6UXK2	M1-K584
IZUMO1	284359	Q8IYV9	M1-R292
JAM2	58494	P57087	M1-S238
JAM3	83700	Q9BX67	M1-N241
KDR	3791	P35968	M1-E764
KIAA0319	9856	Q5VV43	M1-S955
KIAA1324	57535	Q6UXG2	M1-K910
KIR2DL1	3802	P43626	M1-H245
KIR2DL2	3803	P43631	M1-H245
KIR2DL3	3804	P43628	M1-H245
KIR2DL4	3805	Q99706	M1-A243
KIR2DL5A	57292	Q8N109	M1-R236
KIR2DL5B	553128	Q8NHK3	M1-R236
KIR2DS1	3806	Q14954	M1-H245
KIR2DS2	100132285	P43631	M1-H245
KIR2DS3	3808	Q14952	M1-H245
KIR2DS4	3809	P43632	M1-H245
KIR2DS5	3810	Q14953	M1-H245
KIR3DL1	3811	P43629	M1-H340
KIR3DL2	3812	P43630	M1-H340
KIR3DL3	115653	Q8N743	M1-H323
KIR3DS1	3813	Q14943	M1-H340
KIRREL	55243	Q96J84	M1-G496
KIRREL2	84063	Q6UWL6	M1-R510
KIRREL3	84623	Q8IZU9	M1-A535
KIT	3815	P10721	M1-P524
KLRK1	22914	P26718	L79-V216
L1CAM	3897	P32004	M1-G1121
LAG3	3902	P18627	M1-L450
LAMP1	3916	P11279	M1-S381
LAMP2	3920	P13473	M1-N374
LEPR	3953	P48357	M1-A840
LIFR	3977	P42702	M1-S833
LILRA1	11024	O75019	M1-N461
LILRA2	11027	Q8N149	M1-L450
LILRA3	11026	Q8N6C8	M1-E439

LILRA4	23547	P59901	M1-N446
LILRA5	353514	A6NI73	M1-N265
LILRA6	79168	Q6PI73	M1-N447
LILRB1	10859	Q8NHL6	M1-G477
LILRB2	10288	Q8N423	M1-G460
LILRB3	11025	O75022	M1-E443
LILRB4	11006	Q8NHJ6	M1-R255
LILRB5	10990	O75023	M1-G458
LINGO1	84894	Q96FE5	M1-T561
LINGO2	158038	Q7L985	M1-T545
LINGO3	645191	P0C6S8	M1-T531
LINGO4	339398	Q6UY18	M1-A533
LOC374597	391123	P0DPA2	M1-A130
LRFN1	57622	Q9P244	M1-T535
LRFN2	57497	Q9ULH4	M1-T533
LRFN3	79414	Q9BTN0	M1-T538
LRFN4	78999	Q6PJG9	M1-L518
LRFN5	145581	Q96NI6	M1-T528
LRIG1	26018	Q96JA1	M1-G794
LRIG2	9860	O94898	M1-G807
LRIT1	26103	Q9P2V4	M1-Q526
LRIT2	340745	A6NDA9	M1-H462
LRIT3	345193	Q3SXY7	M1-Q580
LRRC19	64922	Q9H756	M1-S269
LRRC24	441381	Q50LG9	M1-T405
LRRC25	126364	Q8N386	M1-T165
LRRC4	64101	Q9HBW1	M1-K527
LRRC4B	94030	Q9NT99	M1-K527
LRRC4C	57689	Q9HCJ2	M1-K527
LRRN1	57633	Q6UXK5	M1-A631
LRRN2	10446	O75325	M1-G630
LRRN3	54674	Q9H3W5	M1-T628
LRRTM3	347731	Q86VH5	M1-K419
LSAMP	4045	Q13449	M1-S317
LTBR	4055	P36941	M1-L226
LY6G6F	259215	Q5SQ64	M1-P234
LY9	4063	Q9HBG7	M1-K454
MADCAM1	8174	Q13477	M1-L318
MAG	4099	P20916	M1-M510
MCAM	4162	P43121	M1-G559
MDGA1	266727	Q8NFP4	M1-S932
MDGA2	161357	Q7Z553	M1-A933
MERTK	10461	Q12866	M1-L503

MFAP3L	9848	O75121	M1-D148
MICA	100507436	Q29983	M1-Q308
MICB	4277	Q29980	M1-D309
MILR1	284021	Q7Z6M3	M1-K227
MOG	4340	Q16653	M1-G154
MPZ	4359	P25189	M1-G155
MPZL1	9019	O95297	M1-V165
MPZL2	10205	O60487	M1-H152
MPZL3	196264	Q6UWV2	M1-S158
MUSK	4593	O15146	M1-T495
MXRA5	25878	Q9NR99	M1-F2828
MXRA8	54587	Q9BRK3	M1-Q341
NCAM1	4684	P13591	M1-A723
NCAM2	4685	O15394	M1-N697
NCR1	9437	O76036	M1-R258
NCR2	9436	O95944	M1-A192
NCR3	259197	O14931	M1-T138
NEGR1	257194	Q7Z3B1	M1-D327
NEO1	4756	Q92859	M1-N1103
NFAM1	150372	Q8NET5	M1-G1216
NFASC	23114	O94856	M1-N250
NGFR	4804	P08138	M1-P1061
NPHS1	4868	O60500	M1-P339
NPTN	27020	Q9Y639	M1-G1168
NRCAM	4897	Q92823	M1-G1168
NRG1	3084	Q02297	M1-Q240
NRG2	9542	O14511	M1-Q403
NRP2	8828	O60462	M1-P864
NTM	50863	Q9P121	M1-N321
NTRK1	4914	P04629	M1-S419
NTRK2	4915	Q16620	M1-H430
NTRK3	4916	Q16288	M1-G431
OPCML	4978	Q14982	M1-N322
OSCAR	126014	Q8IYS5	M1-V271
OSMR	9180	Q99650	M1-S739
PCDHGB6	56100	Q9Y5F9	M1-Y692
PDCD1	5133	Q15116	M1-V170
PDCD1LG2	80380	Q9BQ51	M1-T220
PDGFRA	5156	P16234	M1-A528
PEAR1	375033	Q5VY43	M1-A757
PECAM1	5175	P16284	M1-A639
PIGR	5284	P01833	M1-A197
PILRB	29990	Q9UKJ0	M1-R191

PLXNB2	23654	O15031	M1-S1199
PRLR	5618	P16471	M1-T236
PRTG	283659	Q2VWP7	M1-G950
PTGFRN	5738	Q9P2B2	M1-P832
PTK7	5754	Q13308	M1-T704
PTPRD	5789	P23468	M1-G1266
PTPRF	5792	P10586	M1-L1262
PTPRJ	5795	Q12913	M1-G971
PTPRK	5796	Q15262	M1-K752
PTPRM	5797	P28827	M1-K742
PTPRO	5800	Q16827	M1-N819
PTPRS	5802	Q13332	M1-G1282
PTPRT	11122	O14522	M1-K746
PTPRU	10076	Q92729	M1-L749
PVR	5817	P15151	M1-N343
PVRL1	5818	Q15223	M1-A355
PVRL2	5819	Q92692	M1-G360
NECTIN3	25945	Q9NQS3	M1-D400
PVRL4	81607	Q96NY8	M1-V350
RELT	84957	Q969Z4	M1-Q162
ROBO1	6091	Q9Y6N7	M1-P897
ROBO2	6092	Q9HCK4	M1-A860
ROBO3	64221	Q96MS0	M1-P891
ROR1	4919	Q01973	M1-Y406
ROR2	4920	Q01974	M1-G403
SCN1B	6324	Q07699	M1-E160
SCN2B	6327	O60939	M1-A159
SCN3B	55800	Q9NY72	M1-E159
SCN4B	6330	Q8IWT1	M1-T161
SDK1	221935	Q7Z5N4	M1-E2007
SDK2	54549	Q58EX2	M1-W1930
SEMA3A	10371	Q14563	M1-V725
SEMA4A	64218	Q9H3S1	M1-H683
SEMA4B	10509	Q9NPR2	M1-E712
SEMA4C	54910	Q9C0C4	M1-G663
SEMA4D	10507	Q92854	M1-R734
SEMA4F	10505	O95754	M1-G660
SEMA4G	57715	Q9NTN9	M1-R674
SEMA5B	54437	Q9P283	M1-H1036
SEMA6A	57556	Q9H2E6	M1-Q644
SEMA7A	8482	O75326	M1-A644
SIGIRR	59307	Q6IA17	M1-H118
SIGLEC1	6614	Q9BZZ2	M1-Q1641

SIGLEC10	89790	Q96LC7	M1-N550
SIGLEC11	114132	Q96RL6	M1-G560
SIGLEC12	89858	Q96PQ1	M1-A481
SIGLEC14	100049587	Q08ET2	M1-T359
SIGLEC15	284266	Q6ZMC9	M1-T263
SIGLEC16	400709	A6NMB1	M1-G434
SIGLEC5	8778	O15389	M1-A440
SIGLEC6	946	O43699	M1-G346
SIGLEC7	27036	Q9Y286	M1-G350
SIGLEC8	27181	Q9NYZ4	M1-A363
SIGLEC9	27180	Q9Y336	M1-G348
SIRPA	140885	P78324	M1-Y373
SIRPB1	10326	O00241	M1-P370
SIRPB2	284759	Q5JXA9	M1-G287
SIRPD	128646	Q9H106	M1-K197
SIRPG	55423	Q9P1W8	M1-G361
SIT1	27240	Q9Y3P8	M1-A41
SKINTL	391037	A8MVG2	M1-S242
SLAMF1	6504	Q13291	M1-M226
SLAMF6	114836	Q96DU3	M1-M226
SLAMF7	57823	Q9NQ25	M1-D233
SLAMF8	56833	Q9P0V8	M1-F234
SLAMF9	89886	Q96A28	M1-S210
SLITRK1	114798	Q96PX8	M1-G623
SLITRK2	84631	Q9H156	M1-V620
TAPBPL	55080	Q9BX59	M1-E403
TARM1	441864	B6A8C7	M1-R236
THBD	7056	P07204	M1-G516
THY1	7070	P04216	M1-K129
TIE1	7075	P35590	M1-Q759
TIGIT	201633	Q495A1	M1-P141
TIMD4	91937	Q96H15	M1-Q314
TMEM123	114908	Q8N131	M1-S168
TMEM132E	124842	Q6IEE7	M1-A803
TMEM25	84866	Q86YD3	M1-G237
TMEM81	388730	Q6P7N7	M1-K221
TMIGD1	388364	Q6UXZ0	M1-P220
TMIGD2	126259	Q96BF3	M1-G150
TNFRSF10D	8793	Q9UBN6	M1-H211
TNFRSF11A	8792	Q9Y6Q6	M1-P212
TNFRSF11B	4982	O00300	M1-L401
TNFRSF12A	51330	Q9NP84	M1-I81
TNFRSF13B	23495	O14836	M1-S165

TNFRSF13C	115650	Q96RJ3	M1-G80
TNFRSF14	8764	Q92956	M1-V202
TNFRSF17	608	Q02223	M1-I55
TNFRSF18	8784	Q9Y5U5	M1-P162
TNFRSF19	55504	Q9NS68	M1-A172
TNFRSF1A	7132	P19438	M1-T211
TNFRSF1B	7133	P20333	M1-D257
TNFRSF21	27242	O75509	M1-H349
TNFRSF25	8718	Q93038	M1-Q199
TNFRSF4	7293	P43489	M1-A217
TNFRSF6B	8771	O95407	M1-H300
TNFRSF8	943	P28908	M1-P386
TNFRSF9	3604	Q07011	M1-Q186
TNFSF11	8600	O14788	F70-D317
TNFSF15	9966	O95150	S57-L251
TNFSF8	944	P32971	Q63-D234
TREM1	54210	Q9NP99	M1-P202
TREM2	54209	Q9NZC2	M1-S174
TREML1	340205	Q86YW5	M1-P162
TREML2	79865	Q5T2D2	M1-D265
TREML4	285852	Q6UXN2	M1-G180
TYRO3	7301	Q06418	M1-S428
UNC5A	90249	Q6ZN44	M1-Y306
UNC5B	219699	Q8IZJ1	M1-Y377
UNC5C	8633	O95185	M1-Y380
UNC5D	137970	Q6UXZ4	M1-D379
VCAM1	7412	P19320	M1-E698
VSIG1	340547	Q86XK7	M1-E232
VSIG10	54621	Q8N0Z9	M1-G413
VSIG10L	147645	Q86VR7	M1-G779
VSIG2	23584	Q96IQ7	M1-G244
VSIG4	11326	Q9Y279	M1-P283
VSIG8	391123	P0DPA2	M1-R260
VSTM1	284415	Q6UX27	M1-T135
VSTM2B	342865	A6NLU5	M1-T263
VSTM4	196740	Q8IW00	M1-L177
VTCN1	79679	Q7Z7D3	M1-S259

Table 5. STM library for IgSF experiment

STM library gene symbol	STM library Entrez ID	STM library Uniprot ID	STM library boundaries
ACE	1636	P12821	M1-Q1259
ACE2	59272	Q9BYF1	M1-S740

ACPP	55	P15309	M1-D386
ACPT	93650	Q9BZG2	M1-P390
ACVR1B	91	P36896	M1-E126
ACVR1C	130399	Q8NER5	M1-E113
ACVR2A	92	P27037	M1-N138
ACVR2B	93	Q13705	M1-T137
ACVRL1	94	P37023	M1-Q118
ADAM11	4185	O75078	M1-N734
ADAM12	8038	O43184	M1-A701
ADAM15	8751	Q13444	M1-S693
ADAM17	6868	P78536	M1-N671
ADAM18	8749	Q9Y3Q7	M1-N687
ADAM19	8728	Q9H013	M1-P702
ADAM2	2515	Q99965	M1-R667
ADAM20	8748	O43506	M1-R692
ADAM21	8747	Q9UKJ8	M1-G681
ADAM22	53616	Q9P0K1	M1-N736
ADAM23	8745	O75077	M1-N792
ADAM28	10863	Q9UKQ2	M1-S666
ADAM29	11086	Q9UKF2	M1-K669
ADAM30	11085	Q9UKF2	M1-S685
ADAM32	203102	Q8TC27	M1-T682
ADAM33	80332	Q9BZ11	M1-T701
ADAM7	8756	Q9H2U9	M1-N668
ADAM8	101	P78325	M1-S653
ADAM9	8754	Q13443	M1-G698
ADGRA2	25960	Q96PE1	M1-P771
ADGRA3	166647	Q8IWK6	M1-P761
ADGRF5	221395	Q8IZF2	M1-S1006
AGER	177	Q15109	M1-T340
AJAP1	55966	Q9UKB5	M1-Q282
ALCAM	214	Q13740	M1-K527
ALPL	249	P05186	M1-S502
AMHR2	269	Q16671	M1-S144
AMIGO1	57463	Q86WK6	M1-A373
AMIGO1	57463	Q86WK6	M1-T372
AMIGO2	347902	Q86SJ2	M1-T398
AMIGO2	347902	Q86WK6	M1-T398
AMIGO3	386724	Q86WK7	M1-T383
AMN	81693	Q9BXJ7	M1-G360
ANTXR1	84168	Q9H6X2	M1-S321
ANTXR2	118429	P58335	M1-G318
APCDD1	147495	Q8J025	M1-H492

APLP1	333	P51693	M1-A581
APLP2	334	Q06481	M1-S452
APOO	79135	Q9BUR5	M1-G109
APP	351	P05067	M1-G700
AQPEP	206338	Q6Q4G3	M1-T990
AQPEP	206338	Q6Q4G3	Y37-T990
AREG	374	P15514	M1-K184
ART1	417	P52961	M1-I280
ART3	419	Q13508	M1-A361
ART4	420	Q93070	M1-K284
ASGR1	432	P07306	Q62-L291
ASGR2	433	P07307	Q80-A311
ATP1B1	481	P05026	E63-S303
ATRAID	51374	Q6UW56	M1-S199
ATRNL1	26033	Q5VV63	M1-Q1232
AXL	558	P30530	M1-P449
BACE1	23621	P56817	M1-T457
BACE2	25825	Q9Y5Z0	M1-Y473
BLVRB	645	P30043	M1-G161
BMP10	27302	O95393	M1-R424
BMP5	653	P22003	M1-H454
BMPR1A	657	P36894	M1-R152
BMPR2	659	Q13873	M1-T150
BOC	91653	Q9BWV1	M1-Y855
BST1	683	Q10588	M1-Q290
BST2	684	Q10589	T45-Q180
BTC	685	P35070	M1-Q118
BTLA	151888	Q7Z6A9	M1-P152
BTN1A1	696	Q13410	M1-T244
BTN2A1	11120	Q7KYR7	M1-P246
BTN2A2	10385	Q8WVV5	M1-P250
BTN2A2	10385	Q8WVV5	M1-P263
BTN2A2	10385	Q8WVV5	M1-V237
BTN2A3P	54718	Q96KV6	M1-P244
BTN3A1	11119	O00481	M1-A250
BTN3A2	11118	P78410	M1-P247
BTN3A3	10384	O00478	M1-P247
BTNL2	56244	Q9UIR0	M1-W455
BTNL3	10917	Q6UXE8	M1-S237
BTNL3	10917	Q6UXE8	M1-T226
BTNL8	79908	Q6UXE8	M1-K238
BTNL9	153579	Q6UXE8	M1-K256
C10orf35	219738	Q96D05	M1-S91

C11orf24	53838	Q96F05	M1-T400
C12orf53	196500	Q8IYJ0	M1-Q179
C12orf63	144535	Q96N23	M1-S1127
C14orf37	145407	Q86TY3	M1-M714
C15orf24	56851	Q9NPA0	M1-P164
C16orf91	283951	Q4G0I0	M1-P232
C16orf92	146378	Q96LL3	M1-G101
C17orf80	55028	Q9BSJ5	M1-S552
C18orf1	753	O15165	M1-E64
C19orf18	147685	Q8NEA5	M1-K100
C19orf38	255809	A8MVS5	M1-L119
C19orf38	255809	A8MVS5	M1-T116
C19orf59	199675	Q8IX19	K107-Q187
C1orf159	54991	Q96HA4	M1-S147
C1orf43	25912	Q9BWL3	K32-L253
C1orf85	112770	Q8WWB7	M1-P368
C20orf3	57136	Q9HDC9	E18-V372
C2orf82	389084	Q6UX34	M1-A92
C2orf89	129293	Q86V40	M1-M477
C3orf18	51161	Q9UK00	M1-T61
C4orf32	132720	Q8N8J7	M1-P99
C4orf34	201895	Q96QK8	M1-G50
C5orf15	56951	Q8NC54	M1-H198
C6orf162	57150	Q96KF7	M1-K47
C6orf72	116254	Q9NU53	M1-P261
C9orf11	54586	Q9NQ60	M1-I127
C9orf79	286234	Q6ZUB1	S88-S1445
CA12	771	O43570	M1-G299
CA14	23632	Q9ULX7	M1-E289
CA4	762	P22748	M1-K283
CA9	768	Q16790	M1-D414
CACHD1	57685	Q5VU97	M1-P799
CACNA2D3	55799	Q8IZS8	M1-A1070
CACNA2D4	93589	Q7Z3S7	M1-S1118
CADM1	23705	Q9BY67	M1-H374
CADM2	253559	Q8N3J6	M1-A368
CADM2	253559	Q8N3J6	M1-H367
CADM3	57863	Q8N126	M1-H330
CADM4	199731	Q8NFZ8	M1-A324
CATSPERD	257062	Q86XM0	M1-Q718
CATSPERG	57828	Q6ZRH7	M1-K1064
CCDC107	203260	Q8WV48	Q86-S283
CCDC47	57003	Q96A33	M1-S135

CD101	9398	Q93033	M1-P954
CD109	135228	Q6YHK3	M1-S1423
CD14	929	P08571	M1-N345
CD160	11126	O95971	M1-S160
CD163	9332	Q86VB7	S42-S1050
CD164	8763	Q04900	M1-D162
CD164L2	388611	Q6UWJ8	M1-S141
CD180	4064	Q99467	M1-G626
CD19	930	P15391	M1-K291
CD1A	909	P06126	M1-V300
CD1B	910	P29016	M1-S303
CD1C	911	P29017	M1-N303
CD1D	912	P15813	M1-S301
CD1E	913	P15812	M1-G303
CD2	914	P06729	M1-D209
CD200	4345	P41217	M1-G232
CD200R1	131450	Q8TD46	M1-K238
CD200R1L	344807	Q6Q8B3	M1-S237
CD207	50489	Q9UJ71	P65-P328
CD22	933	P20273	M1-G685
CD226	10666	Q15762	M1-T250
CD24	100133941	P25063	M1-A58
CD244	51744	Q9BZW8	M1-P229
CD248	57124	Q9HCU0	M1-R685
CD27	939	P26842	M1-R191
CD274	29126	Q9NZQ7	M1-T239
CD276	80381	Q5ZPR3	M1-A466
CD28	940	P10747	M1-P152
CD300A	11314	Q9UGN4	M1-P180
CD300C	10871	Q08708	M1-R183
CD300E	342510	Q496F6	M1-H173
CD300LB	124599	A8K4G0	M1-K147
CD300LB	124599	A8K4G0	M38-H187
CD300LD	100131439	Q6UXZ3	M1-H165
CD300LF	146722	Q8TDQ1	M1-S156
CD300LG	146894	Q6UXG3	M1-R247
CD302	9936	Q8IX05	M1-H168
CD320	51293	Q9NPF0	M1-G230
CD33	945	P20138	M1-G260
CD34	947	P28906	M1-T290
CD3D	915	P04234	M1-A105
CD3D	915	P04234	M1-G106
CD3E	916	P07766	M1-D126

CD3G	917	P09693	M1-G117
CD3G	917	P09693	M1-N111
CD4	920	P01730	M1-P396
CD40	958	P25942	M1-A194
CD44	960	P16070	M1-E649
CD46	4179	P15529	M1-D328
CD47	961	Q08722	M1-N142
CD48	962	P09326	M1-R219
CD48	962	P09326	M1-S220
CD5	921	P06127	M1-P372
CD52	1043	P31358	M1-P35
CD55	1604	P08174	M1-T352
CD58	965	P19256	M1-R215
CD6	923	P30203	M1-L402
CD68	968	P34810	M1-S319
CD69	969	Q07108	S62-K199
CD7	924	P09564	M1-A182
CD72	971	P21854	R117-D359
CD79A	973	P11912	M1-R143
CD79B	974	P40259	M1-A43
CD79B	974	P40259	M1-G160
CD80	941	P33681	M1-N242
CD83	9308	Q01151	M1-E144
CD84	8832	Q9UIB8	M1-G225
CD86	942	P42081	M1-H245
CD8A	925	P01732	M1-D182
CD8B	926	P10966	M1-P170
CD8B	926	P10966	M1-T172
CD93	22918	Q9NPY3	M1-K580
CD96	10225	P40200	M1-G518
CD99	4267	P14209	M1-G125
CD99L2	83692	Q8TCZ2	M1-T186
CDCP1	64866	Q9H5V8	M1-D665
CDH12	1010	P55289	M1-L608
CDH13	1012	P55290	M1-A692
CDH15	1013	P55291	M1-A606
CDH16	1014	O75309	M1-S785
CDH17	1015	Q12864	M1-T784
CDH18	1016	Q13634	M1-S608
CDH19	28513	Q9H159	M1-E596
CDH2	1000	P19022	M1-A724
CDH20	28316	Q9HBT6	M1-G620
CDH22	64405	Q9UJ99	M1-A626

CDH24	64403	Q86UP0	M1-T601
CDH26	60437	Q8IXH8	M1-E610
CDH3	1001	P22223	M1-G654
CDH4	1002	P55283	M1-T721
CDH5	1003	P33151	M1-Q599
CDH6	1004	P55285	M1-T609
CDH7	1005	Q9ULB5	M1-S606
CDH8	1006	P55286	M1-A612
CDH9	1007	Q9ULB4	M1-A604
CDHR1	92211	Q96JP9	M1-N697
CDHR2	54825	Q9BYE9	M1-S1154
CDHR3	222256	Q6ZTQ4	M1-V712
CDHR5	53841	Q9HBB8	M1-A670
CDON	50937	Q4KMG0	M1-D963
CEACAM16	388551	Q2WEN9	M1-G363
CEACAM16	388551	Q2WEN9	M1-G425
CEACAM19	56971	Q7Z692	M1-A160
CEACAM20	125931	Q6UY09	M1-A447
CEACAM20	125931	Q6UY09	M1-G446
CEACAM21	90273	Q3KPI0	M1-G240
CEACAM3	1084	P40198	M1-A154
CEACAM3	1084	P40198	M1-G155
CEACAM4	1089	O75871	M1-G155
CEACAM5	1048	P06731	M1-A685
CEACAM6	4680	P40199	M1-S321
CEACAM7	1087	Q14002	M1-A241
CEACAM7	1087	Q14002	M1-S243
CEACAM8	1088	P31997	M1-S327
CHL1	10752	O00533	M1-G1081
CLCA2	9635	Q9UQC9	A681-D899
CLCA2	9635	Q9UQC9	M1-A680
CLCA4	22802	Q14CN2	M1-G894
CLEC10A	10462	Q8IUN9	Q61-H316
CLEC12A	160364	Q5QGZ9	K69-A265
CLEC12B	387837	Q2HXU8	S68-D276
CLEC14A	161198	Q86T13	M1-A397
CLEC17A	388512	Q6ZS10	K194-C378
CLEC2B	9976	Q92478	K26-H149
CLEC2L	154790	P0C7M8	S90-T214
CLEC4A	50856	Q9UMR7	Q70-L237
CLEC4D	338339	Q8WXI8	T42-N215
CLEC4E	26253	Q9ULY5	Q50-L219
CLEC4G	339390	Q6UXB4	S54-C293

CLEC5A	23601	Q9NY25	P28-K188
CLEC7A	64581	Q9BXN2	S71-M201
CLEC9A	283420	Q6UXN8	K57-V241
CLECL1	160365	Q8IZS7	A86-I167
CLMP	79827	Q9H6B4	M1-A235
CLSTN1	22883	O94985	M1-A860
CLSTN3	9746	Q9BQT9	M1-A848
CNTFR	1271	P26992	M1-S342
CNTN1	1272	Q12860	M1-S993
CNTN2	6900	Q02246	M1-N1012
CNTN2	6900	Q02246	M1-S1007
CNTN3	5067	Q9P232	M1-N1008
CNTN4	152330	Q8IWV2	M1-S1000
CNTN5	53942	O94779	M1-A1073
CNTN5	53942	O94779	M1-I1070
CNTN6	27255	Q9UQ52	M1-S998
CNTNAP1	8506	P78357	M1-G1280
CNTNAP2	26047	Q9UHC6	M1-S1261
CNTNAP3	79937	Q9BZ76	M1-R1241
CNTNAP4	85445	Q9C0A0	M1-A1241
CNTNAP5	129684	Q8WYK1	M1-S1237
CORIN	10699	Q9Y5Q5	G70-N1042
CPM	1368	P14384	M1-S406
CR1	1378	P17927	M1-A1972
CR2	1380	P20023	M1-S1031
CRB1	23418	P82279	M1-T1346
CRB2	286204	Q5IJ48	M1-A1226
CRB3	92359	Q9BUF7	M1-E55
CRIM1	51232	Q9NZV1	M1-S939
CRLF1	9244	O75462	M1-R422
CRLF2	64109	Q9HC73	M1-K231
CRTAM	56253	O95727	M1-R283
CSF1	1435	P09603	M1-S496
CSF1R	1436	P07333	M1-F513
CSF1R	1436	P07333	M1-P517
CSF2RA	1438	P15509	M1-N321
CSF2RB	1439	P32927	M1-P441
CSF3R	1441	Q99062	M1-E625
CSF3R	1441	Q99062	M1-H627
CTLA4	1493	P16410	M1-F162
CUZD1	50624	Q86UP6	M1-H570
CX3CL1	6376	P15509	M1-Q341
CXADR	1525	P78310	M1-G237

CXCL16	58191	Q9H2A7	M20-A223
CXorf59	286464	Q6ZTR5	M1-A457
CXorf61	203413	Q5H943	F24-T113
CYYR1	116159	Q96J86	M1-T61
DAG1	1605	Q14118	I655-D748
DAG1	1605	Q14118	M1-G653
DAG1	1605	Q14118	M1-V749
DCBLD1	285761	Q8N8Z6	M1-A460
DCC	1630	P43146	M1-N1097
DCT	1638	P40126	M1-G468
DDR1	780	Q08345	M1-A417
DDR2	4921	Q16832	M1-R399
DGCR2	9993	P98153	M1-G347
DLK1	8788	P80370	M1-C306
DLK2	65989	Q6UY11	M1-S306
DLL1	28514	O00548	M1-P544
DLL3	10683	Q9NYJ7	M1-Y491
DLL4	54567	Q9NR61	M1-S526
DNER	92737	Q8NFT8	M1-Y640
DPEP1	1800	P16444	M1-G386
DPEP2	64174	Q9H4A9	M1-V462
DPEP3	64180	Q9H4B8	M26-R486
DPP6	1804	P42658	T118-D865
DSC1	1823	Q08554	M1-R691
DSC2	1824	Q02487	M1-K694
DSC3	1825	Q14574	M1-K690
DSCAM	1826	O60469	M1-K1594
DSCAML1	57453	Q8TD84	M1-V1589
DSE	29940	Q9UL01	M1-R902
DSG1	1828	Q02413	M1-H545
DSG2	1829	Q14126	M1-A614
DSG2	1829	Q14126	M1-S606
DSG3	1830	P32926	M1-G617
DSG4	147409	Q86SJ6	M1-G632
EDA	1896	Q92838	S165-S396
EDA2R	60401	Q9HAV5	M1-L139
EDAR	10913	Q9UNE0	M1-H183
EFNA3	1944	P52797	M1-S213
EFNA5	1946	P52803	M1-E202
EFNB1	1947	P98172	M1-K237
EFNB2	1948	P52799	M1-G230
EFNB3	1949	Q15768	M1-P226
EGF	1950	P01133	M1-K1032

EGFR	1956	P00533	M1-S645
ELFN1	392617	P0C7U0	M1-Y418
EMB	133418	Q6PCB8	M1-P263
EMCN	51705	Q9ULC0	M1-S190
ENG	2022	P17813	M1-P590
ENPEP	2028	Q07075	T40-G957
ENPP5	59084	Q9UJA9	M1-Y431
EPCAM	4072	P16422	M1-K265
EPGN	255324	Q6UW88	M1-Y111
EPHA1	2041	P21709	M1-E547
EPHA10	284656	Q5JZY3	M1-A565
EPHA2	1969	P29317	M1-G531
EPHA3	2042	P29320	M1-Q541
EPHA4	2043	P54764	M1-T547
EPHA7	2045	Q15375	M1-V555
EPHA8	2046	P29322	M1-T542
EPHB1	2047	P54762	M1-P540
EPHB2	2048	P29323	M1-P542
EPHB3	2049	P54753	M1-P558
EPHB4	2050	P54760	M1-Q537
EPHB6	2051	O15197	M1-L595
EPOR	2057	P19235	M1-P250
ERBB2	2064	P04626	M1-S653
ERBB3	2065	P21860	M1-T643
ERBB4	2066	Q15303	M1-P651
EREG	2069	O14944	M1-L108
ERMAP	114625	Q96PL5	M1-A155
ESAM	90952	Q96AP7	M1-A248
EVA1C	59271	P58658	M1-A323
EVC2	132884	Q86UK5	M1-A300
EVI2A	2123	P22794	M1-M135
EVI2B	2124	P34910	M1-S202
F11R	50848	Q9Y624	M1-V238
F3	2152	P13726	M1-I252
FAM171A1	221061	Q5VUB5	M1-T303
FAM171B	165215	Q6P995	M1-T355
FAM174A	345757	Q8TBP5	M1-A124
FAM187A	100528020	A6NFU0	M1-E379
FAM187B	148109	Q17R55	M1-K335
FAM189A2	9413	Q15884	M1-A89
FAM200A	221786	Q8TCP9	M1-S513
FAM209A	200232	Q5JX71	M1-G54
FAM73A	374986	Q8NAN2	G102-Q632

FAM75A1	647060	Q5TZJ5	M76-I1347
FAM75A3	727830	Q5VYP0	M76-I1347
FAM75A5	727905	Q5VU36	M1-I1347
FAM75A5	727905	Q5VU36	S47-I1347
FAM75A7	727905	Q5VU36	Y48-I1347
FAS	355	P25445	M1-N173
FASLG	356	P48023	H106-L281
FCAMR	83953	Q8WWV6	M1-R450
FCAR	2204	P24071	M1-N227
FCER1A	2205	P12319	M1-Q205
FCER2	2208	P06734	D48-S321
FCER2	2208	P06734	M150-S321
FCGR1A	2209	P12314	M1-H292
FCGR1A	2209	P12314	M1-P288
FCGR1B	2210	Q92637	M1-H198
FCGR2A	2212	P12318	M1-G217
FCGR2B	2213	P31994	M1-G223
FCGR2B	2213	P31994	M1-P221
FCGR2C	9103	P31995	M1-G223
FCGR2C	9103	P31995	M1-P221
FCGR3A	2214	P08637	M1-Q208
FCGR3B	2215	O75015	M1-Q208
FCGR3B	2215	O75015	M1-G206
FCGRT	2217	P55899	M1-S297
FCMR	9214	O60667	M1-G251
FCRL1	115350	Q96LA6	M1-G308
FCRL2	79368	Q96LA5	M1-G400
FCRL3	115352	Q96P31	M1-G571
FCRL3	115352	Q96P31	M1-G576
FCRL4	83417	Q96PJ5	M1-G386
FCRL5	83416	Q96RD9	M1-G851
FCRL6	343413	Q6DN72	M1-N306
FCRLA	84824	Q7L513	A28-E359
FGFR1	2260	P11362	M1-E374
FGFR1	2260	P11362	M1-E376
FGFR2	2263	P21802	M1-E377
FGFR2	2263	P21802	M20-E396
FGFR3	2261	P22607	M1-G375
FGFR3	2261	P22607	M1-S371
FGFR4	2264	P22455	M1-D369
FGFRL1	53834	Q8N441	M1-P378
FIBCD1	84929	Q8N539	N55-R461
FLRT1	23769	Q9NZU1	M1-P524

FLRT2	23768	O43155	M1-P540
FLRT3	23767	Q9NZU0	M1-P528
FLT1	2321	P17948	M1-E758
FLT1	2321	P17948	M1-H687
FLT3	2322	P36888	M1-N541
FLT3	2322	P36888	M1-S543
FLT3LG	2323	P49771	M1-Q159
FLT4	2324	P35916	M1-E775
FNDC3A	22862	Q9Y2H6	M1-R1165
FNDC3B	64778	Q53EP0	M1-D67
FNDC3B	64778	Q53EP0	M1-Q1178
FNDC4	64838	Q9H6D8	M1-E169
FNDC9	408263	Q8TBE3	M1-Q110
FOLR1	2348	P15328	M1-M233
FOLR2	2350	P14207	M1-V229
FRMD3	257019	A2A2Y4	M1-R530
FRMD5	84978	Q7Z6J6	M1-K496
FRRS1L	23732	Q9P0K9	M1-T322
FXYD4	53828	P59646	M1-Q38
FXYD5	53827	Q96DB9	M1-R145
GAS1	2619	P54826	M1-R316
GFRA1	2674	P56159	M1-T428
GFRA2	2675	O00451	M1-P443
GFRA3	2676	O60609	M1-N374
GFRAL	389400	Q6UXV0	M1-E351
GGT1	2678	P19440	P27-Y569
GHR	2690	P10912	M1-Y264
GLG1	2734	Q92896	M1-N1145
GLIPR1	11010	P48060	M1-N231
GLIPR1L2	144321	Q4G1C9	M1-C253
GLT8D2	83468	Q9H1C3	V27-S349
GML	2765	Q99445	M1-K143
GNA13	10672	Q14344	M1-Q377
GP1BA	2811	P07359	M1-D498
GP1BB	2812	P13224	M1-A150
GP5	2814	P40197	M1-G523
GP9	2815	P14770	M1-R145
GPA33	10223	Q99795	M1-A236
GPC1	2817	P35052	M1-S530
GPC3	2719	P51654	M1-P561
GPC4	2239	O75487	M1-D528
GPC6	10082	Q9Y625	M1-D528
GPIHBP1	338328	Q8IV16	M1-A167

GPNMB	10457	Q14956	M1-A500
GUCY2C	2984	P25092	M1-L432
GUCY2D	3000	Q02846	G57-P463
GUCY2F	2986	P51841	M1-A467
GYPA	2993	P02724	M1-E91
GYPC	2995	P04921	M1-D58
HAVCR1	26762	Q96D42	M1-G290
HAVCR1	26762	Q96D42	M1-G295
HAVCR2	84868	Q8TDQ0	M1-G202
HBEGF	1839	Q99075	M1-T161
HEG1	57493	Q9ULI3	M1-L1248
HEPACAM	220296	Q14CZ8	M1-R237
HEPACAM	220296	Q14CZ8	M1-Y236
HEPACAM2	253012	A8MVW5	M1-P351
HEPH	9843	Q9BQS7	M1-E1108
HEPHL1	341208	Q6MZM0	M1-A1115
HFE	3077	Q30201	M1-V306
HFE	3077	Q30201	M1-W297
HFE2	148738	Q6ZVN8	M1-G402
HHLA2	11148	Q9UM44	M1-G346
HHLA2	11148	Q9UM44	M1-N344
HYAL2	8692	Q12891	M1-G447
ICAM1	3383	P05362	M1-E480
ICAM2	3384	P13598	M1-Q223
ICAM2	3384	P13598	M1-Y216
ICAM3	3385	P32942	M1-H485
ICAM4	3386	Q14773	M1-A240
ICAM5	7087	Q9UMF0	M1-W835
ICOS	29851	Q9Y6W8	M1-F141
ICOSLG	23308	O75144	M1-N253
ICOSLG	23308	O75144	M1-S258
IFNAR1	3454	P17181	M1-K436
IFNAR2	3455	P48551	M1-A242
IFNGR1	3459	P15260	M1-G245
IFNGR2	3460	P38484	M1-Q247
IFNLR1	163702	Q8IU57	M1-A228
IGDCC4	57722	Q8TDY8	M1-T957
IGF1R	3480	P08069	M1-H935
IGF2R	3482	P11717	M1-A2305
IGFLR1	79713	Q9H665	M1-N160
IGSF1	3547	Q8N6C5	E581-I1336
IGSF1	3547	Q8N6C5	M1-A520
IGSF11	152404	Q5DX21	M1-G245

IGSF21	84966	Q96ID5	M1-A452
IGSF3	3321	O75054	M1-A1124
IGSF3	3321	O75054	M1-D1123
IGSF5	150084	Q9NSI5	M1-G270
IGSF5	150084	Q9NSI5	M1-V267
IGSF6	10261	O95976	M1-S153
IGSF8	93185	Q969P0	M1-T579
IGSF9	57549	Q9P2J2	M1-G738
IGSF9B	22997	Q9UPX0	M1-G726
IGSF9B	22997	Q9UPX0	M1-P722
IL10RA	3587	Q13651	M1-N235
IL10RB	3588	Q08334	M1-S220
IL11RA	3590	Q14626	M1-Q365
IL12RB1	3594	P42701	M1-D545
IL12RB2	3595	Q99665	M1-N622
IL13RA1	3597	P78552	M1-S342
IL13RA2	3598	Q14627	M1-R343
IL15RA	3601	Q13261	M1-T205
IL17RA	23765	Q96F46	M1-Y322
IL17RC	84818	Q8NAC3	M1-K537
IL17RD	54756	Q8NFM7	M1-R299
IL17RE	132014	Q8NFR9	M1-H454
IL18R1	8809	Q13478	M1-G330
IL18RAP	8807	O95256	M1-K355
IL1R1	3554	P14778	M1-H337
IL1R1	3554	P14778	M1-K336
IL1R2	7850	P27930	M1-E343
IL1RAP	3556	Q9NPH3	M1-C362
IL1RAP	3556	Q9NPH3	M1-T367
IL1RAPL1	11141	Q9NZN1	M1-G341
IL1RAPL1	11141	Q9NZN1	M1-T357
IL1RAPL2	26280	Q9NP60	M1-E356
IL1RL1	9173	Q01638	M1-S328
IL1RL2	8808	Q9HB29	M1-R335
IL20RA	53832	Q9UHF4	M1-K250
IL20RB	53833	Q6UXL0	M1-L233
IL21R	50615	Q9HBE5	M1-H237
IL23R	149233	Q5VWK5	M1-G355
IL27RA	9466	Q6UWB1	M1-G520
IL2RA	3559	P01589	M1-Q240
IL2RB	3560	P14784	M1-P242
IL2RG	3561	P31785	M1-A262
IL31RA	133396	Q8NI17	M1-E519

IL3RA	3563	P26951	M1-R305
IL4R	3566	P24394	M1-C227
IL5RA	3568	Q01344	M1-E341
IL6R	3570	P08887	M1-T366
IL6ST	3572	P40189	M1-A620
IL7R	3575	P16871	M1-P240
IL9R	3581	Q01113	M1-G271
ILDR1	286676	Q86SU0	M1-H167
ILDR1	286676	Q86SU0	M1-V161
ILDR2	387597	Q71H61	M1-E186
IMPG2	50939	Q9BZV3	M1-V1100
INSR	3643	P06213	M1-K956
INSRR	3645	P14616	A747-H921
ISLR2	57611	Q6UXK2	M1-K584
ISLR2	57611	Q6UXK2	M1-S589
ITFG1	81533	Q8TB96	M1-N565
ITGA1	3672	P56199	M1-P1141
ITGA2B	3674	P08514	M1-K886
ITGA2B	3674	P08514	M1-P996
ITGA5	3678	P08648	M1-P998
ITGB6	3694	P18564	M1-I708
ITLN1	55600	Q8WWA0	M1-R313
ITM2A	9452	O43736	M79-E263
ITM2B	9445	Q9Y287	K77-K242
ITM2B	9445	Q9Y287	K77-S266
ITM2C	81618	Q9NQX7	R81-K241
ITM2C	81618	Q9NQX7	R81-V267
IYD	389434	Q6PHW0	M1-N213
IZUMO1	284359	Q8IYV9	M1-R292
JAG1	182	P78504	M1-D1067
JAG2	3714	Q9Y219	M1-G1081
JAM2	58494	P57087	M1-S238
JAM3	83700	Q9BX67	M1-N241
JAML	120425	Q86YT9	M1-Q274
JTB	10899	O76095	M1-R104
KDR	3791	P35968	M1-E764
KIAA0090	23065	Q8N766	M1-D958
KIAA0319	9856	Q5VV43	M1-S955
KIAA0319L	79932	Q8IZA0	M1-L931
KIAA1024	23251	Q9UPX6	M1-K878
KIAA1324	57535	Q6UXG2	M1-K910
KIAA1324L	222223	A8MWY0	M1-K929
KIAA1467	57613	A2RU67	P128-I622

KIR2DL1	3802	P43626	M1-H245
KIR2DL1	3802	P43626	M1-R242
KIR2DL2	3803	P43627	M1-H245
KIR2DL3	3804	P43628	M1-H245
KIR2DL3	3804	P43628	M1-R242
KIR2DL4	3805	Q99706	M1-A243
KIR2DL5A	57292	Q8N109	M1-I235
KIR2DL5A	57292	Q8N109	M1-R236
KIR2DL5B	553128	Q8NHK3	M1-H238
KIR2DL5B	553128	Q8NHK3	M1-R236
KIR2DS1	3806	Q14954	M1-H243
KIR2DS1	3806	Q14954	M1-H245
KIR2DS2	100132285	P43631	M1-H245
KIR2DS3	3808	Q14952	M1-H243
KIR2DS3	3808	Q14952	M1-H245
KIR2DS4	3809	P43632	M1-H245
KIR2DS4	3809	P43632	M1-R242
KIR2DS5	3810	Q14953	M1-H243
KIR2DS5	3810	Q14953	M1-H245
KIR3DL1	3811	P43629	M1-H340
KIR3DL2	3812	P43630	M1-H338
KIR3DL2	3812	P43630	M1-H340
KIR3DL3	115653	Q8N743	M1-H321
KIR3DL3	115653	Q8N743	M1-H323
KIR3DL3	115653	Q8N743	M1-V410
KIR3DS1	3813	O43469	M1-H340
KIRREL	55243	Q96J84	M1-G496
KIRREL2	84063	Q6UWL6	M1-R510
KIRREL3	84623	Q8IZU9	M1-A535
KIRREL3	84623	Q8IZU9	M1-S531
KIT	3815	P10721	M1-P524
KIT	3815	P10721	M1-T520
KITLG	4254	P21583	M1-S212
KL	9365	Q9UEF7	M1-R979
KLRAP1	10748	O75889	I69-E194
KLRAP1	10748	O75889	I69-Y215
KLRB1	3820	Q12918	Q67-S225
KLRC1	3821	P26715	S95-L233
KLRC2	3822	P26717	E98-L231
KLRD1	3824	Q13241	K32-I179
KLRF1	51348	Q9NZS2	S63-T124
KLRF1	51348	Q9NZS2	S63-Y231
KLRG1	10219	Q96E93	L60-F195

KLRK1	22914	P26718	N80-V216
KREMEN1	83999	Q96MU8	M1-T392
L1CAM	3897	P32004	M1-E1120
L1CAM	3897	P32004	M1-G1121
LAG3	3902	P18627	M1-L450
LAMP3	27074	Q9UQV4	M1-T381
LAMP5	24141	Q9UJQ1	M1-E235
LAYN	143903	Q6UX15	M1-N232
LCTL	197021	Q6UWM7	M1-E541
LDLR	3949	P01130	M1-R788
LDLRAD1	388633	Q5T700	P63-P205
LDLRAD3	143458	Q86YD5	M1-S171
LECT1	11061	O75829	E215-V334
LEPR	3953	P48357	M1-A840
LEPR	3953	P48357	M1-D839
LIFR	3977	P42702	M1-S833
LILRA1	11024	O75019	M1-N461
LILRA2	11027	Q8N149	M1-L450
LILRA3	11026	Q8N6C8	M1-E439
LILRA4	23547	P59901	M1-N446
LILRA5	353514	A6NI73	M1-N265
LILRA6	79168	Q6PI73	M1-N447
LILRB1	10859	Q8NHL6	M1-H458
LILRB2	10288	Q8N423	M1-G460
LILRB3	11025	O75022	M1-E443
LILRB4	11006	Q8NHJ6	M1-E259
LILRB4	11006	Q8NHJ6	M1-R255
LILRB5	10990	O75023	M1-G458
LILRB5	10990	O75023	M1-R455
LINGO1	84894	Q96FE5	M1-T556
LINGO1	84894	Q96FE5	M1-T561
LINGO2	158038	Q7L985	M1-T540
LINGO2	158038	Q7L985	M1-T545
LINGO3	645191	P0C6S8	M1-T531
LINGO4	339398	Q6UY18	M1-A533
LINGO4	339398	Q6UY18	M1-G531
LMLN	89782	Q96KR4	M1-H655
LOC256223	256223	A8MXV6	M1-A211
LRCH1	23143	Q9Y2L9	M1-K690
LRCH4	4034	O75427	M1-G661
LRFN1	57622	Q9P244	M1-T535
LRFN2	57497	Q9ULH4	M1-Q528
LRFN2	57497	Q9ULH4	M1-T533

LRFN3	79414	Q9BTN0	M1-G535
LRFN3	79414	Q9BTN0	M1-T538
LRFN4	78999	Q6PJG9	M1-L518
LRFN5	145581	Q96NI6	M1-Q523
LRFN5	145581	Q96NI6	M1-T528
LRIG1	26018	Q96JA1	M1-G794
LRIG1	26018	Q96JA1	M1-T792
LRIG2	9860	O94898	M1-G807
LRIT1	26103	Q9P2V4	M1-Q526
LRIT2	340745	A6NDA9	M1-H462
LRIT3	345193	Q3SXY7	M1-Q580
LRIT3	345193	Q3SXY7	M1-W536
LRP10	26020	Q7Z4F1	M1-R439
LRP11	84918	Q86VZ4	M1-G450
LRP12	29967	Q9Y561	M1-R492
LRP3	4037	O75074	M1-R495
LRP4	4038	O75096	M1-H1723
LRP5	4041	O75197	M1-A1386
LRP6	4040	O75581	M1-T1373
LRP8	7804	Q14114	M1-A826
LRPAP1	4043	P30533	M1-L357
LRRC19	64922	Q9H756	M1-S269
LRRC24	441381	Q50LG9	M1-T405
LRRC25	126364	Q8N386	M1-T165
LRRC3	81543	Q9BY71	M1-D204
LRRC32	2615	Q14392	M1-N627
LRRC33	375387	Q86YC3	M1-G649
LRRC37B	114659	Q96QE4	M1-K905
LRRC38	126755	Q5VT99	M1-I250
LRRC3B	116135	Q96PB8	M1-K199
LRRC4	64101	Q9HBW1	M1-K527
LRRC4	64101	Q9HBW1	M1-T526
LRRC4B	94030	Q9NT99	M1-K576
LRRC4C	57689	Q9HCJ2	M1-K527
LRRC52	440699	Q8N7C0	M1-D244
LRRC55	219527	Q6ZSA7	M1-D300
LRRC66	339977	Q68CR7	M1-L375
LRRN1	57633	Q6UXK5	M1-A631
LRRN2	10446	O75325	M1-G630
LRRN2	10446	O75325	M1-P629
LRRN3	54674	Q9H3W5	M1-T627
LRRN3	54674	Q9H3W5	M1-T628
LRRN4	164312	Q8WUT4	M1-A681

LRRN4CL	221091	Q8ND94	M1-L195
LRRTM1	347730	Q86UE6	M1-K427
LRRTM2	26045	O43300	M1-R422
LRRTM3	347731	Q86VH5	M1-F417
LRRTM3	347731	Q86VH5	M1-K419
LRRTM4	80059	Q86VH4	M1-K424
LRTM1	57408	Q9HBL6	M1-H284
LRTM2	654429	Q8N967	M1-R306
LSAMP	4045	Q13449	M1-S317
LSR	51599	Q86X29	M1-D259
LTBR	4055	P36941	M1-T224
LTK	4058	P29376	M1-P424
LY6D	8581	Q14210	M1-A105
LY6E	4061	Q16553	M1-F100
LY6G6C	80740	O95867	M1-A100
LY6G6D	58530	O95868	M1-A105
LY6G6F	259215	Q5SQ64	M1-P234
LY6G6F	259215	Q5SQ64	M1-W235
LY6H	4062	O94772	M1-A116
LY6K	54742	Q17RY6	M59-E200
LY75	4065	O60449	M1-A1669
LY9	4063	Q9HBG7	M1-K454
LYPD1	116372	Q8N2G4	M1-A120
LYPD3	27076	O95274	M1-G325
LYPD5	284348	Q6UWN5	M1-S226
LYPD6	130574	Q86Y78	M1-G151
LYPD6B	130576	Q8NI32	M1-G163
LYSMD3	116068	Q7Z3D4	M1-G215
LYSMD4	145748	Q5XG99	M1-Q218
LYVE1	10894	Q9Y5Y7	M1-T238
M6PR	4074	P20645	M1-S190
MADCAM1	8174	Q13477	M1-L318
MAG	4099	P20916	M1-H507
MAG	4099	P20916	M1-M510
MAMDC4	158056	Q6UXC1	M1-A1154
MANSC1	54682	Q9H8J5	M1-K383
MCAM	4162	P43121	M1-G559
MDGA1	266727	Q8NFP4	M1-S932
MDGA2	161357	Q7Z553	M1-A933
MDGA2	161357	Q7Z553	M1-V930
MEGF10	84466	Q96KG7	M1-I856
MEGF11	84465	A6BM72	M1-S848
MEGF8	1954	Q7Z7M0	M1-D2647

MEGF9	1955	Q9H1U4	M1-N514
MEP1A	4224	Q16819	M1-V712
MEP1B	4225	Q16820	M1-T652
MERTK	10461	Q12866	M1-L503
MEST	4232	Q5EB52	P32-F335
MET	4233	P08581	M1-G933
MFAP3	4238	P55082	M1-S148
MFAP3L	9848	O75121	M1-D148
MFI2	4241	P08582	M1-Q708
MFRP	83552	Q9BY79	Q91-P579
MGC39681	283197	Q8NCQ3	K48-A95
MICA	100507436	Q29983	M1-Q308
MICB	4277	Q29980	M1-D266
MICB	4277	Q29980	M1-D309
MILR1	284021	Q7Z6M3	M1-K227
MME	4311	P08473	D53-W750
MMP14	4323	P50281	M1-S538
MMP15	4324	P51511	M1-N625
MMP16	4325	P51512	M1-A564
MMP23B	8510	O75900	R39-G390
MMP24	10893	Q9Y5R2	M1-A602
MOG	4340	Q16653	M1-G154
MPEG1	219972	Q2M385	M1-G655
MPL	4352	P40238	M1-T489
MPZ	4359	P25189	M1-G155
MPZL1	9019	O95297	M1-V165
MPZL2	10205	O60487	M1-H152
MPZL3	196264	Q6UWV2	M1-S158
MRC1	4360	P22897	M1-R1377
MRC2	9902	Q9UBG0	M1-A1414
MSLN	10232	Q13421	M1-A621
MST1R	4486	Q04912	M1-G960
MUC13	56667	Q9H3R2	M1-L421
MUC15	143662	Q8N387	M28-T263
MUC21	394263	Q5SSG8	M1-E479
MUSK	4593	O15146	M1-T495
MXRA5	25878	Q9NR99	M1-F2828
MXRA8	54587	Q9BRK3	M1-Q341
MYEOV	26579	Q96EZ4	M1-G293
NAALAD2	10003	Q9Y3Q0	E36-L740
NAALADL1	10004	Q9UQQ1	K31-L791
NAGPA	51172	Q9UK23	M1-T448
NCAM1	4684	P13591	M1-A723

NCAM1	4684	P13591	M1-L719
NCAM2	4685	O15394	M1-N697
NCAM2	4685	O15394	M1-T694
NCR1	9437	O76036	M1-N255
NCR1	9437	O76036	M1-R258
NCR2	9436	O95944	M1-A192
NCR2	9436	O95944	M1-P190
NCR3	259197	O14931	M1-T138
NCSTN	23385	Q92542	M1-E669
NECTIN1	5818	Q15223	M1-A355
NECTIN2	5819	Q92692	M1-G360
NECTIN3	25945	Q9NQS3	M1-D400
NECTIN4	81607	Q96NY8	M1-V350
NEGR1	257194	Q7Z3B1	M1-D327
NEO1	4756	Q92859	M1-N1103
NETO2	81831	Q8NC67	M1-E333
NFAM1	150372	Q8NET5	M1-K163
NFASC	23114	O94856	M1-G1216
NGFR	4804	P08138	M1-N250
NLGN1	22871	Q8N2Q7	M1-V678
NLGN3	54413	Q9NZ94	M1-S709
NLGN4X	57502	Q8N0W4	M1-K668
NOMO1	23420	Q15155	M1-S1160
NOTCH1	4851	P46531	M1-H1735
NOTCH2	4853	Q04721	M1-Q1677
NOTCH3	4854	Q9UM47	M1-L1643
NOTCH4	4855	Q99466	M1-V1449
NPDC1	56654	Q9NQX5	M1-G182
NPHS1	4868	O60500	M1-P1061
NPHS1	4868	O60500	M1-S1055
NPR1	4881	P16066	M1-E473
NPR2	4882	P20594	M1-T455
NPR3	4883	P17342	M1-E481
NPTN	27020	Q9Y639	M1-P339
NRCAM	4897	Q92823	M1-G1168
NRG1	3084	Q02297	M1-Q240
NRG2	9542	O14511	M1-Q403
NRG4	145957	Q8WWG1	M1-E63
NRN1	51299	Q9NPD7	M1-A118
NRN1L	123904	Q496H8	M1-P140
NRP1	8829	O14786	M1-R845
NRP2	8828	O60462	M1-P864
NRXN1	9378	Q9ULB1	M1-T1401

NRXN2	9379	Q9P2S2	M1-G1637
NRXN3	9369	Q9Y4C0	M1-G1569
NT5E	4907	P21589	M1-F548
NTM	50863	Q9P121	M1-N321
NTNG1	22854	Q9Y2I2	M1-F438
NTRK1	4914	P04629	M1-S419
NTRK2	4915	Q16620	M1-H430
NTRK3	4916	Q16288	M1-G431
NTRK3	4916	Q16288	M1-T429
OMG	4974	P23515	M1-S417
OPCML	4978	Q14982	M1-N322
OPCML	4978	Q14982	M1-V321
OSMR	9180	Q99650	M1-S739
OSTM1	28962	Q86WC4	M1-P284
P2RX2	22953	Q9UBL9	Q64-S337
PARM1	25849	Q6UWI2	M1-S258
PBOV1	59351	Q9GZY1	M1-I135
PCDH10	57575	Q9P2E7	M1-D713
PCDH11Y	83259	Q9BZA8	M1-K844
PCDH12	51294	Q9NPG4	M1-S715
PCDH17	27253	O14917	M1-D703
PCDH18	54510	Q9HCL0	M1-S699
PCDH19	57526	Q8TAB3	M1-S678
PCDH20	64881	Q8N6Y1	M1-T862
PCDH9	5101	Q9HC56	M1-T814
PCDHA13	56136	Q9Y5I0	M1-N697
PCDHA7	56141	Q9UN72	M1-N697
PCDHA8	56140	Q9Y5H6	M1-N697
PCDHAC1	56135	Q9H158	M1-Y683
PCDHB1	29930	Q9Y5F3	M1-K689
PCDHB10	56126	Q9UN67	M1-L692
PCDHB11	56125	Q9Y5F2	M1-T687
PCDHB13	56123	Q9Y5F0	M1-T687
PCDHB3	56132	Q9Y5E6	M1-T687
PCDHB4	56131	Q9Y5E5	M1-T686
PCDHB5	26167	Q9Y5E4	M1-T686
PCDHB6	56130	Q9Y5E3	M1-T685
PCDHB7	56129	Q9Y5E2	M1-S683
PCDHB9	56127	Q9Y5E1	M1-T687
PCDHGA11	56105	Q9Y5H2	M1-D689
PCDHGA2	56113	Q9Y5H1	M1-Y692
PCDHGA4	56111	Q9Y5G9	M1-Y692
PCDHGA7	56108	Q9Y5G6	M1-Y692

PCDHGA8	9708	Q9Y5G5	M1-Y692
PCDHGA9	56107	Q9Y5G4	M1-D688
PCDHGB4	8641	Q9UN71	M1-Y689
PCDHGB5	56101	Q9Y5G0	M1-Q685
PCDHGC4	56098	Q9Y5F7	M1-Y693
PCSK4	54760	Q6UW60	M1-A709
PDCD1	5133	Q15116	M1-V170
PDCD1LG2	80380	Q9BQ51	M1-T220
PDGFRA	5156	P16234	M1-A528
PEAR1	375033	Q5VY43	M1-A757
PECAM1	5175	P16284	M1-G602
PECAM1	5175	P16284	M1-K600
PGBD5	79605	Q8N414	M1-Q404
PI16	221476	Q6UXB8	M1-H443
PIGR	5284	P01833	M1-A639
PIGR	5284	P01833	M1-R638
PIK3IP1	113791	Q96FE7	M1-L173
PILRB	29990	Q9UKJ0	M1-R191
PLA2R1	22925	Q13018	M1-P1400
PLB1	151056	Q6P1J6	M1-E1414
PLSCR4	57088	Q9NRQ2	M1-D301
PLVAP	83483	Q9BX97	G50-G442
PLXDC1	57125	Q9BX97	M1-P409
PLXDC2	84898	Q6UX71	M1-G455
PLXNA1	5361	Q9UIW2	M1-A1245
PLXNA4	91584	Q9HCM2	M1-A1238
PLXNB1	5364	O43157	M1-Q1490
PLXNB2	23654	O15031	M1-S1199
PLXNB3	5365	Q9ULL4	M1-Q1255
PLXNC1	10154	O60486	M1-T944
PLXND1	23129	Q9Y4D7	M1-A1271
PMEL	6490	P40967	M1-Q595
PODXL	5420	O00592	M1-M460
PODXL2	50512	Q9NZ53	M1-T500
PRLR	5618	P16471	M1-T235
PRLR	5618	P16471	M1-T236
PRND	23627	Q9UKY0	M1-R151
PRNP	5621	P04156	M1-G229
PROCR	10544	Q9UNN8	M1-S210
PRRG1	5638	O14668	M1-L83
PRRG2	5639	O14669	M1-D106
PRRG3	79057	Q9BZD7	M1-D78
PRRG4	79056	Q9BZD6	M1-D113

PRSS21	10942	Q9Y6M0	M1-Q287
PRSS55	203074	Q6UWB4	M1-G326
PRSS8	5652	Q16651	M1-G319
PRTG	283659	Q2VWP7	M1-G950
PTCRA	171558	Q6ISU1	M1-A147
PTGFRN	5738	Q9P2B2	M1-K830
PTGFRN	5738	Q9P2B2	M1-P832
PTK7	5754	Q13308	M1-T704
PTPRA	5786	P18433	M1-P142
PTPRB	5787	P23467	M1-G1622
PTPRC	5788	P08575	D193-A576
PTPRC	5788	P08575	M1-A576
PTPRD	5789	P23468	M1-G1266
PTPRF	5792	P10586	M1-L1262
PTPRG	5793	P23470	M1-E736
PTPRH	5794	Q9HD43	M1-S751
PTPRJ	5795	Q12913	M1-G971
PTPRK	5796	Q15262	M1-K752
PTPRM	5797	P28827	M1-K742
PTPRN	5798	Q16849	M1-E446
PTPRN	5798	Q16849	M1-S576
PTPRN2	5799	Q92932	M1-K614
PTPRO	5800	Q16827	M1-N819
PTPRR	5801	Q15256	M1-G227
PTPRS	5802	Q13332	M1-G1282
PTPRT	11122	O14522	M1-K746
PTPRT	11122	O14522	M1-M766
PTPRU	10076	Q92729	M1-L749
PTPRZ1	5803	P23471	M1-K1635
PVR	5817	P15151	M1-N343
QSOX1	5768	O00391	M1-D709
QSOX2	169714	Q6ZRP7	M1-S662
RAET1E	135250	Q8TD07	M1-T212
RAET1G	353091	Q6H3X3	M1-V213
RAET1L	154064	Q5VY80	M1-S217
RAMP1	10267	O60894	M1-S117
RAMP2	10266	O60895	M1-D144
RAMP3	10268	O60896	M1-V118
RARRES1	5918	P49788	A38-F294
RECK	8434	O95980	M1-P941
RELT	84957	Q969Z4	M1-Q162
RET	5979	P07949	M1-T636
RGMA	56963	Q96B86	M1-G427

RGMB	285704	Q6NW40	M1-G412
ROBO1	6091	Q9Y6N7	M1-P897
ROBO2	6092	Q9HCK4	M1-A860
ROBO3	64221	Q96MS0	M1-P891
ROR1	4919	Q01973	M1-Y406
ROR2	4920	Q01974	M1-G403
ROR2	4920	Q01974	M1-M402
ROS1	6098	P08922	M1-S1861
RTN4R	65078	Q9BZR6	M1-S447
RTN4RL1	146760	Q86UN2	M1-A422
RTP3	83597	Q9BQQ7	M1-N210
RTP4	64108	Q96DX8	M1-D224
RYK	6259	P34925	M1-R224
SARAF	51669	Q96BY9	M1-N172
SAYSD1	55776	Q9NPB0	M1-K105
SCARB1	949	Q8WTV0	K37-H442
SCARF1	8578	Q14162	M1-A422
SCARF2	91179	Q96GP6	M1-R440
SCN1B	6324	Q07699	M1-E160
SCN2B	6327	O60939	M1-A159
SCN3B	55800	Q9NY72	M1-E159
SCN4B	6330	Q8IWT1	M1-T161
SDC1	6382	P18827	M1-E251
SDC2	6383	P34741	M1-E144
SDC3	9672	O75056	M1-R382
SDC4	6385	P31431	M1-E145
SDK1	221935	Q7Z5N4	M1-E2007
SDK2	54549	Q58EX2	M1-W1930
SECTM1	6398	Q8WVN6	M1-G145
SEL1L3	23231	Q68CR1	M1-R1051
SELE	6401	P16581	M1-N554
SELL	6402	P14151	M1-P333
SELPLG	6404	Q14242	M1-C310
SEMA4A	64218	Q9H3S1	M1-H683
SEMA4A	64218	Q9H3S1	M1-S679
SEMA4B	10509	Q9NPR2	M1-D711
SEMA4B	10509	Q9NPR2	M1-E712
SEMA4C	54910	Q9C0C4	M1-G663
SEMA4D	10507	Q92854	M1-R734
SEMA4F	10505	O95754	M1-G660
SEMA4F	10505	O95754	M1-T658
SEMA4G	57715	Q9NTN9	M1-R674
SEMA5A	9037	Q9P283	M1-N967

SEMA5B	54437	Q9P283	M1-H1036
SEMA6A	57556	Q9H2E6	M1-Q644
SEMA6B	10501	Q9H3T3	M1-S603
SEMA6C	10500	Q9H3T2	M1-P604
SEMA7A	8482	O75326	M1-A644
SEMA7A	8482	O75326	M1-L647
SERPINB7	8710	O75635	Q47-P380
SEZ6	124925	Q53EL9	M1-A928
SEZ6L	23544	Q9BYH1	M1-A958
SEZ6L2	26470	Q6UXD5	M1-N844
SGCA	6442	Q16586	M1-D285
SGCB	6443	Q16585	R91-H318
SGCD	6444	Q92629	K58-L290
SGCE	8910	O43556	M1-F317
SGCG	6445	Q13326	K59-L291
SGCZ	137868	Q96LD1	K72-S312
SHISA2	387914	Q6UWI4	M1-V116
SHISA3	152573	A0PJX4	M1-P94
SHISA4	149345	Q96DD7	M1-G88
SHISA5	51246	Q8N114	M1-T109
SIGIRR	59307	Q6IA17	M1-H118
SIGLEC1	6614	Q9BZZ2	M1-Q1641
SIGLEC10	89790	Q96LC7	M1-N550
SIGLEC11	114132	Q96RL6	M1-G558
SIGLEC11	114132	Q96RL6	M1-G560
SIGLEC12	89858	Q96PQ1	M1-A481
SIGLEC12	89858	Q96PQ1	M1-T478
SIGLEC15	284266	Q6ZMC9	M1-T263
SIGLEC16	400709	A6NMB1	M1-G434
SIGLEC5	8778	O15389	M1-A440
SIGLEC5	8778	O15389	M1-S353
SIGLEC5	8778	O15389	M1-T359
SIGLEC6	946	O43699	M1-G346
SIGLEC7	27036	Q9Y286	M1-G350
SIGLEC8	27181	Q9NYZ4	M1-A363
SIGLEC9	27180	Q9Y336	M1-G348
SIGLECP16	400709	A6NMB1	M1-T433
SIRPA	140885	P78324	M1-Y373
SIRPB1	10326	O00241	M1-P370
SIRPB2	284759	Q5JXA9	M1-G287
SIRPD	128646	Q9H106	H31-K197
SIRPD	128646	Q9H106	M1-K197
SIRPD	128646	Q9H106	M1-Q181

SIRPG	55423	Q9P1W8	M1-G361
SIRPG	55423	Q9P1W8	M1-T359
SKINT1	391037	A8MVG2	M1-S242
SLAMF1	6504	Q13291	M1-P237
SLAMF6	114836	Q96DU3	M1-M226
SLAMF7	57823	Q9NQ25	M1-M226
SLAMF8	56833	Q9P0V8	M1-D233
SLAMF9	89886	Q96A28	M1-C235
SLAMF9	89886	Q96A28	M1-F234
SLAMF9	89886	Q96A28	M1-S210
SLITRK1	114798	Q96PX8	M1-G623
SLITRK2	84631	Q9H156	M1-P617
SLITRK2	84631	Q9H156	M1-V620
SLITRK3	22865	O94933	M1-S654
SLITRK4	139065	Q8IW52	M1-P616
SLITRK6	84189	Q9H5Y7	M1-P606
SMCR7	125170	Q96C03	K48-L454
SMCR7L	54471	Q9NQG6	K47-T463
SNPH	9751	O15079	M1-R423
SORCS1	114815	Q8WY21	M1-A1102
SORL1	6653	Q92673	M1-A2138
SORT1	6272	Q99523	M1-S756
SPACA1	81833	Q9HBV2	M1-D216
SPACA4	171169	Q8TDM5	M1-T104
SPATA9	83890	Q9BWV2	M1-S146
SPINT1	6692	O43278	M1-K446
SPINT2	10653	O43291	M1-N189
SPN	6693	P16150	M1-R253
ST14	6768	Q9Y5Y6	Q80-V855
STAB1	23166	Q9NY15	M1-G2479
STAB2	55576	Q8WWQ8	M1-G2463
STIM1	6786	Q13586	M1-D213
SUSD1	64420	Q6UWL2	M1-Q724
SUSD2	56241	Q9UGT4	M1-A785
SUSD3	203328	Q96L08	M1-K103
SUSD4	55061	Q5VX71	M1-T321
SUSD5	26032	O60279	M1-G573
TACSTD2	4070	P09758	M1-K271
TAPBPL	55080	Q9BX59	M1-E403
TARM1	441864	B6A8C7	M1-N233
TARM1	441864	B6A8C7	M1-R236
TCP11	6954	Q8WWU5	M1-Q266
TCTN2	79867	Q96GX1	M1-K671

TCTN3	26123	Q6NUS6	M1-C586
TDGF1	6997	P13385	H33-Y188
TDGF1	6997	P13385	M1-P168
TECTA	7007	O75443	M1-R2081
TECTB	6975	Q96PL2	M1-L301
TEK	7010	Q02763	M1-K745
TEX101	83639	Q9BY14	M1-E221
TEX29	121793	Q8N6K0	M1-V55
TFR2	7036	Q9UP52	R105-F801
TGFA	7039	P01135	M1-A89
TGOLN2	10618	O43493	M1-H384
THBD	7056	P07204	M1-G516
THSD1	55901	Q9NS62	M1-N413
THSD7A	221981	Q9UPZ6	M1-T1606
THSD7B	80731	Q9C0I4	M1-K1558
THY1	7070	P04216	M1-K129
THY1	7070	P04216	M1-L161
TIE1	7075	P35590	M1-Q759
TIGIT	201633	Q495A1	M1-P141
TIMD4	91937	Q96H15	M1-Q314
TLR1	7096	Q15399	M1-T580
TLR10	81793	Q9BXR5	M1-T576
TLR2	7097	O60603	M1-T588
TLR3	7098	O15455	M1-L704
TLR4	7099	O00206	M1-K631
TLR5	7100	O60602	M1-K639
TLR6	10333	Q9Y2C9	M1-T585
TLR8	51311	Q9NR97	M1-D825
TLR9	54106	Q9NR96	M1-A820
TMEFF1	8577	Q8IYR6	M1-H329
TMEFF2	23671	Q9UIK5	M1-V320
TMEM106A	113277	Q96A25	P116-P262
TMEM108	66000	Q6UXF1	M1-D468
TMEM119	338773	Q4V9L6	M1-M96
TMEM123	114908	Q8N131	M1-S168
TMEM123	114908	Q8N131	M1-T166
TMEM130	222865	Q8N3G9	M1-P339
TMEM132A	54972	Q24JP5	M1-A852
TMEM132E	124842	Q6IEE7	M1-A803
TMEM154	201799	Q6P9G4	M1-E75
TMEM156	80008	Q8N614	M1-K213
TMEM158	25907	Q8WZ71	M1-A226
TMEM167A	153339	Q8TBQ9	M1-K53

TMEM183A	92703	Q8IXX5	M1-T299
TMEM190	147744	Q8WZ59	M1-H80
TMEM207	131920	Q6UWW9	M1-G49
TMEM25	84866	Q86YD3	M1-G237
TMEM27	57393	Q9HBJ8	L163-L222
TMEM27	57393	Q9HBJ8	M1-P141
TMEM53	79639	Q6P2H8	H196-C277
TMEM59	9528	Q9BXS4	M1-G239
TMEM59L	25789	Q9UK28	M1-R267
TMEM81	388730	Q6P7N7	M1-K221
TMEM95	339168	Q3KNT9	M1-K145
TMEM98	26022	Q9NQ34	Q29-I226
TMEM9B	56674	Q9NQ34	M1-T104
TMIE	259236	Q8NEW7	M1-R55
TMIGD1	388364	Q6UXZ0	M1-P220
TMIGD2	126259	Q96BF3	M1-G150
TMPRSS11D	9407	O60235	F43-I418
TMPRSS11F	389208	Q6ZWK6	E54-M438
TMPRSS12	283471	Q86WS5	M1-Q323
TMPRSS13	84000	Q9BYE2	Q182-V581
TMPRSS4	56649	Q9NRS4	D58-L437
TMPRSS5	80975	Q9H3S3	Y71-L457
TMPRSS7	344805	Q7RTY8	M1-L717
TMX4	56255	Q9H1E5	M1-S188
TNFRSF10D	8793	Q9UBN6	M1-P209
TNFRSF11A	8792	Q9Y6Q6	M1-H208
TNFRSF12A	51330	Q9NP84	M1-I81
TNFRSF13B	23495	O14836	M1-V160
TNFRSF13C	115650	Q96RJ3	M1-G80
TNFRSF14	8764	Q92956	M1-V202
TNFRSF17	608	Q02223	M1-G51
TNFRSF18	8784	Q9Y5U5	M1-P162
TNFRSF19	55504	Q9NS68	M1-A172
TNFRSF1A	7132	P19438	M1-N201
TNFRSF1B	7133	P20333	M1-D257
TNFRSF21	27242	O75509	M1-H349
TNFRSF25	8718	Q93038	M1-Q199
TNFRSF4	7293	P43489	M1-A217
TNFRSF8	943	P28908	M1-P386
TNFRSF9	3604	Q12933	M1-Q186
TNFSF10	8743	P50591	T39-G299
TNFSF14	8740	O43557	Q60-V240
TNFSF15	9966	O95150	L72-L251

TNFSF18	8995	Q9UNG2	Q50-S177
TNFSF8	944	P32971	Q63-D234
TNFSF9	8744	P41273	S56-E254
TNMD	64102	Q9H2S6	K51-V317
TPBG	7162	Q13641	M1-S355
TPO	7173	P23467	M1-T848
TPSG1	25823	Q9NRR2	I38-R281
TPSG1	25823	Q9NRR2	M1-R281
TREH	11181	O43280	M1-A558
TREM1	54210	Q9NP99	M1-P202
TREM2	54209	Q9NZC2	M1-S174
TREML1	340205	Q86YW5	M1-P162
TREML2	79865	Q5T2D2	M1-D265
TREML4	285852	Q6UXN2	M1-G180
TRHDE	29953	Q9UKU6	R64-H1024
TRIL	9865	Q7L0X0	M1-Q696
TXNDC15	79770	Q96J42	M1-D323
TYRO3	7301	Q06418	M1-S428
TYRP1	7306	P17643	M1-E477
ULBP1	80329	Q9BZM6	M1-A214
ULBP2	80328	Q9BZM5	M1-G218
ULBP3	79465	Q9BZM4	M1-A215
UMOD	7369	P07911	M1-V613
UNC5A	90249	Q6ZN44	M1-Y306
UNC5B	219699	Q8IZJ1	M1-Y377
UNC5C	8633	O95185	M1-D376
UNC5C	8633	O95185	M1-Y380
UNC5D	137970	Q6UXZ4	M1-D379
UPK3BL	100134938	B0FP48	M1-T202
UXS1	80146	Q8NBZ7	E85-Q402
VASN	114990	Q6EMK4	M1-P575
VCAM1	7412	P19320	M1-E698
VLDLR	7436	P98155	M1-S797
VNN2	8875	O95498	M1-S492
VSIG1	340547	Q86XK7	M1-E232
VSIG10	54621	Q8N0Z9	M1-G413
VSIG10	54621	Q8N0Z9	M1-N410
VSIG10L	147645	Q86VR7	M1-G779
VSIG2	23584	Q96IQ7	M1-G244
VSIG4	11326	Q9Y279	M1-P283
VSIG8	391123	Q5VU13	M1-A130
VSIG8	391123	Q5VU13	M1-R260
VSIR	64115	Q9H7M9	M1-A195

VSIR	64115	Q9H7M9	M1-T192
VSTM1	284415	Q6UX27	M1-T135
VSTM2B	342865	A6NLU5	M1-T263
VSTM4	196740	Q8IW00	M1-L177
VSTM4	196740	Q8IW00	M1-Y180
VTCN1	79679	Q7Z7D3	M1-K246
VTCN1	79679	Q7Z7D3	M1-L260
VTCN1	79679	Q7Z7D3	M1-S259
WBP1	23559	Q96G27	M1-L56
WBP1	23559	Q96G27	R76-P269
WDR11	55717	Q9BZH6	M1-K1126
ZAN	7455	Q9Y493	M1-R2753
ZP1	22917	P60852	M1-P601
ZP2	7783	Q05996	M1-A716
ZP3	7784	P21754	M1-V387
ZP4	57829	Q12836	M1-K505
ZPLD1	131368	Q8TCW7	M1-S372

Table 6. Predicted IgSF interactome

IgSF query symbol	Prey gene symbol	Positive P	Negative P	Non-specific P
ACVR1B	TDGF1	1	0	0
ACVR1B	TDGF1	0.998	0	0.002
ALCAM	CD6	0.998	0	0.002
ALCAM	ALCAM	1	0	0
ALCAM	ALCAM	1	0	0
JAML	FCRL4	0.998	0.002	0
JAML	CXADR	1	0	0
JAML	CD320	0.998	0	0.002
JAML	CLMP	1	0	0
BTLA	PCDHB7	0.986	0	0.014
BTLA	IL10RB	0.98	0.014	0.006
BTLA	TMEFF2	0.986	0.006	0.008
BTLA	MGC39681	0.962	0.006	0.032
BTLA	KIR2DS3	0.984	0.01	0.006
BTLA	CHL1	0.992	0.002	0.006
BTLA	F3	0.988	0.008	0.004
BTLA	CD1D	0.982	0.008	0.01
BTLA	ADGRF5	0.994	0	0.006
BTLA	SLITRK6	0.992	0	0.008
BTLA	SCN1B	0.996	0	0.004
BTLA	BTNL8	0.99	0.004	0.006
BTLA	CD79A	0.99	0.006	0.004

BTLA	TNFSF15	0.992	0.002	0.006
BTLA	TNFRSF4	0.992	0.004	0.004
BTLA	EPHB3	0.998	0	0.002
BTLA	JTB	0.992	0.004	0.004
BTLA	TMEM123	0.996	0	0.004
BTLA	FLRT2	0.858	0	0.142
BTLA	TYRP1	0.992	0.002	0.006
BTLA	TNFSF14	0.99	0.006	0.004
BTN1A1	CD72	0.78	0.002	0.218
BTN2A1	FAM187B	0.998	0	0.002
BTN3A1	LRRC4C	0.964	0.002	0.034
BTN3A1	LRRC4B	1	0	0
BTN3A1	CDH9	0.998	0.002	0
BTN3A1	TGOLN2	0.988	0.01	0.002
BTN3A1	ST14	0.958	0.04	0.002
BTN3A1	VSIG8	1	0	0
BTN3A2	LRRC4B	0.98	0.002	0.018
BTN3A2	CD72	0.89	0.002	0.108
BTN3A3	LRRC4B	1	0	0
VSIR	CD72	0.836	0.002	0.162
VSIR	IGSF11	1	0	0
VSIR	VSIG8	0.966	0.002	0.032
VSIR	SEMA4F	1	0	0
CADM3	LRCH4	1	0	0
CADM3	CADM2	1	0	0
CADM3	IMPG2	1	0	0
CADM3	CADM3	1	0	0
CADM3	CADM4	1	0	0
CADM3	C12orf63	0.992	0.006	0.002
CADM3	PEAR1	0.982	0.006	0.012
CADM3	CADM1	1	0	0
CADM3	IL2RG	0.996	0.004	0
CADM3	CADM2	1	0	0
CADM4	SDK2	0.996	0.004	0
CADM4	CADM2	1	0	0
CADM4	CADM2	1	0	0
CADM4	PRRG4	0.996	0.004	0
CADM4	CADM3	1	0	0
CD14	PLXND1	0.994	0.006	0
CD1B	IL6ST	1	0	0
CD2	NLGN3	0.996	0	0.004
CD2	CD58	1	0	0
CD200	MET	0.992	0.004	0.004

CD200	ESAM	0.986	0.006	0.008
CD200	CD22	0.918	0.008	0.074
CD200	CDON	0.99	0.006	0.004
CD200	TEX29	0.984	0.008	0.008
CD200	PTPRZ1	0.93	0.008	0.062
CD200	CSF3R	0.996	0	0.004
CD200	LYPD6	0.978	0.002	0.02
CD200	MPZL1	0.992	0.004	0.004
CD200	TMEM190	0.996	0	0.004
CD200	EPGN	0.994	0.002	0.004
CD200	GPC1	0.988	0.002	0.01
CD200	IL11RA	0.996	0	0.004
CD200	KIR2DS5	0.978	0.004	0.018
CD200	LRP3	0.992	0.004	0.004
CD200	LRCH4	0.992	0.002	0.006
CD200R1	CD200	1	0	0
CD226	MCAM	0.998	0	0.002
CD226	NECTIN2	1	0	0
CD226	PVR	1	0	0
CD244	CD79B	0.966	0.004	0.03
CD244	CSF3R	0.928	0.006	0.066
CD244	IYD	0.998	0	0.002
CD244	MUC15	0.958	0	0.042
CD274	EPHA3	0.764	0.006	0.23
CD274	PDCD1	1	0	0
CD274	CD80	1	0	0
CD274	PDCD1	1	0	0
CD276	IL20RA	1	0	0
CD28	TMEM95	0.996	0.004	0
CD28	ICOSLG	1	0	0
CD28	CD86	1	0	0
CD28	CD86	1	0	0
CD28	CD80	1	0	0
CD300A	IGSF5	0.998	0	0.002
CD300C	IGSF5	0.998	0	0.002
CD300C	PTPRO	1	0	0
CD300C	NTNG1	0.958	0.006	0.036
CD300LB	LRRC52	1	0	0
CD300LB	FLT1	1	0	0
CD300LF	IGSF5	0.94	0	0.06
CD300LF	FLT1	1	0	0
CD300LG	IYD	0.996	0	0.004
CD300LG	CSF3R	0.994	0.002	0.004

CD300LG	PRRG3	0.986	0.004	0.01
CD300LG	CD69	0.956	0.032	0.012
CD300LG	CD44	0.95	0.038	0.012
CD300LG	SIRPA	0.992	0	0.008
CD300LG	CD22	0.946	0.008	0.046
CD300LG	TREM2	0.988	0.008	0.004
CD300LG	EPHA3	0.788	0	0.212
CD300LG	SEMA6A	0.992	0.004	0.004
CD300LG	CD300LF	0.994	0	0.006
CD300LG	CD79B	0.996	0	0.004
CD300LG	FLRT2	0.804	0.008	0.188
CD300LG	CLEC9A	0.954	0.034	0.012
CD300LG	VLDLR	0.954	0.034	0.012
CD300LG	MUC15	0.994	0	0.006
CD300LG	BMP5	0.956	0.024	0.02
CD300LG	KIR2DS5	0.99	0	0.01
CD300LG	CD300LB	0.978	0.006	0.016
CD300LG	CD300A	0.962	0.006	0.032
CD300LG	ADAM21	0.976	0	0.024
CD300LG	LRPAP1	0.942	0.03	0.028
CD300LG	TIMD4	0.9	0.002	0.098
CD300LG	ILDR2	0.948	0.002	0.05
CD300LG	CDH16	0.99	0.004	0.006
CD300LG	DAG1	0.942	0.026	0.032
CD300LG	DSE	0.948	0.04	0.012
CD300LG	CNTNAP5	0.954	0.034	0.012
CD300LG	TIMD4	0.85	0.024	0.126
CD320	TMEM167A	0.958	0.032	0.01
CD320	SIGLEC7	0.998	0	0.002
CD320	ROR2	1	0	0
CD320	LRPAP1	0.994	0.002	0.004
CD320	IGSF5	0.998	0	0.002
CD320	SIGLEC7	1	0	0
CD33	KIRREL3	0.998	0	0.002
CD3D	CD72	0.776	0.006	0.218
CD3D	CDHR2	0.976	0	0.024
CD40	IL11RA	0.958	0.042	0
CD47	SIRPG	1	0	0
CD47	SIGLEC1	0.992	0.008	0
CD47	SIRPA	1	0	0
CD47	PCSK4	0.99	0.01	0
CD47	SIRPG	1	0	0
CD47	SCN1B	1	0	0

CD5	TNFRSF25	0.998	0.002	0
CD58	CD2	1	0	0
CD59	TNFSF15	0.974	0.004	0.022
CD59	SIGLEC1	1	0	0
CD59	STAB1	0.982	0	0.018
CD6	DAG1	0.99	0.008	0.002
CD6	ALCAM	1	0	0
CD6	ALCAM	1	0	0
CD6	SIGLEC7	0.842	0.014	0.144
CD6	HBEGF	0.98	0.008	0.012
CD6	SIGLEC8	0.968	0.004	0.028
CD7	ADAM15	1	0	0
CD79A	VSIG8	0.986	0	0.014
CD79B	KREMEN1	0.998	0.002	0
CD80	CD274	1	0	0
CD80	CD274	1	0	0
CD80	NGFR	1	0	0
CD80	CD28	1	0	0
CD80	CD28	1	0	0
CD80	CTLA4	1	0	0
CD96	NAALADL1	0.96	0.04	0
CD96	PVR	0.964	0	0.036
CD96	PVR	0.992	0.002	0.006
CEACAM3	CEACAM7	1	0	0
CEACAM3	CEACAM7	1	0	0
CEACAM4	FLT4	0.978	0.01	0.012
CEACAM4	PDCD1LG2	1	0	0
CEACAM4	PDCD1LG2	1	0	0
CEACAM4	FLT4	0.996	0	0.004
CEACAM5	CEACAM3	1	0	0
CEACAM5	CEACAM7	0.962	0.004	0.034
CEACAM5	CEACAM6	1	0	0
CEACAM5	CEACAM7	0.988	0	0.012
CEACAM5	CEACAM8	1	0	0
CEACAM5	CEACAM5	0.998	0	0.002
CEACAM5	CEACAM3	1	0	0
CEACAM5	LRP8	0.994	0.006	0
CEACAM6	UXS1	0.998	0	0.002
CEACAM6	STAB1	1	0	0
CEACAM6	ITGA1	1	0	0
CEACAM6	CEACAM7	1	0	0
CEACAM6	CEACAM5	1	0	0
CEACAM6	CEACAM7	1	0	0

CEACAM6	CEACAM8	1	0	0
CEACAM8	BTN2A2	0.996	0.002	0.002
CEACAM8	TECTB	0.998	0	0.002
CEACAM8	PTPRO	0.98	0	0.02
CHL1	CNTN5	1	0	0
CHL1	L1CAM	0.996	0.004	0
CHL1	TMEM132A	0.996	0.004	0
CHL1	CNTN5	1	0	0
CHL1	L1CAM	0.998	0	0.002
CLEC12B	ADAM21	0.906	0	0.094
CLEC14A	IL20RA	0.95	0	0.05
CLEC14A	AGER	0.994	0.004	0.002
CLEC14A	NCAM1	1	0	0
CLEC14A	NCAM1	1	0	0
CLMP	JAML	0.992	0	0.008
CNTFR	LILRB4	1	0	0
CNTFR	LILRB4	1	0	0
CNTN1	NFASC	0.998	0	0.002
CNTN1	FCGRT	0.944	0.05	0.006
CNTN1	MCAM	0.996	0	0.004
CNTN1	CDH6	0.992	0	0.008
CNTN1	NRCAM	0.998	0	0.002
CNTN1	NFASC	0.998	0	0.002
CNTN1	PCDHB7	0.994	0	0.006
CNTN1	SGCG	0.994	0	0.006
CNTN1	PTPRZ1	0.998	0	0.002
CNTN1	CHL1	0.982	0.002	0.016
CNTN1	NRCAM	0.998	0	0.002
CNTN1	LAMP3	0.79	0.004	0.206
CNTN1	FCGRT	0.978	0.008	0.014
CNTN1	IL23R	0.95	0.036	0.014
CNTN2	NRCAM	1	0	0
CNTN2	KREMEN1	0.998	0.002	0
CNTN2	CNTN2	0.988	0	0.012
CNTN2	NRCAM	1	0	0
CNTN2	CNTN2	1	0	0
CNTN3	PTPRG	1	0	0
CNTN3	APP	1	0	0
CNTN3	APLP1	1	0	0
CNTN4	APP	1	0	0
CNTN4	AQPEP	1	0	0
CNTN4	PTPRG	1	0	0
CNTN4	APLP1	1	0	0

CNTN6	PTPRG	1	0	0
CRTAM	CADM1	1	0	0
CRTAM	DSC3	1	0	0
CRTAM	ADAM21	0.904	0.002	0.094
CRTAM	ILDR2	0.87	0.006	0.124
CRTAM	MUC15	0.996	0	0.004
CRTAM	NTRK3	1	0	0
CSF1R	PRTG	1	0	0
CSF1R	MGC39681	0.978	0.002	0.02
CSF1R	TEK	1	0	0
CTLA4	CD80	1	0	0
CTLA4	CD86	1	0	0
CTLA4	CD86	1	0	0
CTLA4	FAM200A	0.994	0.006	0
CTLA4	WBP1	0.992	0.004	0.004
CTLA4	PCDHGB4	0.992	0.004	0.004
CXADR	JAML	1	0	0
CXADR	KLRAP1	1	0	0
DAG1	SARAF	1	0	0
DLK1	ERBB4	0.998	0.002	0
DLK1	ACVR2B	1	0	0
DSCAM	PTPRT	1	0	0
DSCAM	PTPRT	1	0	0
DSCAM	DSCAM	0.996	0.004	0
DSCAML1	DSCAML1	1	0	0
EDA2R	FCGR3B	1	0	0
EDA2R	TRIL	0.81	0.008	0.182
EDA2R	KIR3DL3	0.968	0.006	0.026
EDA2R	LAMP3	0.938	0	0.062
EDAR	LILRB1	0.996	0.004	0
EDAR	EDA	1	0	0
EDAR	LILRB1	0.998	0	0.002
EFNB1	NAALAD2	1	0	0
EFNB1	TRHDE	0.952	0.048	0
EFNB1	EVC2	1	0	0
EFNB1	DAG1	1	0	0
EFNB1	FAM187B	0.998	0	0.002
EFNB1	DSG4	0.998	0	0.002
EFNB1	SLAMF9	0.996	0.004	0
EFNB1	ITLN1	0.996	0.004	0
EFNB1	AQPEP	1	0	0
EFNB1	EPHA3	0.798	0.002	0.2
EFNB2	EPHB2	1	0	0

EFNB2	KLRAP1	0.988	0.008	0.004
EFNB2	EPHA3	0.956	0	0.044
EFNB2	TCTN2	0.952	0.028	0.02
EFNB2	EPHA8	1	0	0
EFNB2	EPHB4	1	0	0
EFNB2	EPHA4	1	0	0
EFNB2	KIR2DS3	0.982	0.006	0.012
EFNB2	EPHB6	0.998	0	0.002
EFNB2	C19orf38	1	0	0
EFNB2	MGC39681	1	0	0
EFNB2	EPHA10	1	0	0
EFNB2	EPHB3	1	0	0
EFNB2	EPHB1	1	0	0
EFNB3	EPHB4	1	0	0
EFNB3	EPHA4	1	0	0
EFNB3	MGC39681	1	0	0
EFNB3	EPHB2	1	0	0
EFNB3	EPHB6	1	0	0
EFNB3	EPHB1	1	0	0
EFNB3	EPHA10	1	0	0
EFNB3	EPHB3	1	0	0
EFNB3	C19orf38	0.99	0.002	0.008
EFNB3	EPHA3	0.956	0	0.044
EPHB6	FLT1	0.998	0	0.002
EPHB6	EFNB2	1	0	0
EPHB6	EFNB3	1	0	0
EPHB6	EFNB1	1	0	0
ESAM	ROBO3	0.998	0	0.002
F3	ULBP3	1	0	0
FAS	FASLG	1	0	0
FCAR	TNFRSF14	0.992	0	0.008
FCER1A	PEAR1	1	0	0
FCGRT	CD300E	0.998	0	0.002
FCGRT	SHISA4	1	0	0
FCGRT	IGFLR1	0.996	0	0.004
FCRL1	TCTN3	0.996	0.004	0
FCRL1	LRIT1	0.994	0.004	0.002
FCRL1	FLT4	0.994	0.002	0.004
FCRL1	LRFN3	0.996	0.004	0
FCRL1	VSIG8	0.996	0	0.004
FCRL1	TNFSF9	0.996	0.004	0
FCRL1	EFNB2	1	0	0
FCRL1	NT5E	0.998	0	0.002

FCRL1	NETO2	0.998	0	0.002
FGFR1	KL	1	0	0
FGFR2	RAMP1	1	0	0
FGFR3	LRRTM2	0.934	0.006	0.06
FGFR3	IL1RAPL2	1	0	0
FGFR3	KL	1	0	0
FGFR4	GPC3	0.948	0	0.052
FGFR4	GPC6	1	0	0
FGFR4	NRXN3	0.996	0.002	0.002
FGFR4	KL	1	0	0
FGFR4	NRXN2	0.994	0	0.006
FGFR4	GPC4	1	0	0
FGFRL1	GPC6	0.994	0	0.006
FGFRL1	NRXN3	1	0	0
FGFRL1	PLVAP	1	0	0
FGFRL1	NRXN2	0.972	0	0.028
FGFRL1	GPC4	1	0	0
FLT1	GPC4	0.95	0.006	0.044
FLT1	GPC3	0.878	0.002	0.12
FLT1	APP	0.996	0	0.004
FLT1	ELFN1	1	0	0
FLT1	NRP1	1	0	0
FLT3	FLT3LG	1	0	0
FLT4	MUC15	0.974	0.002	0.024
FLT4	KIR2DS5	0.87	0.012	0.118
FLT4	DSG1	0.856	0.022	0.122
FLT4	FLRT2	0.792	0.012	0.196
FLT4	LILRB1	0.978	0	0.022
FLT4	ADAM21	0.874	0.008	0.118
FLT4	NRP2	0.996	0.004	0
FLT4	ILDR2	0.782	0.016	0.202
GP5	LAYN	0.998	0	0.002
ADGRF5	TREML2	0.952	0.006	0.042
HHLA2	KIR3DL3	0.994	0.004	0.002
HHLA2	KIR3DL3	0.996	0.004	0
HHLA2	TMIGD2	1	0	0
ICOSLG	ICOS	1	0	0
IGDCC4	GPC4	0.932	0.01	0.058
IGDCC4	PLB1	0.998	0	0.002
IGSF11	CLEC2L	0.998	0	0.002
IGSF11	EPGN	0.996	0.002	0.002
IGSF11	TMEM190	1	0	0
IGSF11	PCDHB3	1	0	0

IGSF21	ILDR2	0.958	0.002	0.04
IGSF21	MUC15	0.998	0	0.002
IGSF21	IYD	1	0	0
IGSF21	NRXN2	1	0	0
IGSF21	HAVCR1	0.998	0.002	0
IGSF21	CD22	0.922	0.008	0.07
IGSF21	KIR2DS5	0.994	0.002	0.004
IGSF21	HAVCR1	0.994	0.004	0.002
IGSF21	ADAM21	0.834	0.006	0.16
IGSF21	CSF3R	0.932	0.01	0.058
IGSF21	CD79B	0.992	0	0.008
IGSF8	IL17RC	1	0	0
IL18R1	NETO2	1	0	0
IL1RAP	PTPRF	0.996	0.004	0
IL1RAP	PTPRS	0.97	0	0.03
IL1RAPL1	PTPRS	0.996	0	0.004
IL1RAPL1	SIGLEC12	1	0	0
IL1RAPL1	APOO	1	0	0
IL1RAPL1	PTPRG	0.94	0.006	0.054
IL1RAPL1	MILR1	1	0	0
IL1RAPL1	CNTN5	1	0	0
IL1RAPL1	ADAM20	1	0	0
IL1RAPL2	FGFR3	1	0	0
IL1RAPL2	PTPRS	0.996	0	0.004
IL1RAPL2	CNTN5	1	0	0
IL1RAPL2	APOO	1	0	0
IL1RAPL2	MILR1	0.998	0	0.002
IL1RAPL2	ADAM20	1	0	0
IL1RAPL2	FGFR3	0.994	0.004	0.002
IL1RL1	AXL	1	0	0
IL1RL1	AXL	1	0	0
IL1RL1	EDA	0.966	0.002	0.032
IL20RA	LYPD6	1	0	0
IL20RA	PCDHAC1	1	0	0
IL6R	BTNL9	0.992	0.004	0.004
IL6R	LRTM2	1	0	0
IL6R	SIGLEC5	0.96	0	0.04
IL6ST	IL11RA	1	0	0
ILDR1	KIAA0319L	1	0	0
ILDR1	CR2	1	0	0
ILDR1	LILRB1	0.994	0.004	0.002
ILDR1	TRIL	0.994	0	0.006
ILDR1	LILRB1	1	0	0

KIR2DL5A	VSIG4	1	0	0
KIR2DL5A	LEPR	1	0	0
KIR2DL5A	PVR	0.996	0	0.004
KIR2DL5A	TMEM167A	1	0	0
KIR3DL3	HHLA2	1	0	0
KIR3DL3	HHLA2	1	0	0
KIRREL	CORIN	0.992	0.004	0.004
KIRREL	KIRREL	1	0	0
KIRREL	KIRREL	1	0	0
KIRREL	CDHR2	0.964	0	0.036
KIT	KITLG	1	0	0
L1CAM	L1CAM	0.994	0.004	0.002
L1CAM	CHL1	1	0	0
L1CAM	L1CAM	0.998	0	0.002
L1CAM	AQPEP	0.998	0.002	0
LILRA1	NETO2	0.984	0	0.016
LILRA1	LILRA1	0.964	0.006	0.03
LILRA1	CD300E	0.842	0.008	0.15
LILRA1	KIR3DL2	0.864	0.008	0.128
LILRA1	KIR3DL2	0.982	0	0.018
LILRA3	IGSF9B	0.996	0.004	0
LILRA3	NETO2	0.996	0	0.004
LILRA3	IGSF9B	0.97	0.002	0.028
LILRA5	LILRB1	0.998	0.002	0
LILRA5	IZUMO1	1	0	0
LILRA6	LCTL	1	0	0
LILRA6	CD300E	0.912	0	0.088
LILRB1	IL6R	1	0	0
LILRB1	ILDR1	1	0	0
LILRB1	LILRA5	0.998	0.002	0
LILRB1	LILRA5	1	0	0
LILRB5	LDLR	1	0	0
LRFN4	PTPRS	0.992	0	0.008
LRFN5	TNFRSF14	1	0	0
LRFN5	TNFRSF14	1	0	0
LRFN5	PTPRF	0.958	0.004	0.038
LRFN5	PTPRS	0.992	0	0.008
LRRC4	PRSS55	1	0	0
LRRC4	LRRN1	1	0	0
LRRC4	NETO2	0.952	0.008	0.04
LRRC4B	BTN3A3	1	0	0
LRRC4B	PTPRS	0.838	0.006	0.156
LRRC4B	PTPRF	1	0	0

LRRC4C	TMEM53	0.992	0.006	0.002
LRRC4C	LRRTM4	0.994	0.004	0.002
LRRC4C	CORIN	0.996	0.004	0
LRRC4C	SIGLEC7	0.756	0.014	0.23
LRRC4C	LRRN1	1	0	0
LRRC4C	LDLR	0.998	0	0.002
LRRC4C	SIGLEC7	0.998	0	0.002
LRRC4C	NTNG1	1	0	0
LRRN1	LRRC4C	1	0	0
LRRN1	LRRC4	1	0	0
LRRN1	LRRC4C	0.996	0.004	0
LRRN1	LRRC4	1	0	0
LRRN3	KITLG	1	0	0
LY6G6F	LILRB3	0.996	0.004	0
LY6G6F	LILRA6	0.996	0.004	0
LY6G6F	CSF1R	0.994	0.004	0.002
LY6G6F	LILRA6	0.996	0.002	0.002
LY6G6F	DDR1	1	0	0
LY6G6F	LILRA5	0.974	0.004	0.022
LY6G6F	ROBO3	1	0	0
LY6G6F	LILRA5	0.998	0.002	0
LY6G6F	LAYN	0.978	0.002	0.02
MADCAM1	SIGLEC7	0.998	0	0.002
MADCAM1	SIGLEC7	0.998	0	0.002
MCAM	TMEM132A	0.976	0.002	0.022
MCAM	CNTN1	0.998	0	0.002
MCAM	FGFR4	1	0	0
MDGA1	NLGN4X	1	0	0
MDGA1	NLGN3	0.968	0	0.032
MERTK	IGSF5	0.998	0	0.002
MFAP3L	PI16	1	0	0
MICA	PCDHAC1	0.878	0.004	0.118
MOG	KIR2DL4	0.994	0	0.006
MOG	LRRTM3	0.996	0	0.004
MOG	LRRTM2	1	0	0
MOG	HBEGF	0.938	0.022	0.04
MOG	LRRTM3	0.992	0.004	0.004
MOG	LRIG1	0.998	0	0.002
MOG	GLG1	0.952	0.01	0.038
MOG	LRIG1	0.978	0.004	0.018
MOG	APCDD1	0.994	0	0.006
MOG	TRIL	1	0	0
MOG	KIR2DL4	0.988	0	0.012

MOG	IL20RA	0.926	0.002	0.072
MOG	NRG2	0.998	0	0.002
MOG	CD4	0.996	0	0.004
MOG	VSTM4	0.984	0.006	0.01
MPZL2	MPZL3	1	0	0
MPZL3	MPZL2	1	0	0
MPZL3	KIAA0319L	0.874	0.008	0.118
MUSK	DLL1	1	0	0
MUSK	PTPRO	1	0	0
MXRA5	CD69	1	0	0
MXRA8	JAM3	1	0	0
NCAM1	NCAM1	1	0	0
NCAM1	PTPRS	0.994	0	0.006
NCAM1	CLEC14A	0.994	0.004	0.002
NCAM1	NCAM1	1	0	0
NCAM1	NPTN	0.996	0.004	0
NCAM1	CLEC2L	1	0	0
NCAM1	ISLR2	1	0	0
NCAM2	NCAM2	0.998	0	0.002
NCAM2	CDH13	0.998	0	0.002
NCR1	CD4	1	0	0
NEGR1	IGSF9B	0.996	0.004	0
NEGR1	TNFRSF17	0.996	0	0.004
NEGR1	NEGR1	0.998	0	0.002
NEGR1	KIR2DS3	1	0	0
NEGR1	OPCML	0.958	0.042	0
NEGR1	LSAMP	1	0	0
NEGR1	NTM	0.994	0.004	0.002
NEO1	HFE2	1	0	0
NEO1	RGMA	1	0	0
NFASC	LINGO4	1	0	0
NFASC	NRCAM	1	0	0
NFASC	NRCAM	1	0	0
NGFR	LRRTM3	0.998	0	0.002
NGFR	CD80	1	0	0
NGFR	LRRTM3	1	0	0
NRCAM	CNTN2	1	0	0
NRCAM	CNTN1	1	0	0
NRCAM	LCTL	1	0	0
NRCAM	NFASC	0.998	0	0.002
NRCAM	NFASC	0.978	0	0.022
NRCAM	CNTN2	1	0	0
NRP2	SLITRK3	0.994	0	0.006

NRP2	LRRTM3	0.992	0.002	0.006
NRP2	KIR3DL1	0.982	0.002	0.016
NRP2	LILRA1	0.96	0.022	0.018
NRP2	NFASC	0.978	0.002	0.02
NRP2	NRG2	0.93	0.03	0.04
NRP2	LRPAP1	0.98	0.006	0.014
NRP2	SIGLEC7	0.93	0.002	0.068
NRP2	LAMP3	0.958	0	0.042
NRP2	SIGLEC5	0.948	0	0.052
NRP2	FLRT3	0.934	0.024	0.042
NRP2	FCRL6	0.994	0	0.006
NRP2	FCRL2	0.762	0.02	0.218
NRP2	TRIL	0.988	0	0.012
NRP2	SIGLEC12	0.962	0.02	0.018
NRP2	THY1	0.994	0	0.006
NRP2	ADAM9	0.99	0.004	0.006
NRP2	NFASC	0.994	0	0.006
NRP2	SIRPD	0.992	0.002	0.006
NRP2	GP5	0.992	0.002	0.006
NRP2	KIR3DL2	0.992	0.002	0.006
NRP2	KIR3DL2	0.992	0.002	0.006
NRP2	FLT4	0.948	0.038	0.014
NRP2	FCRL6	0.952	0.034	0.014
NRP2	PMEL	0.92	0.038	0.042
NRP2	FCGR3B	0.986	0	0.014
NTM	VSIG8	0.996	0	0.004
NTM	AMIGO2	1	0	0
NTM	THSD7A	0.998	0.002	0
NTM	LRRC4C	0.998	0	0.002
NTM	CD79B	1	0	0
NTM	STAB1	1	0	0
NTM	LRRN3	1	0	0
NTM	TNFRSF17	1	0	0
NTM	ICOSLG	1	0	0
NTRK1	AQPEP	0.992	0.002	0.006
NTRK1	LTK	0.944	0.034	0.022
NTRK1	CEACAM19	0.986	0.006	0.008
NTRK1	ADAM11	0.984	0	0.016
NTRK1	PTPRG	0.998	0	0.002
NTRK1	PRRG3	0.992	0	0.008
NTRK1	CXorf61	0.984	0.006	0.01
NTRK1	TNFRSF17	0.836	0.016	0.148
NTRK1	SEMA4G	0.91	0.01	0.08

NTRK1	CNTN5	0.994	0	0.006
NTRK2	KIR2DS5	0.938	0.026	0.036
NTRK2	LILRA6	0.884	0.03	0.086
NTRK2	LMLN	0.91	0.032	0.058
NTRK2	LY6G6F	0.944	0.032	0.024
NTRK2	EPHB2	0.902	0.006	0.092
NTRK2	INSR	0.944	0.038	0.018
NTRK2	CD8A	0.906	0.008	0.086
NTRK2	LY6G6F	0.926	0.024	0.05
NTRK2	PCDHB5	0.894	0.032	0.074
NTRK2	KLRC1	0.944	0.034	0.022
NTRK2	PCDHGA11	0.99	0.002	0.008
NTRK2	NCR3	0.944	0.034	0.022
NTRK2	KIRREL3	0.976	0.004	0.02
NTRK2	GPA33	0.954	0.024	0.022
NTRK2	SLAMF9	0.924	0.03	0.046
NTRK2	TNFSF15	0.956	0.022	0.022
NTRK2	CD274	0.936	0.026	0.038
NTRK2	SEMA4G	0.884	0.03	0.086
NTRK3	PTPRS	0.996	0	0.004
OPCML	LSAMP	1	0	0
OPCML	NTM	0.994	0.004	0.002
OPCML	OPCML	1	0	0
OPCML	NEGR1	1	0	0
OPCML	OPCML	0.956	0.042	0.002
PCDHGB6	PLXDC1	0.996	0.004	0
PCDHGB6	IL4R	1	0	0
PCDHGB6	FCAMR	0.894	0.006	0.1
PDCD1	PDCD1LG2	1	0	0
PDCD1	FCGR2A	0.984	0.004	0.012
PDCD1	CD48	0.992	0.006	0.002
PDCD1	CD274	1	0	0
PDCD1	CD274	1	0	0
PDCD1	CD274	1	0	0
PDCD1	PDCD1LG2	1	0	0
PDCD1LG2	PDCD1	1	0	0
PDCD1LG2	PDCD1	1	0	0
PDCD1LG2	CEACAM4	1	0	0
PDCD1LG2	TNFRSF11A	1	0	0
PECAM1	PECAM1	0.96	0.04	0
PECAM1	PECAM1	0.998	0	0.002
PIGR	CD8A	0.924	0.002	0.074
PIGR	AGER	0.764	0.03	0.206

PIGR	IL10RA	0.91	0.032	0.058
PIGR	CDH7	0.994	0	0.006
PIGR	KIRREL3	0.914	0.026	0.06
PIGR	DSG4	0.876	0.026	0.098
PIGR	TREML4	0.994	0.002	0.004
PIGR	SUSD2	0.954	0.032	0.014
PIGR	THY1	0.908	0.034	0.058
PIGR	EPHB2	0.816	0.032	0.152
PIGR	GPA33	0.954	0.024	0.022
PIGR	LY6G6F	0.946	0.03	0.024
PIGR	HFE	0.95	0.036	0.014
PIGR	TNFRSF1B	0.982	0.004	0.014
PIGR	PCDHGC4	0.946	0.026	0.028
PIGR	PCDHGA11	0.938	0.026	0.036
PIGR	PDCD1LG2	0.954	0.006	0.04
PIGR	LILRA6	0.908	0.026	0.066
PILRB	EPHA10	0.992	0	0.008
PILRB	EPHA7	0.998	0.002	0
PLXNB2	SEMA4D	1	0	0
PLXNB2	SEMA4B	1	0	0
PLXNB2	SEMA4A	1	0	0
PLXNB2	SEMA4B	1	0	0
PLXNB2	SEMA4A	1	0	0
PLXNB2	SEMA4C	1	0	0
PLXNB2	SEMA4G	0.994	0.004	0.002
PLXNB2	SEMA4C	1	0	0
PLXNB2	SEMA4G	1	0	0
PLXNB2	SEMA4D	0.994	0.004	0.002
PRLR	NCR2	1	0	0
PRLR	NCR2	0.998	0	0.002
PRLR	KIAA0090	0.982	0.006	0.012
PRLR	CADM3	0.954	0.006	0.04
PRLR	IMPG2	0.952	0.002	0.046
PTGFRN	IGSF3	1	0	0
PTGFRN	TMEM59L	0.996	0.002	0.002
PTGFRN	SGCG	0.984	0.002	0.014
PTGFRN	CDH6	0.932	0.004	0.064
PTPRD	NTRK3	0.988	0.004	0.008
PTPRD	IL1RAPL2	0.994	0	0.006
PTPRD	IL1RAPL1	0.994	0	0.006
PTPRD	RARRES1	0.994	0	0.006
PTPRD	KIRREL3	0.938	0.024	0.038
PTPRD	KIAA0090	0.988	0.006	0.006

PTPRD	IMPG2	0.994	0	0.006
PTPRD	BTN1A1	0.988	0.006	0.006
PTPRD	RAMP1	0.992	0.002	0.006
PTPRD	SLITRK2	0.936	0.05	0.014
PTPRD	CD8A	0.876	0.026	0.098
PTPRD	LRP12	0.878	0.032	0.09
PTPRD	NTRK1	0.984	0.01	0.006
PTPRD	LRFN4	0.992	0.002	0.006
PTPRD	LRFN5	0.992	0.002	0.006
PTPRD	CDH4	0.91	0.03	0.06
PTPRD	LMLN	0.848	0.04	0.112
PTPRD	CNTN2	0.994	0	0.006
PTPRD	SLITRK3	0.994	0	0.006
PTPRD	CADM3	0.994	0	0.006
PTPRD	NOTCH2	0.988	0.006	0.006
PTPRD	DSG4	0.856	0.024	0.12
PTPRD	LRFN1	0.992	0.002	0.006
PTPRD	LRRC4B	0.988	0	0.012
PTPRD	IL1RAP	0.994	0	0.006
PTPRD	IGFLR1	0.994	0	0.006
PTPRD	DDR2	0.994	0	0.006
PTPRD	NTRK3	0.958	0.022	0.02
PTPRD	IL1RAP	0.992	0.002	0.006
PTPRD	SLITRK1	0.994	0	0.006
PTPRD	CUZD1	0.99	0.004	0.006
PTPRD	SLITRK6	0.994	0	0.006
PTPRM	PTPRM	0.996	0.002	0.002
PTPRS	NTRK3	1	0	0
PTPRS	LRFN4	1	0	0
PTPRS	SLITRK4	0.992	0.004	0.004
PTPRS	LRFN5	0.998	0	0.002
PTPRS	IL1RAP	1	0	0
PTPRS	SLITRK3	1	0	0
PTPRS	IL1RAPL1	1	0	0
PTPRS	IL1RAPL2	1	0	0
PTPRS	IL1RAP	1	0	0
PTPRS	SLITRK2	0.996	0.004	0
PTPRS	LRFN1	0.992	0.002	0.006
PTPRS	SLITRK1	0.996	0	0.004
PTPRS	SLITRK6	1	0	0
PTPRS	LRFN5	0.996	0	0.004
PTPRS	NTRK3	1	0	0
PTPRT	PTPRT	1	0	0

PTPRT	PTPRT	0.996	0.004	0
PVR	TIGIT	1	0	0
PVR	KIR2DL5A	0.994	0.004	0.002
PVR	TIGIT	1	0	0
PVR	NECTIN3	1	0	0
NECTIN2	CD226	1	0	0
NECTIN2	NECTIN4	1	0	0
NECTIN2	TIGIT	1	0	0
NECTIN2	TIGIT	1	0	0
NECTIN2	NECTIN3	1	0	0
NECTIN2	NECTIN2	1	0	0
NECTIN3	PVR	1	0	0
NECTIN3	CD34	0.994	0.004	0.002
NECTIN3	NECTIN1	1	0	0
NECTIN3	NECTIN2	1	0	0
NECTIN3	TIGIT	1	0	0
NECTIN3	TIGIT	1	0	0
NECTIN3	GUCY2D	0.998	0	0.002
NECTIN3	PVR	1	0	0
NECTIN4	NECTIN1	1	0	0
NECTIN4	GUCY2D	0.998	0	0.002
NECTIN4	TIGIT	1	0	0
NECTIN4	TIGIT	1	0	0
NECTIN4	CD34	0.994	0.004	0.002
NECTIN4	PVR	0.958	0.002	0.04
ROBO3	LY6G6F	0.996	0.004	0
ROBO3	LY6G6F	1	0	0
SEMA4A	PLXNB2	0.998	0	0.002
SEMA4A	PLXNB1	1	0	0
SEMA4B	PLXNB2	1	0	0
SEMA4B	PLXNB1	1	0	0
SEMA4C	PLXNB2	1	0	0
SEMA4C	PLXNB1	0.996	0	0.004
SEMA4D	PLXNB3	1	0	0
SEMA4D	PLXNB2	1	0	0
SEMA4D	PLXNB1	1	0	0
SEMA4G	PLXNB1	0.992	0	0.008
SEMA4G	PLXNB3	1	0	0
SEMA4G	PLXNB2	0.992	0	0.008
SEMA6A	PLXNA4	1	0	0
SEMA7A	PLXNC1	1	0	0
SIGLEC10	PTPRM	1	0	0
SIGLEC10	PTPRM	1	0	0

SIGLEC15	UNC5D	0.996	0.004	0
SIGLEC15	LRRC4C	0.934	0	0.066
SIGLEC15	LRRC4C	0.924	0.004	0.072
SIGLEC15	UNC5D	1	0	0
SIGLEC15	FGFR4	0.994	0.002	0.004
SIGLEC6	CD4	0.998	0	0.002
SIGLEC6	NCR1	0.998	0	0.002
SIGLEC6	NCR1	1	0	0
SIGLEC6	CA12	1	0	0
SIGLEC6	KIR2DL4	1	0	0
SIGLEC6	KIR2DL4	0.994	0.004	0.002
SIGLEC7	TIMD4	1	0	0
SIGLEC7	PTPRO	1	0	0
SIGLEC7	NCR1	0.904	0.008	0.088
SIGLEC7	TIMD4	0.996	0	0.004
SIGLEC7	NCR1	0.98	0	0.02
SIGLEC7	LRP12	1	0	0
SIGLEC7	PCDHAC1	0.848	0.012	0.14
SIGLEC7	LRRC4C	0.878	0.006	0.116
SIGLEC7	MXRA5	0.988	0.004	0.008
SIGLEC8	NRXN2	0.96	0.002	0.038
SIGLEC8	IL4R	0.996	0.002	0.002
SIGLEC8	NCR1	0.994	0	0.006
SIGLEC8	TREML4	1	0	0
SIGLEC8	SIGLEC8	0.962	0.006	0.032
SIGLEC8	LRFN2	0.99	0.004	0.006
SIGLEC8	PTPRO	0.97	0.002	0.028
SIGLEC8	NCR1	0.994	0	0.006
SIGLEC8	PCDHGA7	0.984	0.008	0.008
SIGLEC8	NTNG1	0.998	0	0.002
SIGLEC8	TEX101	0.994	0	0.006
SIGLEC8	KIAA0319L	0.996	0	0.004
SIGLEC8	LRRC4C	0.994	0	0.006
SIRPA	TPSG1	0.998	0.002	0
SIRPA	LRPAP1	0.998	0.002	0
SIRPA	CD69	0.996	0.002	0.002
SIRPA	TIGIT	0.81	0.012	0.178
SIRPA	CD47	1	0	0
SIRPA	CHL1	1	0	0
SIRPG	CD47	1	0	0
SLAMF6	SLAMF6	1	0	0
SLAMF7	SLAMF7	0.998	0	0.002
SLITRK1	ENPEP	0.952	0.048	0

SLITRK1	PTPRS	0.942	0	0.058
TIE1	LRFN5	1	0	0
TIE1	NTRK1	1	0	0
TIGIT	NECTIN3	0.998	0	0.002
TIGIT	PVR	1	0	0
TIGIT	RECK	1	0	0
TIGIT	ACE2	0.998	0	0.002
TIGIT	PVR	1	0	0
TMEM123	LRRN2	1	0	0
TMIGD2	HHLA2	1	0	0
TMIGD2	HHLA2	1	0	0
TNFRSF11A	ACE2	1	0	0
TNFRSF11A	MYEOV	0.96	0.04	0
TNFRSF11B	PCDHAC1	1	0	0
TNFRSF11B	GPC1	0.992	0.004	0.004
TNFRSF11B	ACE2	1	0	0
TNFRSF11B	GPC3	1	0	0
TNFRSF11B	C14orf37	0.984	0.01	0.006
TNFRSF11B	NRP1	0.992	0.002	0.006
TNFRSF11B	GPC4	0.996	0	0.004
TNFRSF11B	IL7R	0.998	0	0.002
TNFRSF11B	GPC6	0.996	0	0.004
TNFRSF11B	SLITRK1	0.996	0	0.004
TNFRSF11B	NRXN2	0.994	0	0.006
TNFRSF11B	NRXN3	0.996	0.002	0.002
TNFRSF11B	EGF	0.978	0.014	0.008
TNFRSF17	CD300E	1	0	0
TNFRSF17	LY9	1	0	0
TNFRSF18	TNFSF18	0.996	0.004	0
TNFRSF21	PI16	1	0	0
TNFRSF25	PRNP	1	0	0
TNFRSF8	TNFSF8	1	0	0
TNFRSF9	TNFSF9	0.996	0.004	0
TREM2	FCRL2	0.762	0.014	0.224
TREM2	GFRA1	0.97	0.004	0.026
TREM2	FLT1	1	0	0
TREM2	LRRC52	1	0	0
TREML1	KIR3DL1	0.994	0.002	0.004
TREML2	ANTXR1	0.996	0.004	0
UNC5A	FLRT3	1	0	0
UNC5A	LRRC4C	0.906	0.016	0.078
UNC5A	FLRT2	1	0	0
UNC5A	CDHR2	0.898	0.002	0.1

UNC5A	FLRT1	1	0	0
UNC5A	KIAA0319L	0.998	0	0.002
UNC5B	FLRT3	0.998	0	0.002
UNC5B	NOTCH4	0.998	0	0.002
UNC5B	GLG1	0.96	0.004	0.036
UNC5B	FLRT1	0.982	0	0.018
UNC5B	FLRT2	0.982	0	0.018
UNC5C	FLRT1	1	0	0
UNC5C	FLRT3	1	0	0
UNC5C	FLRT2	0.8	0.006	0.194
UNC5C	GPC3	1	0	0
UNC5D	SEMA7A	0.958	0.032	0.01
UNC5D	GPC3	1	0	0
UNC5D	FLRT1	1	0	0
UNC5D	SELL	0.906	0.006	0.088
UNC5D	FLRT2	1	0	0
UNC5D	FLRT3	1	0	0
UNC5D	LRRC4B	0.856	0.038	0.106
VSIG10	IL6ST	0.954	0.004	0.042
VSIG10L	GPC3	1	0	0
VSIG10L	AXL	1	0	0
VSIG10L	AXL	1	0	0
VSIG8	HHLA2	0.982	0.002	0.016
VSIG8	KIR3DL1	0.944	0.006	0.05
VSIG8	TREM1	0.996	0	0.004
VSIG8	CEACAM20	0.994	0.004	0.002
VSIG8	TRIL	0.818	0.008	0.174
VSIG8	FCAR	0.996	0.004	0
VSIG8	AQPEP	0.998	0.002	0
VSTM2B	ACPT	0.996	0.004	0
VSTM2B	NRXN2	1	0	0
VSTM2B	NRXN1	1	0	0
VSTM2B	TREM1	0.986	0.002	0.012
VSTM2B	HHLA2	0.986	0.002	0.012

Table 7. Tagged STM library for PDPN experiment

Prey short name	Prey Entrez ID
1110032F04RIK	68725
A1BG	1
ACE	1636
ACE2	59272
ACPP	55

ACPT	93650
ACVR1	90
ACVR1B	91
ACVR1C	130399
ACVR2A	92
ACVR2B	93
ACVRL1	94
ADAM10	102
ADAM11	4185
ADAM12	8038
ADAM15	8751
ADAM17	6868
ADAM18	8749
ADAM19	8728
ADAM2	2515
ADAM20	8748
ADAM21	8747
ADAM22	53616
ADAM23	8745
ADAM28	10863
ADAM29	11086
ADAM30	11085
ADAM32	203102
ADAM33	80332
ADAM7	8756
ADAM8	101
ADAM9	8754
AGER	177
AJAP1	55966
ALCAM	214
ALK	238
ALPI	248
ALPL	249
ALPP	250
AMHR2	269
AMICA1	120425
AMIGO1	57463
AMIGO2	347902
AMIGO3	386724
AMN	81693
ANTXR1	84168
ANTXR2	118429
APCDD1	147495

APCDD1L	164284
APLP1	333
APLP2	334
APOO	79135
APP	351
AREG	374
ART1	417
ART3	419
ART4	420
ATRAID	51374
ATRN	8455
ATRNL1	26033
AXL	558
AZGP1	563
BACE1	23621
BACE2	25825
BAMBI	25805
BCAM	4059
BCAN	63827
BMPR1A	657
BMPR1B	658
BMPR2	659
BOC	91653
BSG	682
BST1	683
BST2	684
BTC	685
BTLA	151888
BTN1A1	696
BTN2A1	11120
BTN2A2	10385
BTN2A3P	54718
BTN3A1	11119
BTN3A2	11118
BTN3A3	10384
BTNL2	56244
BTNL3	10917
BTNL8	79908
BTNL9	153579
BUTR1	100129094
C10orf26	54838
C10orf35	219738
C10orf54	64115

C11orf24	53838
C11orf87	399947
C11orf92	399948
C12orf53	196500
C12orf59	120939
C14orf132	100132684
C14orf180	400258
C14orf37	145407
C15orf24	56851
C16orf54	728070
C16orf91	283951
C16orf92	146378
C17orf80	55028
C18orf1	753
C19orf18	147685
C19orf24	55009
C19orf38	255809
C19orf63	284361
C19orf75	284369
C1orf101	257044
C1orf130	400746
C1orf159	54991
C1orf85	112770
C2orf82	389084
C2orf89	129293
C3orf18	51161
C3orf35	339883
C3orf45	132228
C4orf32	132720
C4orf34	201895
C5orf15	56951
C6orf25	80739
C6orf72	116254
C9orf11	54586
CA12	771
CA14	23632
CA4	762
CA9	768
CACHD1	57685
CACNA2D3	55799
CACNA2D4	93589
CADM1	23705
CADM2	253559

CADM3	57863
CADM4	199731
CATSPERD	257062
CATSPERG	57828
CAV3	859
CCDC107	203260
CCDC47	57003
CD101	9398
CD109	135228
CD14	929
CD160	11126
CD163	9332
CD164	8763
CD164L2	388611
CD177	57126
CD180	4064
CD19	930
CD1A	909
CD1B	910
CD1C	911
CD1D	912
CD1E	913
CD2	914
CD200	4345
CD200R1	131450
CD200R1L	344807
CD22	933
CD226	10666
CD24	100133941
CD244	51744
CD247	919
CD248	57124
CD27	939
CD274	29126
CD276	80381
CD28	940
CD300A	11314
CD300C	10871
CD300E	342510
CD300LB	124599
CD300LD	100131439
CD300LF	146722
CD300LG	146894

CD302	9936
CD320	51293
CD33	945
CD34	947
CD3D	915
CD3E	916
CD3G	917
CD4	920
CD40	958
CD44	960
CD46	4179
CD47	961
CD48	962
CD5	921
CD52	1043
CD55	1604
CD58	965
CD6	923
CD68	968
CD7	924
CD79A	973
CD79B	974
CD80	941
CD83	9308
CD84	8832
CD86	942
CD8A	925
CD8B	926
CD93	22918
CD96	10225
CD99	4267
CD99L2	83692
CDCP1	64866
CDH1	999
CDH10	1008
CDH11	1009
CDH12	1010
CDH13	1012
CDH15	1013
CDH16	1014
CDH17	1015
CDH18	1016
CDH19	28513

CDH2	1000
CDH20	28316
CDH22	64405
CDH24	64403
CDH26	60437
CDH3	1001
CDH4	1002
CDH5	1003
CDH6	1004
CDH7	1005
CDH8	1006
CDH9	1007
CDHR3	222256
CDHR5	53841
CDON	50937
CEACAM1	634
CEACAM16	388551
CEACAM18	729767
CEACAM19	56971
CEACAM20	125931
CEACAM21	90273
CEACAM3	1084
CEACAM4	1089
CEACAM5	1048
CEACAM6	4680
CEACAM7	1087
CEACAM8	1088
CHL1	10752
CHODL	140578
CILP	8483
CILP2	148113
CLCA2	9635
CLCA4	22802
CLEC14A	161198
CLMP	79827
CLSTN1	22883
CLSTN2	64084
CLSTN3	9746
CNTFR	1271
CNTN1	1272
CNTN2	6900
CNTN3	5067
CNTN4	152330

CNTN5	53942
CNTN6	27255
CNTNAP1	8506
CNTNAP2	26047
CNTNAP3	79937
CNTNAP4	85445
CNTNAP5	129684
CPM	1368
CR1	1378
CR2	1380
CRB1	23418
CRB2	286204
CRB3	92359
CRIM1	51232
CRLF1	9244
CRLF2	64109
CRTAM	56253
CSF1	1435
CSF1R	1436
CSF2RA	1438
CSF2RB	1439
CSF3R	1441
CSPG4	1464
CSPG5	10675
CTLA4	1493
CUZD1	50624
CX3CL1	6376
CXADR	1525
CXCL16	58191
CXorf68	100132963
CYYR1	116159
DAG1	1605
DCBLD1	285761
DCBLD2	131566
DCC	1630
DDOST	1650
DDR1	780
DDR2	4921
DGCR2	9993
DLK1	8788
DLK2	65989
DLL1	28514
DLL3	10683

DLL4	54567
DNER	92737
DPCR1	135656
DPEP1	1800
DPEP2	64174
DPEP3	64180
DSC1	1823
DSC2	1824
DSC3	1825
DSCAM	1826
DSCAML1	57453
DSG1	1828
DSG2	1829
DSG3	1830
DSG4	147409
DTPQ5903	147645
ECSM2	641700
EDA2R	60401
EDAR	10913
EFNA3	1944
EFNA5	1946
EFNB1	1947
EFNB2	1948
EFNB3	1949
EGF	1950
EGFR	1956
ELFN1	392617
ELFN2	114794
EMB	133418
EMCN	51705
ENG	2022
ENPP5	59084
EPCAM	4072
EPGN	255324
EPHA1	2041
EPHA10	284656
EPHA2	1969
EPHA3	2042
EPHA4	2043
EPHA5	2044
EPHA6	285220
EPHA7	2045
EPHA8	2046

EPHB1	2047
EPHB2	2048
EPHB3	2049
EPHB4	2050
EPHB6	2051
EPOR	2057
ERBB2	2064
ERBB3	2065
ERBB4	2066
EREG	2069
ERMAP	114625
ERN2	10595
ESAM	90952
EVA1C	59271
EVC2	132884
EVI2A	2123
EVI2B	2124
F11R	50848
F3	2152
FAIM3	9214
FAM171A1	221061
FAM171B	165215
FAM174A	345757
FAM174B	400451
FAM187A	66784
FAM187B	148109
FAM189A2	9413
FAM200A	221786
FAM209A	200232
FAM209B	388799
FAS	355
FCAMR	83953
FCAR	2204
FCER1A	2205
FCGR1A	2209
FCGR1B	2210
FCGR1C	100132417
FCGR2A	2212
FCGR2B	2213
FCGR2C	9103
FCGR3A	2214
FCGR3B	2215
FCGRT	2217

FCRL1	115350
FCRL2	79368
FCRL3	115352
FCRL4	83417
FCRL5	83416
FCRL6	343413
FCRLA	84824
FCRLB	127943
FGFR1	2260
FGFR2	2263
FGFR3	2261
FGFR4	2264
FGFRL1	53834
FLRT1	23769
FLRT2	23768
FLRT3	23767
FLT1	2321
FLT3	2322
FLT3LG	2323
FLT4	2324
FNDC3A	22862
FNDC4	64838
FNDC9	408263
FOLR1	2348
FOLR2	2350
FRRS1L	23732
FSTL4	23105
FSTL5	56884
FURIN	5045
FXYD5	53827
GAS1	2619
GFRA1	2674
GFRA2	2675
GFRA3	2676
GFRA4	64096
GFRAL	389400
GHR	2690
GLG1	2734
GLIPR1	11010
GLIPR1L2	144321
GML	2765
GP1BA	2811
GP1BB	2812

GP2	2813
GP5	2814
GP6	51206
GP9	2815
GPA33	10223
GPC1	2817
GPC2	221914
GPC3	2719
GPC4	2239
GPC6	10082
GPIHBP1	338328
GPNMB	10457
GPR116	221395
GPR124	25960
GPR125	166647
GUCY2C	2984
GUCY2D	3000
GUCY2F	2986
GYPA	2993
GYPB	2994
GYPC	2995
GYPE	2996
HAPLN2	60484
HAPLN3	145864
HAPLN4	404037
HAVCR1	26762
HAVCR2	84868
HBEGF	1839
HCST	10870
HEG1	57493
HEPACAM	220296
HEPACAM2	253012
HEPH	9843
HEPHL1	341208
HFE	3077
HFE2	148738
HHLA2	11148
HYAL2	8692
ICAM1	3383
ICAM2	3384
ICAM3	3385
ICAM4	3386
ICAM5	7087

ICOS	29851
ICOSLG	23308
IFNAR1	3454
IFNAR2	3455
IFNGR1	3459
IFNGR2	3460
IFNLR1	163702
IGDCC3	9543
IGDCC4	57722
IGF1R	3480
IGF2R	3482
IGFBP7	3490
IGFBPL1	347252
IGFLR1	79713
IGLON5	402665
IGSF1	3547
IGSF11	152404
IGSF21	84966
IGSF3	3321
IGSF5	150084
IGSF6	10261
IGSF8	93185
IGSF9	57549
IGSF9B	22997
IL10RA	3587
IL10RB	3588
IL11RA	3590
IL12B	3593
IL12RB1	3594
IL12RB2	3595
IL13RA1	3597
IL13RA2	3598
IL15RA	3601
IL17RA	23765
IL17RB	55540
IL17RC	84818
IL17RD	54756
IL17RE	132014
IL18BP	10068
IL18R1	8809
IL18RAP	8807
IL1R1	3554
IL1R2	7850

IL1RAP	3556
IL1RAPL1	11141
IL1RAPL2	26280
IL1RL1	9173
IL1RL2	8808
IL20RA	53832
IL20RB	53833
IL21R	50615
IL22RA1	58985
IL23R	149233
IL27RA	9466
IL2RA	3559
IL2RB	3560
IL2RG	3561
IL31RA	133396
IL3RA	3563
IL4R	3566
IL5RA	3568
IL6R	3570
IL6ST	3572
IL7R	3575
IL9R	3581
ILDR1	286676
ILDR2	387597
IMPG2	50939
INSR	3643
INSRR	3645
ISLR	3671
ISLR2	57611
ITFG1	81533
ITGA1	3672
ITGA10	8515
ITGA11	22801
ITGA2	3673
ITGA2B	3674
ITGA3	3675
ITGA4	3676
ITGA5	3678
ITGA6	3655
ITGA7	3679
ITGA8	8516
ITGA9	3680
ITGAD	3681

ITGAE	3682
ITGAL	3683
ITGAM	3684
ITGAV	3685
ITGAX	3687
ITLN1	55600
IZUMO1	284359
IZUMO2	126123
JAG1	182
JAG2	3714
JAM2	58494
JAM3	83700
JTB	10899
KAZALD1	81621
KCNE4	23704
KDR	3791
KIAA0090	23065
KIAA0319	9856
KIAA0319L	79932
KIAA1024	23251
KIAA1324	57535
KIAA1324L	222223
KIAA1644	85352
KIR2DL1	3802
KIR2DL2	3803
KIR2DL3	3804
KIR2DL4	3805
KIR2DL5A	57292
KIR2DL5B	553128
KIR2DS1	3806
KIR2DS2	100132285
KIR2DS3	3808
KIR2DS4	3809
KIR2DS5	3810
KIR3DL1	3811
KIR3DL2	3812
KIR3DL3	115653
KIR3DP1	548594
KIR3DS1	3813
KIR3DX1	90011
KIRREL	55243
KIRREL2	84063
KIRREL3	84623

KIT	3815
KITLG	4254
KL	9365
KLB	152831
KLRAP1	10748
KREMEN1	83999
KREMEN2	79412
L1CAM	3897
LAG3	3902
LAIR1	3903
LAIR2	3904
LAMP1	3916
LAMP2	3920
LAMP3	27074
LAMP5	24141
LAX1	54900
LAYN	143903
LCTL	197021
LDLR	3949
LDLRAD2	401944
LDLRAD3	143458
LEPR	3953
LIFR	3977
LILRA1	11024
LILRA2	11027
LILRA3	11026
LILRA4	23547
LILRA5	353514
LILRA6	79168
LILRB1	10859
LILRB2	10288
LILRB3	11025
LILRB4	11006
LILRB5	10990
LINGO1	84894
LINGO2	158038
LINGO3	645191
LINGO4	339398
LMLN	89782
LOC160348	160348
LOC256223	256223
LOC374383	374383
LOC376666	376666

LOC652900	652900
LRCH4	4034
LRFN1	57622
LRFN2	57497
LRFN3	79414
LRFN4	78999
LRFN5	145581
LRIG1	26018
LRIG2	9860
LRIG3	121227
LRIT1	26103
LRIT2	340745
LRIT3	345193
LRP10	26020
LRP11	84918
LRP12	29967
LRP3	4037
LRP4	4038
LRP5	4041
LRP6	4040
LRP8	7804
LRPAP1	4043
LRRC15	131578
LRRC19	64922
LRRC24	441381
LRRC25	126364
LRRC26	389816
LRRC3	81543
LRRC32	2615
LRRC33	375387
LRRC37A	9884
LRRC37A2	474170
LRRC37A3	374819
LRRC37B	114659
LRRC38	126755
LRRC3B	116135
LRRC4	64101
LRRC4B	94030
LRRC4C	57689
LRRC52	440699
LRRC55	219527
LRRC66	339977
LRRN1	57633

LRRN2	10446
LRRN3	54674
LRRN4	164312
LRRN4CL	221091
LRRTM1	347730
LRRTM2	26045
LRRTM3	347731
LRRTM4	80059
LRTM1	57408
LRTM2	654429
LSAMP	4045
LSR	51599
LTBR	4055
LTK	4058
LY6D	8581
LY6E	4061
LY6G6C	80740
LY6G6D	58530
LY6G6F	259215
LY6H	4062
LY6K	54742
LY75	4065
LY9	4063
LYPD1	116372
LYPD3	27076
LYPD5	284348
LYPD6	130574
LYPD6B	130576
LYSMD3	116068
LYSMD4	145748
LYVE1	10894
M6PR	4074
MADCAM1	8174
MAG	4099
MAMDC4	158056
MANSC1	54682
MCAM	4162
MDGA1	266727
MDGA2	161357
MEGF10	84466
MEGF11	84465
MEGF8	1954
MEGF9	1955

MEP1A	4224
MEP1B	4225
MERTK	10461
MET	4233
MFAP3	4238
MFAP3L	9848
MFI2	4241
MICA	4276
MICB	4277
MILR1	284021
MMGT1	93380
MMP14	4323
MMP15	4324
MMP16	4325
MMP24	10893
MOG	4340
MPEG1	219972
MPL	4352
MPZ	4359
MPZL1	9019
MPZL2	10205
MPZL3	196264
MR1	3140
MRC1	4360
MRC2	9902
MSLN	10232
MST1R	4486
MUC1	4582
MUC13	56667
MUC15	143662
MUC21	394263
MUSK	4593
MXRA5	25878
MXRA7	439921
MXRA8	54587
MYEOV	26579
NAGPA	51172
NCAM1	4684
NCAM2	4685
NCAN	1463
NCLN	56926
NCR1	9437
NCR2	9436

NCR3	259197
NCSTN	23385
NEGR1	257194
NEO1	4756
NETO1	81832
NETO2	81831
NFAM1	150372
NFASC	23114
NGFR	4804
NLGN1	22871
NLGN2	57555
NLGN3	54413
NLGN4X	57502
NLGN4Y	22829
NOMO1	23420
NOMO3	408050
NOTCH1	4851
NOTCH2	4853
NOTCH3	4854
NOTCH4	4855
NPDC1	56654
NPHS1	4868
NPR1	4881
NPR2	4882
NPR3	4883
NPTN	27020
NRCAM	4897
NRG1	3084
NRG2	9542
NRG4	145957
NRN1	51299
NRN1L	123904
NRP1	8829
NRP2	8828
NRXN1	9378
NRXN2	9379
NRXN3	9369
NT5E	4907
NTM	50863
NTNG1	22854
NTRK1	4914
NTRK2	4915
NTRK3	4916

OMG	4974
OPCML	4978
OSCAR	126014
OSMR	9180
OSTM1	28962
OTOA	146183
P2RX2	22953
PAPLN	89932
PARM1	25849
PCDHGB6	56100
PCDHGC3	5098
PCDHGC5	93708
PCSK4	54760
PCSK7	9159
PDCD1	5133
PDCD1LG2	80380
PDGFRA	5156
PDGFRB	5159
PDGFRL	5157
PDPN	10630
PEAR1	375033
PECAM1	5175
Phospholipase Inhibitor	
PI16	221476
PIGR	5284
PIK3IP1	113791
PILRA	29992
PILRB	29990
PLA2R1	22925
PLB1	151056
PLXDC1	57125
PLXDC2	84898
PLXNA1	5361
PLXNA2	5362
PLXNA3	55558
PLXNA4	91584
PLXNB1	5364
PLXNB2	23654
PLXNB3	5365
PLXNC1	10154
PLXND1	23129
PMEL	6490

PMEPA1	56937
PODXL	5420
PODXL2	50512
PRIMA1	145270
PRLR	5618
PRND	23627
PRNP	5621
PROCR	10544
PRRG2	5639
PRRG3	79057
PRRG4	79056
PRSS21	10942
PRSS41	360226
PRSS55	203074
PRSS8	5652
PRTG	283659
PSG1	5669
PSG2	5670
PSG3	5671
PSG4	5672
PSG5	5673
PSG6	5675
PSG7	5676
PSG8	440533
PSG9	5678
PTCRA	171558
PTGFRN	5738
PTK7	5754
PTPRA	5786
PTPRB	5787
PTPRC	5788
PTPRCAP	5790
PTPRD	5789
PTPRE	5791
PTPRF	5792
PTPRG	5793
PTPRH	5794
PTPRJ	5795
PTPRK	5796
PTPRM	5797
PTPRN	5798
PTPRN2	5799
PTPRO	5800

PTPRR	5801
PTPRS	5802
PTPRT	11122
PTPRU	10076
PTPRZ1	5803
PVR	5817
PVRL1	5818
PVRL2	5819
NECTIN3	25945
PVRL4	81607
PXDN	7837
PXDNL	137902
QSOX1	5768
QSOX2	169714
RAET1E	135250
RAET1G	353091
RAET1L	154064
RAMP1	10267
RAMP2	10266
RAMP3	10268
RECK	8434
RELL1	768211
RELT	84957
RET	5979
RGMA	56963
RGMB	285704
ROBO1	6091
ROBO2	6092
ROBO3	64221
ROBO4	54538
ROR1	4919
ROR2	4920
ROS1	6098
RPN1	6184
RPRML	388394
RTN4R	65078
RTN4RL1	146760
RYK	6259
SARAF	51669
SCARF1	8578
SCARF2	91179
SCN1B	6324
SCN2B	6327

SCN3B	55800
SCN4B	6330
SDC1	6382
SDC2	6383
SDC3	9672
SDC4	6385
SDK1	221935
SDK2	237979
SECTM1	6398
SEL1L3	23231
SELE	6401
SELL	6402
SELP	6403
SELPLG	6404
SEMA3A	10371
SEMA3B	7869
SEMA3C	10512
SEMA3D	223117
SEMA3E	9723
SEMA3F	6405
SEMA3G	56920
SEMA4A	64218
SEMA4B	10509
SEMA4C	54910
SEMA4D	10507
SEMA4F	10505
SEMA4G	57715
SEMA5A	9037
SEMA5B	54437
SEMA6A	57556
SEMA6B	10501
SEMA6C	10500
SEMA6D	80031
SEMA7A	8482
SERTM1	400120
SEZ6	124925
SEZ6L	23544
SEZ6L2	26470
SGCA	6442
SGCE	8910
SHISA2	387914
SHISA3	152573
SHISA4	149345

SHISA5	51246
SIGIRR	59307
SIGLEC1	6614
SIGLEC10	89790
SIGLEC11	114132
SIGLEC12	89858
SIGLEC14	100049587
SIGLEC15	284266
SIGLEC16	400709
SIGLEC5	8778
SIGLEC6	946
SIGLEC7	27036
SIGLEC8	27181
SIGLEC9	27180
SIRPA	140885
SIRPB1	10326
SIRPB2	284759
SIRPD	128646
SIRPG	55423
SIT1	27240
SKINTL	391037
SLAMF1	6504
SLAMF6	114836
SLAMF7	57823
SLAMF8	56833
SLAMF9	89886
SLITRK1	114798
SLITRK2	84631
SLITRK3	22865
SLITRK4	139065
SLITRK5	26050
SLITRK6	84189
SMAGP	57228
SOGA3	387104
SORCS1	114815
SORCS2	57537
SORCS3	22986
SORL1	6653
SORT1	6272
SPACA1	81833
SPACA4	171169
SPATA9	83890
SPINT1	6692

SPINT2	10653
SPN	6693
SPRN	503542
STAB1	23166
STAB2	55576
STIM1	6786
SUSD1	64420
SUSD2	56241
SUSD3	203328
SUSD4	55061
SUSD5	26032
TACSTD2	4070
TAPBP	6892
TAPBPL	55080
TARM1	441864
TCP11	6954
TCTN2	79867
TCTN3	26123
TDGF1	6997
TECTA	7007
TECTB	6975
TEK	7010
TEX101	83639
TEX29	121793
TGFA	7039
TGFBR1	7046
TGFBR2	7048
TGFBR3	7049
TGOLN2	10618
THBD	7056
THSD1	55901
THSD7A	221981
THSD7B	80731
THY1	7070
TIE1	7075
TIGIT	201633
TIMD4	91937
TLR1	7096
TLR10	81793
TLR2	7097
TLR3	7098
TLR4	7099
TLR5	7100

TLR6	10333
TLR7	51284
TLR8	51311
TLR9	54106
TMEFF1	8577
TMEFF2	23671
TMEM108	66000
TMEM119	338773
TMEM123	114908
TMEM130	222865
TMEM132A	54972
TMEM132B	114795
TMEM132D	121256
TMEM132E	124842
TMEM154	201799
TMEM156	80008
TMEM158	25907
TMEM167A	153339
TMEM167B	56900
TMEM183A	92703
TMEM183B	653659
TMEM190	147744
TMEM207	131920
TMEM213	155006
TMEM240	339453
TMEM25	84866
TMEM27	57393
TMEM52	339456
TMEM59	9528
TMEM59L	25789
TMEM81	388730
TMEM92	162461
TMEM95	339168
TMEM9B	56674
TMIE	259236
TMIGD1	388364
TMIGD2	126259
TMPRSS12	283471
TMX4	56255
TNFRSF10A	8797
TNFRSF10B	8795
TNFRSF10C	8794
TNFRSF10D	8793

TNFRSF11A	8792
TNFRSF11B	4982
TNFRSF12A	51330
TNFRSF13B	23495
TNFRSF13C	115650
TNFRSF14	8764
TNFRSF17	608
TNFRSF18	8784
TNFRSF19	55504
TNFRSF1A	7132
TNFRSF1B	7133
TNFRSF21	27242
TNFRSF25	8718
TNFRSF4	7293
TNFRSF6B	8771
TNFRSF8	943
TNFRSF9	3604
TNFSF15	9966
TP53I13	90313
TPBG	7162
TPO	7173
TPSG1	25823
TREH	11181
TREM1	54210
TREM2	54209
TREML1	340205
TREML2	79865
TREML4	285852
TRIL	9865
TXNDC15	79770
TYRO3	7301
TYROBP	7305
ULBP1	80329
ULBP2	80328
ULBP3	79465
UMOD	7369
UMODL1	89766
UNC5A	90249
UNC5B	219699
UNC5C	8633
UNC5D	137970
UPK3BL	100134938
VASN	114990

VCAM1	7412
VLDLR	7436
VNN1	8876
VNN2	8875
VNN3	55350
VPREB1	7441
VPREB3	29802
VSIG1	340547
VSIG10	54621
VSIG2	23584
VSIG4	11326
VSTM1	284415
VSTM2A	222008
VSTM2B	342865
VSTM2L	128434
VSTM4	196740
VSTM5	387804
VTCN1	79679
WFIKKN1	117166
WFIKKN2	124857
XG	7499
XPNPEP2	7512
ZAN	7455
ZP1	22917
ZP2	7783
ZP3	7784
ZP4	57829
ZPBP	11055
ZPBP2	124626
ZPLD1	131368

Table 8. Untagged STM library for PDPN experiment

Prey short name	Prey Entrez ID
ABHD13	84945
ABHD14A	25864
ABHD15	116236
ABHD3	171586
AC010320.10	
AC092653.3	
AC138393.2	

ACE	1636
ACE2	59272
ACPT	93650
ACVR1	90
ACVR1C	130399
ACVR2A	92
ACVR2B	93
ACVRL1	94
ADAM11	4185
ADAM12	8038
ADAM15	8751
ADAM18	8749
ADAM19	8728
ADAM2	2515
ADAM20	8748
ADAM21	8747
ADAM29	11086
ADAM30	11085
ADAM32	203102
ADAM33	80332
ADAM8	101
ADCK2	90956
ADCK4	79934
ADCK5	203054
ADIG	149685
ALCAM	214
ALK	238
ALPI	248
ALPL	249
ALPP	250
AMHR2	269
AMICA1	120425
AMIGO1	57463
AMIGO2	347902
AMIGO3	386724
AMN	81693
ANKAR	150709
ANKRD32	84250
ANPEP	290
AOC3	8639
APCDD1	147495
APCDD1L	164284
APLP1	333

APLP2	334
APOO	79135
APP	351
AQPEP	206338
AREG	374
ARMC10	83787
ARMCX2	9823
ARMCX3	51566
ARMCX6	54470
ARQM13373	
ART1	417
ART3	419
ASGR1	432
ASGR2	433
ASIC4	55515
ASPHD1	253982
ATP1B1	481
ATP1B2	482
ATP1B3	483
ATP4B	496
ATP6AP1	537
ATPAF1-AS1	374973
ATRAID	51374
ATRNL1	26033
AUP1	550
AXL	558
BACE1	23621
BACE2	25825
BAMBI	25805
BCAM	4059
BLVRB	645
BMPR1A	657
BMPR1B	658
BMPR2	659
BOC	91653
BSG	682
BTC	685
BTLA	151888
BTN1A1	696
BTN2A1	11120
BTN2A3P	54718
BTN3A1	11119
BTN3A2	11118

BTN3A3	10384
BTNL3	10917
BTNL9	153579
C10orf111	221060
C10orf128	170371
C10orf26	54838
C10orf35	219738
C10orf54	64115
C11orf24	53838
C11orf75	56935
C11orf9	745
C11orf92	399948
C12orf59	120939
C12orf63	144535
C14orf118	55668
C14orf132	56967
C14orf37	145407
C15orf24	56851
C15orf48	84419
C15orf54	400360
C16orf42	11539
C16orf54	283897
C16orf58	64755
C16orf91	283951
C16orf92	146378
C17orf101	79701
C17orf56	100489372
C17orf78	284099
C17orf80	55028
C18orf1	753
C18orf26	284254
C18orf62	284274
C19orf18	147685
C19orf24	55009
C19orf26	255057
C19orf38	255809
C19orf59	199675
C19orf63	284361
C19orf75	284369
C19orf77	284422
C1GALT1C1	29071
C1orf101	257044
C1orf162	128346

C1orf210	149466
C1orf212	113444
C1orf43	25912
C1orf85	112770
C1orf87	127795
C20orf3	57136
C2CD2L	9854
C2orf43	60526
C3orf17	25871
C3orf18	51161
C3orf35	339883
C3orf45	132228
C3orf75	54859
C4orf32	132720
C4orf34	201895
C5orf15	56951
C5orf43	643155
C6orf162	57150
C7orf44	55744
C7orf45	136263
C7orf53	286006
C8orf40	114926
C9orf11	54586
C9orf46	55848
C9orf57	138240
C9orf79	286234
C9orf89	84270
CA12	771
CA14	23632
CA4	762
CA9	768
CABP7	164633
CACHD1	57685
CACNA2D4	93589
CADM2	253559
CADM3	57863
CADM4	199731
CARNS1	57571
CATSPERG	57828
CAV1	857
CAV3	859
CCDC107	203260
CCDC127	133957

CCDC155	147872
CCDC47	57003
CD101	9398
CD14	929
CD160	11126
CD163	9332
CD164	8763
CD180	4064
CD19	930
CD1A	909
CD1B	910
CD1C	911
CD1D	912
CD2	914
CD200	4345
CD200R1L	344807
CD207	50489
CD209	30835
CD22	933
CD226	10666
CD24	100133941
CD244	51744
CD247	919
CD27	939
CD274	29126
CD276	80381
CD28	940
CD300A	11314
CD300C	10871
CD300E	342510
CD300LB	124599
CD300LD	100131439
CD300LF	146722
CD300LG	146894
CD302	9936
CD320	51293
CD33	945
CD34	947
CD38	952
CD3D	915
CD3E	916
CD3G	917
CD4	920

CD40	958
CD40LG	959
CD44	960
CD46	4179
CD48	962
CD5	921
CD52	1043
CD55	1604
CD58	965
CD6	923
CD68	968
CD69	969
CD7	924
CD70	970
CD72	971
CD74	972
CD79A	973
CD79B	974
CD80	941
CD83	9308
CD84	8832
CD86	942
CD8A	925
CD8B	926
CD93	22918
CD96	10225
CD99L2	83692
CDCP1	64866
CDH1	999
CDH11	1009
CDH12	1010
CDH13	1012
CDH15	1013
CDH16	1014
CDH17	1015
CDH18	1016
CDH19	28513
CDH2	1000
CDH20	28316
CDH22	64405
CDH24	64403
CDH26	60437
CDH4	1002

CDH6	1004
CDH7	1005
CDH8	1006
CDH9	1007
CDHR1	92211
CDHR2	54825
CDHR3	222256
CDON	50937
CEACAM16	388551
CEACAM19	56971
CEACAM20	125931
CEACAM21	90273
CEACAM4	1089
CEACAM5	1048
CEACAM6	4680
CEND1	51286
CHIC2	26511
CHL1	10752
CHODL	140578
CLCA2	9635
CLEC10A	10462
CLEC12A	160364
CLEC12B	387837
CLEC14A	161198
CLEC17A	388512
CLEC1A	51267
CLEC1B	51266
CLEC2A	387836
CLEC2B	9976
CLEC2D	29121
CLEC2L	154790
CLEC4A	50856
CLEC4C	170482
CLEC4D	338339
CLEC4E	26253
CLEC4F	165530
CLEC4G	339390
CLEC5A	23601
CLEC6A	93978
CLEC7A	64581
CLEC9A	283420
CLECL1	160365
CLMN	79789

CLMP	79827
CLSTN1	22883
CLSTN2	64084
CLSTN3	9746
CNPPD1	27013
CNST	163882
CNTFR	1271
CNTN2	6900
CNTN3	5067
CNTN6	27255
CNTNAP1	8506
CNTNAP2	26047
CNTNAP3	79937
CNTNAP5	129684
COLEC12	81035
CORIN	10699
CPM	1368
CR2	1380
CRB3	92359
CREB3L2	64764
CRIM1	51232
CRLF2	64109
CRTAM	56253
CRYM-AS1	400508
CSF1	1435
CSF1R	1436
CSF2RA	1438
CSF2RB	1439
CSF3R	1441
CSMD1	64478
CSPG5	10675
CTAGE4	100128553
CTAGE6P	340307
CTC1	80169
CTNNAL1	8727
CTXN1	404217
CX3CL1	6376
CXADR	1525
CXCL16	58191
CXorf59	286464
CXorf61	203413
CXorf66	347487
DAG1	1605

DCT	1638
DDR2	4921
DEXI	28955
DGCR2	9993
DLK1	8788
DLK2	65989
DLL1	28514
DLL3	10683
DLL4	54567
DNER	92737
DPCR1	135656
DPEP1	1800
DPEP2	64174
DPEP3	64180
DPP4	1803
DPP6	1804
DSC3	1825
DSCAM	1826
DSG1	1828
DSG2	1829
DSG4	147409
ECE1	1889
ECEL1	9427
EDA	1896
EDA2R	60401
EDAR	10913
EFHA2	286097
EFNA3	1944
EFNA5	1946
EFNB1	1947
EFNB2	1948
EFNB3	1949
EGF	1950
EGFR	1956
ELFN1	392617
EMB	133418
EMCN	51705
ENG	2022
ENPEP	2028
ENPP3	5169
ENPP5	59084
EPCAM	4072
EPGN	255324

EPHA1	2041
EPHA10	284656
EPHA2	1969
EPHA3	2042
EPHA4	2043
EPHA5	2044
EPHA6	285220
EPHA7	2045
EPHB1	2047
EPHB2	2048
EPHB3	2049
EPHB4	2050
EPHB6	2051
EPHX3	79852
EPOR	2057
ERBB2	2064
ERBB3	2065
ERMAP	114625
ESAM	90952
ESYT3	83850
EVA1C	59271
EVC	2121
EVI2A	2123
EVI2B	2124
F11R	50848
F3	2152
FAAH2	158584
FAIM3	9214
FAM105A	54491
FAM118A	55007
FAM151A	338094
FAM159A	348378
FAM162B	221303
FAM163A	148753
FAM171A1	221061
FAM171B	165215
FAM173A	65990
FAM173B	134145
FAM174A	345757
FAM174B	400451
FAM176B	55194
FAM177B	400823
FAM178A	55719

FAM187A	100528020
FAM187B	148109
FAM189A2	9413
FAM198B	51313
FAM200A	221786
FAM209A	200232
FAM209B	388799
FAM210A	125228
FAM24B	196792
FAM3A	60343
FAM69A	388650
FAM69B	138311
FAM73A	374986
FAM75A1	647060
FAM75A3	727830
FAM75A5	727905
FAM75A7	26165
FAM75D1	389763
FAP	2191
FAS	355
FASLG	356
FATE1	89885
FCAMR	83953
FCAR	2204
FCER1A	2205
FCER1G	2207
FCGR1A	2209
FCGR2A	2212
FCGR2B	2213
FCGR2C	9103
FCGR3B	2215
FCGRT	2217
FCRL1	115350
FCRL2	79368
FCRL3	115352
FCRL5	83416
FCRL6	343413
FCRLA	84824
FGFR1	2260
FGFR2	2263
FGFR3	2261
FGFR4	2264
FGFRL1	53834

FIBCD1	84929
FIG4	9896
FLJ33768	283673
FLRT1	23769
FLRT2	23768
FLRT3	23767
FLT1	2321
FLT3LG	2323
FLT4	2324
FNDC3A	22862
FNDC3B	64778
FNDC4	64838
FNDC9	408263
FOLR1	2348
FOLR2	2350
FRMD3	257019
FRMD5	84978
FRRS1L	23732
FURIN	5045
FUT1	2523
FXYD1	5348
FXYD3	5349
FXYD4	53828
FXYD5	53827
FXYD6	53826
GAS1	2619
GEMIN8	54960
GFRA1	2674
GFRA2	2675
GFRA3	2676
GFRA4	64096
GFRAL	389400
GGT1	2678
GGT5	2687
GGTA1	2681
GGTA1P	2681
GHR	2690
GKGM353	
GLDN	342035
GLIPR1L2	144321
GLT8D2	83468
GML	2765
GOLM1	51280

GP1BA	2811
GP1BB	2812
GP2	2813
GP5	2814
GP6	51206
GP9	2815
GPA33	10223
GPC1	2817
GPC2	221914
GPC3	2719
GPC6	10082
GPIHBP1	338328
GPNMB	10457
GPX8	493869
GRAMD1B	57476
GRAMD1C	54762
GRAMD2	196996
GRAMD3	65983
GUCY2C	2984
GUCY2D	3000
GUCY2F	2986
GYPC	2995
HAVCR1	26762
HAVCR2	84868
HBEGF	1839
HCST	10870
HEPACAM	220296
HEPACAM2	253012
HEPH	9843
HFE	3077
HFE2	148738
HHLA2	11148
HILPDA	29923
HPN	3249
HRASLS	57110
HRASLS2	54979
HYAL2	8692
HYAL4	23553
ICAM1	3383
ICAM2	3384
ICAM3	3385
ICAM5	7087
ICOS	29851

ICOSLG	23308
IFNAR1	3454
IFNAR2	3455
IFNGR1	3459
IFNGR2	3460
IGDCC3	9543
IGDCC4	57722
IGF1R	3480
IGFLR1	79713
IGSF11	152404
IGSF21	84966
IGSF3	3321
IGSF5	150084
IGSF6	10261
IGSF8	93185
IGSF9	57549
IGSF9B	22997
IL10RA	3587
IL10RB	3588
IL11RA	3590
IL12RB1	3594
IL12RB2	3595
IL13RA1	3597
IL13RA2	3598
IL17RA	23765
IL17RB	55540
IL17RC	84818
IL17RD	54756
IL18R1	8809
IL18RAP	8807
IL1R1	3554
IL1R2	7850
IL1RAP	3556
IL1RAPL1	11141
IL1RAPL2	26280
IL1RL1	9173
IL1RL2	8808
IL20RA	53832
IL20RB	53833
IL21R	50615
IL22RA1	58985
IL23R	149233
IL27RA	9466

IL2RA	3559
IL2RB	3560
IL2RG	3561
IL31RA	133396
IL3RA	3563
IL4R	3566
IL5RA	3568
IL6R	3570
IL6ST	3572
IL9R	3581
ILDR1	286676
ILDR2	387597
INSR	3643
INSRR	3645
IQCF1	132141
IQSEC2	23096
ISLR2	57611
ITFG1	81533
ITFG3	83986
ITGA1	3672
ITGA10	8515
ITGA11	22801
ITGA2	3673
ITGA2B	3674
ITGA3	3675
ITGA4	3676
ITGA5	3678
ITGA6	3655
ITGA7	3679
ITGA8	8516
ITGA9	3680
ITGAE	3682
ITGAL	3683
ITGAM	3684
ITGAX	3687
ITGB1	3688
ITGB2	3689
ITGB3	3690
ITGB5	3693
ITGB6	3694
ITGB7	3695
ITGB8	3696
ITLN1	55600

ITM2A	9452
ITM2B	9445
ITM2C	81618
ITPRIPL2	162073
IYD	389434
IZUMO1	284359
IZUMO2	126123
JAG1	182
JAG2	3714
JAM2	58494
JAM3	83700
JTB	10899
KCNE1	3753
KCNE2	9992
KCNE3	10008
KCNE4	23704
KEL	3792
KIAA0090	23065
KIAA0247	9766
KIAA0317	9870
KIAA0319	9856
KIAA0319L	79932
KIAA0494	9813
KIAA1024	23251
KIAA1467	57613
KIR2DL1	3802
KIR2DL2	3803
KIR2DL3	3804
KIR2DL4	3805
KIR2DL5A	57292
KIR2DL5B	553128
KIR2DS1	3806
KIR2DS3	3808
KIR2DS4	3809
KIR2DS5	3810
KIR3DL1	3811
KIR3DL3	115653
KIRREL	55243
KIRREL2	84063
KIRREL3	84623
KITLG	4254
KL	9365
KLB	152831

KLRAP1	10748
KLRB1	3820
KLRC1	3821
KLRC2	3822
KLRC3	3823
KLRC4	8302
KLRD1	3824
KLRF1	51348
KLRG1	10219
KLRK1	22914
KREMEN1	83999
KREMEN2	79412
L1CAM	3897
LAG3	3902
LAIR1	3903
LAMP1	3916
LAMP2	3920
LAMP3	27074
LAMP5	24141
LAT	27040
LAT2	7462
LAX1	54900
LAYN	143903
LCTL	197021
LDLR	3949
LDLRAD1	388633
LDLRAD2	401944
LDLRAD3	143458
LECT1	11061
LEPR	3953
LIFR	3977
LILRA1	11024
LILRA2	11027
LILRA4	23547
LILRA5	353514
LILRA6	79168
LILRB1	10859
LILRB2	10288
LILRB3	11025
LILRB4	11006
LILRB5	10990
LIME1	54923
LINGO1	84894

LINGO2	158038
LINGO3	645191
LINGO4	339398
LMLN	89782
LMTK2	22853
LNPEP	4012
LOC100133864	
LOC256223	
LOC652900	
LOC653303	
LOC653560	
LOC727778	
LRAT	9227
LRCH1	23143
LRCH4	4034
LRFN1	57622
LRFN2	57497
LRFN4	78999
LRFN5	145581
LRIG1	26018
LRIG3	121227
LRIT1	26103
LRIT2	340745
LRIT3	345193
LRP1	4035
LRP10	26020
LRP11	84918
LRP12	29967
LRP3	4037
LRP4	4038
LRP5	4041
LRP6	4040
LRP8	7804
LRPAP1	4043
LRRC15	131578
LRRC19	64922
LRRC24	441381
LRRC25	126364
LRRC26	389816
LRRC3	81543
LRRC32	2615
LRRC33	303875
LRRC37A2	474170

LRRC37B	114659
LRRC3B	116135
LRRC4	64101
LRRC4B	94030
LRRC4C	57689
LRRC52	440699
LRRC55	219527
LRRC59	55379
LRRC66	339977
LRRN1	57633
LRRN2	10446
LRRN3	54674
LRRN4	164312
LRRN4CL	221091
LRRTM1	347730
LRRTM2	26045
LRRTM3	347731
LRRTM4	80059
LRTM1	57408
LRTM2	654429
LSAMP	4045
LSR	51599
LTB	4050
LTBR	4055
LTK	4058
LY6D	8581
LY6E	4061
LY6G5C	80741
LY6H	4062
LY6K	54742
LY9	4063
LYPD1	116372
LYPD3	27076
LYPD6	130574
LYPD6B	130576
LYSMD3	116068
LYSMD4	145748
LYVE1	10894
M6PR	4074
MADCAM1	8174
MAG	4099
MAGOHB	55110
MANSC1	54682

MCAM	4162
MDGA1	266727
MDGA2	161357
MEGF10	84466
MEGF11	84465
MEP1A	4224
MEP1B	4225
MEST	4232
MET	4233
MFAP3	4238
MFAP3L	9848
MFI2	4241
MGC35338	130619
MGC39681	293197
MGC5590	79024
MICB	4277
MICU1	10367
MILR1	284021
MLANA	2315
MME	4311
MMEL1	79258
MMGT1	93380
MMP14	4323
MMP15	4324
MMP16	4325
MMP23B	8510
MMP24	10893
MOG	4340
MPEG1	219972
MPL	4352
MPP1	4354
MPZ	4359
MPZL1	9019
MPZL2	10205
MRC1	4360
MRC2	9902
MSLN	10232
MTDH	92140
MUC1	4582
MUC15	143662
MUC21	394263
MUSK	4593
MXRA7	439921

MXRA8	54587
MYEOV	26579
NAA25	80018
NAALAD2	10003
NAALADL1	10004
NAGPA	51172
NCAM1	4684
NCAM2	4685
NCKAP1	10787
NCR1	9437
NCR2	9436
NCSTN	23385
NEGR1	257194
NEO1	4756
NETO1	81832
NETO2	81831
NFASC	23114
NGFR	4804
NLGN1	22871
NLGN2	57555
NLGN3	54413
NLGN4X	57502
NOMO3	408050
NPDC1	56654
NPHS1	4868
NPHS2	7827
NPR1	4881
NPR2	4882
NPR3	4883
NPTN	27020
NRCAM	4897
NRG2	9542
NRG4	145957
NRN1	51299
NRN1L	123904
NRP1	8829
NRP2	8828
NRXN1	9378
NRXN2	9379
NTNG1	22854
NTRK1	4914
NTRK2	4915
NTRK3	4916

NUS1	116150
OLR1	4973
OMG	4974
OPALIN	93377
OPCML	4978
OSMR	9180
OSTBETA	123264
OSTM1	28962
P2RX2	22953
PARM1	25849
PCDH10	57575
PCDH11Y	83259
PCDH12	51294
PCDH17	27253
PCDH18	54510
PCDH19	57526
PCDH7	5099
PCDH8	5100
PCDH9	5101
PCDHA7	56141
PCDHA8	56140
PCDHB1	29930
PCDHB10	56126
PCDHB11	56125
PCDHB12	56124
PCDHB13	56123
PCDHB15	56121
PCDHB16	57717
PCDHB2	56133
PCDHB3	56132
PCDHB4	56131
PCDHB5	26167
PCDHB6	56130
PCDHB7	56129
PCDHB8	56128
PCDHB9	56127
PCDHGA11	56105
PCDHGA2	56113
PCDHGA8	9708
PCSK4	54760
PCSK7	9159
PDCD1	5133
PDCD1LG2	80380

PDGFRA	5156
PDGFRB	5159
PDPN	10630
PDZK1IP1	10158
PGRMC1	10857
PHEX	5251
PI16	221476
PIGR	5284
PIK3IP1	113791
PILRA	29992
PILRB	29990
PLA2R1	22925
PLB1	151056
PLSCR3	57048
PLSCR4	57088
PLVAP	83483
PLXDC1	57125
PLXDC2	84898
PLXNA2	5362
PLXNA4	91584
PLXNB2	23654
PLXNB3	5365
PLXNC1	10154
PLXND1	23129
PMEL	6490
PMEPA1	56937
PNKD	25953
PODXL	5420
PPP1R3A	5506
PRIMA1	145270
PRLR	5618
PRND	23627
PRNP	5621
PROCR	10544
PRR24	255783
PRR7	80758
PRRG1	5638
PRRG2	5639
PRRG3	79057
PRRG4	79056
PRSS21	10942
PRSS41	360226
PRSS55	203074

PRSS8	5652
PRTG	283659
PSD2	84249
PTCRA	171558
PTGFRN	5738
PTK7	5754
PTPRA	5786
PTPRC	5788
PTPRCAP	5790
PTPRE	5791
PTPRF	5792
PTPRG	5793
PTPRH	5794
PTPRJ	5795
PTPRK	5796
PTPRN	5798
PTPRN2	5799
PTPRO	5800
PTPRR	5801
PTPRS	5802
PTPRT	11122
PVR	5817
PVRL1	5818
PVRL2	5819
NECTIN3	25945
PVRL4	81607
QSOX1	5768
QSOX2	169714
RAET1E	135250
RAET1G	353091
RAET1L	154064
RAMP1	10267
RAMP2	10266
RAMP3	10268
RARRES1	5918
RECK	8434
RELL1	768211
RELL2	285613
RELT	84957
RET	5979
RGMA	56963
ROBO1	6091
ROBO2	6092

ROBO3	64221
ROBO4	54538
ROMO1	140823
ROR1	4919
ROR2	4920
ROS1	6098
RPRML	388394
RTN4R	65078
RTN4RL1	146760
RTP1	132112
RTP2	344892
RTP4	64108
RYK	6259
SARAF	51669
SAYSD1	55776
SCAI	286205
SCARA5	286133
SCARF2	91179
SCN1B	6324
SCN2B	6327
SCN3B	55800
SCN4B	6330
SDC1	6382
SDC2	6383
SDC3	9672
SDC4	6385
SECTM1	6398
SEL1L3	23231
SELL	6402
SELP	6403
SELPLG	6404
SELT	51714
SEMA4A	64218
SEMA4B	10509
SEMA4C	54910
SEMA4D	10507
SEMA4G	57715
SEMA5A	9037
SEMA5B	54437
SEMA6A	57556
SEMA6B	10501
SEMA6C	10500
SEMA6D	80031

SEMA7A	8482
SERPINA9	327657
SERPINB3	6317
SERPINB7	8710
SERTM1	400120
SEZ6	124925
SEZ6L	23544
SFTPC	6440
SGCA	6442
SGCB	6443
SGCD	6444
SGCE	8910
SHISA2	387914
SHISA3	152573
SHISA4	149345
SHISA5	51246
SIGIRR	59307
SIGLEC1	6614
SIGLEC10	89790
SIGLEC11	114132
SIGLEC12	89858
SIGLEC15	284266
SIGLEC5	8778
SIGLEC6	946
SIGLEC7	27036
SIGLEC8	27181
SIGLEC9	27180
SIGLECP16	400709
SIRPA	140885
SIRPB2	284759
SIRPD	128646
SIRPG	55423
SIT1	27240
SLAMF1	6504
SLAMF6	114836
SLAMF7	57823
SLAMF8	56833
SLAMF9	89886
SLC25A35	399512
SLC3A1	6519
SLC3A2	6520
SLITRK1	114798
SLITRK2	84631

SLITRK3	22865
SLITRK4	139065
SLITRK5	26050
SLITRK6	84189
SLMAP	7871
SMAGP	57228
SMCR7	140774
SMCR7L	54471
SNN	8303
SNPH	9751
SOGA3	387104
SORCS2	57537
SORCS3	22986
SORT1	6272
SPACA1	81833
SPACA4	171169
SPATA9	83890
SPEM1	374768
SPINT1	6692
SPINT2	10653
SPN	6693
SPRED1	161742
SPRN	503542
SRMS	6725
ST14	6768
ST6GAL1	6480
STBD1	8987
STIM1	6786
STON2	85439
STYK1	55359
SUN3	256979
SUSD1	64420
SUSD2	56241
SUSD3	203328
SUSD4	55061
SUSD5	26032
TACSTD2	4070
TAPBPL	55080
TARM1	441864
TCP11	6954
TCTA	6988
TCTN2	79867
TCTN3	26123

TDGF1	6997
TECTB	6975
TEK	7010
TEX101	83639
TEX2	55852
TEX29	121793
TFR2	7036
TFRC	7037
TGFA	7039
TGFBR1	7046
TGFBR2	7048
TGFBR3	7049
TGOLN2	10618
THBD	7056
THSD1	55901
THSD7A	221981
THSD7B	80731
THY1	7070
TIE1	7075
TIGIT	201633
TIMD4	91937
TLR1	7096
TLR10	81793
TLR2	7097
TLR3	7098
TLR4	7099
TLR5	7100
TLR6	10333
TLR7	51284
TLR8	51311
TLR9	54106
TMCO1	54499
TMCO2	127391
TMCO5A	145942
TMCO7	79613
TMEFF1	8577
TMEFF2	23671
TMEM105	284186
TMEM106B	54664
TMEM108	66000
TMEM123	114908
TMEM130	222865
TMEM132B	114795

TMEM132C	92293
TMEM132D	121256
TMEM132E	124842
TMEM139	135932
TMEM154	201799
TMEM156	80008
TMEM158	25907
TMEM167A	153339
TMEM183A	92703
TMEM190	147744
TMEM2	23670
TMEM207	131920
TMEM213	155006
TMEM25	84866
TMEM27	57393
TMEM53	79639
TMEM59	9528
TMEM59L	25789
TMEM81	388730
TMEM95	339168
TMEM98	26022
TMEM9B	56674
TMIGD1	388364
TMIGD2	126259
TMPRSS11B	132724
TMPRSS11D	9407
TMPRSS11F	389208
TMPRSS12	283471
TMPRSS13	84000
TMPRSS15	5651
TMPRSS2	7113
TMPRSS4	56649
TMPRSS5	80975
TMPRSS6	164656
TMPRSS7	344805
TMPRSS9	360200
TMX4	56255
TNFRSF10B	8795
TNFRSF10C	8794
TNFRSF10D	8793
TNFRSF11A	8792
TNFRSF12A	51330
TNFRSF13B	23495

TNFRSF13C	115650
TNFRSF14	8764
TNFRSF17	608
TNFRSF19	55504
TNFRSF1A	7132
TNFRSF1B	7133
TNFRSF21	27242
TNFRSF25	8718
TNFRSF4	7293
TNFRSF8	943
TNFRSF9	3604
TNFSF10	8743
TNFSF11	8600
TNFSF13	8741
TNFSF13B	10673
TNFSF14	8740
TNFSF15	9966
TNFSF18	8995
TNFSF4	7292
TNFSF8	944
TNFSF9	8744
TNMD	64102
TPBG	7162
TPO	7173
TPSG1	25823
TRAT1	50852
TREH	11181
TREM2	54209
TREML1	340205
TREML2	79865
TREML4	285852
TRHDE	29953
TRIL	9865
TSVS4718	
TXNDC15	79770
TYRO3	7301
TYROBP	7305
TYRP1	7306
TYW1	55253
ULBP1	80329
ULBP2	80328
ULBP3	79465
UMOD	7369

UMODL1	89766
UNC5A	90249
UNC5B	219699
UNC5C	8633
UNC5D	137970
UPK3BL	100134938
USMG5	84833
UXS1	80146
VAPB	9217
VASN	114990
VCAM1	7412
VEZT	55591
VLDLR	7436
VNN3	55350
VSIG1	340547
VSIG10	54621
VSIG2	23584
VSIG4	11326
VSTM1	284415
VSTM4	196740
WBP1	23559
WDR11	55717
WFDC9	259240
XG	7499
XPNPEP2	7512
XXYLT1	152002
ZP1	22917
ZP2	7783
ZP4	57829
ZPLD1	131368

Table 9. PTPRD mutants

Query (internal name)	Prey	Genotype	Normalized Absorbance	IG Family
PTPRD DELG61DELE106	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD G285EIG3	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD S912FFN7	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD S912FFN7	IL1RAP	PTPRD WT	0.583456973	IL1RAP

PTPRD R995CFN7	IL1RAP	PTPRD WT	0.493426669	IL1RAP
PTPRD P249LIG3	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD E406KFN1	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD R1088CFN8	IL1RAP	PTPRD WT	0.663809169	IL1RAP
PTPRD R1088CFN8	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD DELG61DELE106	IL1RAP	PTPRD WT	0.171856389	IL1RAP
PTPRD S431LFN2	IL1RAP	PTPRD WT	0.825183974	IL1RAP
PTPRD R561QFN3	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD R995CFN7	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD S431LFN2	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD E406KFN1	IL1RAP	PTPRD WT	0.790237242	IL1RAP
PTPRD P249LIG3	IL1RAP	PTPRD WT	0.708968451	IL1RAP
PTPRD G285EIG3	IL1RAP	PTPRD WT	0.761173661	IL1RAP
PTPRD G203EK204EIG2	IL1RAP	PTPRD WT	0.404269082	IL1RAP
PTPRD R561QFN3	IL1RAP	PTPRD WT	0.682956104	IL1RAP
PTPRD R232CR233CIG2	IL1RAP	PTPRD WT	0.793858161	IL1RAP
PTPRD P666SFN4	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD V892IFN6	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD V892IFN6	IL1RAP	PTPRD WT	0.815869786	IL1RAP
PTPRD P666SFN4	IL1RAP	PTPRD WT	0.851003875	IL1RAP
PTPRD E755KFN5	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD E755KFN5	IL1RAP	PTPRD WT	0.80789111	IL1RAP
PTPRD G203EK204EIG2	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD R232CR233CIG2	IL1RAP	PTPRD MUTANT	0.908904419	IL1RAP
PTPRD DELG61DELE106	IL1RAPL1	PTPRD WT	0.091686222	IL1RAP

PTPRD G203EK204EIG2	IL1RAPL1	PTPRD WT	0.40838459	IL1RAP
PTPRD P666SFN4	IL1RAPL1	PTPRD WT	0.841186161	IL1RAP
PTPRD R232CR233CIG2	IL1RAPL1	PTPRD WT	0.802150905	IL1RAP
PTPRD R561QFN3	IL1RAPL1	PTPRD WT	0.734719042	IL1RAP
PTPRD E755KFN5	IL1RAPL1	PTPRD WT	0.842930153	IL1RAP
PTPRD R995CFN7	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD P666SFN4	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD V892IFN6	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD S912FFN7	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD G203EK204EIG2	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD G285EIG3	IL1RAPL1	PTPRD WT	0.743707171	IL1RAP
PTPRD R1088CFN8	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD E755KFN5	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD E406KFN1	IL1RAPL1	PTPRD WT	0.8384161	IL1RAP
PTPRD V892IFN6	IL1RAPL1	PTPRD WT	0.805621806	IL1RAP
PTPRD R995CFN7	IL1RAPL1	PTPRD WT	0.497917631	IL1RAP
PTPRD P249LIG3	IL1RAPL1	PTPRD WT	0.756883932	IL1RAP
PTPRD DELG61DELE106	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD R232CR233CIG2	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD P249LIG3	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD G285EIG3	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD S912FFN7	IL1RAPL1	PTPRD WT	0.721570817	IL1RAP
PTPRD E406KFN1	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD R1088CFN8	IL1RAPL1	PTPRD WT	0.73535994	IL1RAP
PTPRD S431LFN2	IL1RAPL1	PTPRD WT	0.849690985	IL1RAP
PTPRD R561QFN3	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP

PTPRD S431LFN2	IL1RAPL1	PTPRD MUTANT	0.870808769	IL1RAP
PTPRD R1088CFN8	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD P249LIG3	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD R561QFN3	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD R1088CFN8	IL1RAPL2	PTPRD WT	0.659542836	IL1RAP
PTPRD E406KFN1	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD R561QFN3	IL1RAPL2	PTPRD WT	0.707555556	IL1RAP
PTPRD S431LFN2	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD P666SFN4	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD S431LFN2	IL1RAPL2	PTPRD WT	0.826023273	IL1RAP
PTPRD P666SFN4	IL1RAPL2	PTPRD WT	0.858480749	IL1RAP
PTPRD E755KFN5	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD E755KFN5	IL1RAPL2	PTPRD WT	0.835990112	IL1RAP
PTPRD G203EK204EIG2	IL1RAPL2	PTPRD WT	0.258887359	IL1RAP
PTPRD G285EIG3	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD V892IFN6	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD G203EK204EIG2	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD S912FFN7	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD DELG61DELE106	IL1RAPL2	PTPRD WT	0.096264856	IL1RAP
PTPRD R232CR233CIG2	IL1RAPL2	PTPRD WT	0.816430108	IL1RAP
PTPRD V892IFN6	IL1RAPL2	PTPRD WT	0.820083326	IL1RAP
PTPRD R995CFN7	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD E406KFN1	IL1RAPL2	PTPRD WT	0.812553593	IL1RAP
PTPRD R232CR233CIG2	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD R995CFN7	IL1RAPL2	PTPRD WT	0.529331164	IL1RAP

PTPRD DELG61DELE106	IL1RAPL2	PTPRD MUTANT	0.870087944	IL1RAP
PTPRD S912FFN7	IL1RAPL2	PTPRD WT	0.609555804	IL1RAP
PTPRD G285EIG3	IL1RAPL2	PTPRD WT	0.778343085	IL1RAP
PTPRD P249LIG3	IL1RAPL2	PTPRD WT	0.748732094	IL1RAP
PTPRD R561QFN3	LRFN1	PTPRD WT	0.064057436	LRFN
PTPRD P666SFN4	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD P666SFN4	LRFN1	PTPRD WT	0.150799431	LRFN
PTPRD V892IFN6	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD E755KFN5	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD R1088CFN8	LRFN1	PTPRD WT	0.082285462	LRFN
PTPRD G203EK204EIG2	LRFN1	PTPRD WT	0.004291979	LRFN
PTPRD G203EK204EIG2	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD DELG61DELE106	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD R232CR233CIG2	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD R561QFN3	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD R232CR233CIG2	LRFN1	PTPRD WT	0.00633128	LRFN
PTPRD S431LFN2	LRFN1	PTPRD WT	0.008609402	LRFN
PTPRD E755KFN5	LRFN1	PTPRD WT	0.031976146	LRFN
PTPRD V892IFN6	LRFN1	PTPRD WT	0.013097621	LRFN
PTPRD P249LIG3	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD DELG61DELE106	LRFN1	PTPRD WT	0.004490513	LRFN
PTPRD R995CFN7	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD R995CFN7	LRFN1	PTPRD WT	0.012409514	LRFN
PTPRD S912FFN7	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD G285EIG3	LRFN1	PTPRD MUTANT	0.882889903	LRFN

PTPRD S431LFN2	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD E406KFN1	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD G285EIG3	LRFN1	PTPRD WT	0.008270135	LRFN
PTPRD S912FFN7	LRFN1	PTPRD WT	0.081130356	LRFN
PTPRD P249LIG3	LRFN1	PTPRD WT	0.074002393	LRFN
PTPRD E406KFN1	LRFN1	PTPRD WT	0.010664312	LRFN
PTPRD R1088CFN8	LRFN1	PTPRD MUTANT	0.882889903	LRFN
PTPRD S912FFN7	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD E406KFN1	LRFN4	PTPRD WT	0.777644847	LRFN
PTPRD E406KFN1	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD P249LIG3	LRFN4	PTPRD WT	0.736647927	LRFN
PTPRD R1088CFN8	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD DELG61DELE106	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD P249LIG3	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD G285EIG3	LRFN4	PTPRD WT	0.744967588	LRFN
PTPRD S431LFN2	LRFN4	PTPRD WT	0.844047229	LRFN
PTPRD G285EIG3	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD S431LFN2	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD R561QFN3	LRFN4	PTPRD WT	0.581704223	LRFN
PTPRD R1088CFN8	LRFN4	PTPRD WT	0.649351843	LRFN
PTPRD R995CFN7	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD G203EK204EIG2	LRFN4	PTPRD WT	0.09333118	LRFN
PTPRD P666SFN4	LRFN4	PTPRD WT	0.877205001	LRFN
PTPRD R232CR233CIG2	LRFN4	PTPRD WT	0.651827355	LRFN
PTPRD E755KFN5	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD R561QFN3	LRFN4	PTPRD MUTANT	0.883468208	LRFN

PTPRD P666SFN4	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD V892IFN6	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD G203EK204EIG2	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD DELG61DELE106	LRFN4	PTPRD WT	0.062552975	LRFN
PTPRD S912FFN7	LRFN4	PTPRD WT	0.607343851	LRFN
PTPRD V892IFN6	LRFN4	PTPRD WT	0.812010444	LRFN
PTPRD R232CR233CIG2	LRFN4	PTPRD MUTANT	0.883468208	LRFN
PTPRD E755KFN5	LRFN4	PTPRD WT	0.838693124	LRFN
PTPRD R995CFN7	LRFN4	PTPRD WT	0.479424217	LRFN
PTPRD P666SFN4	LRFN5	PTPRD WT	0.829983526	LRFN
PTPRD DELG61DELE106	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD R232CR233CIG2	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD E755KFN5	LRFN5	PTPRD WT	0.838841567	LRFN
PTPRD V892IFN6	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD V892IFN6	LRFN5	PTPRD WT	0.814991482	LRFN
PTPRD P666SFN4	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD E755KFN5	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD R995CFN7	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD G203EK204EIG2	LRFN5	PTPRD WT	0.080446747	LRFN
PTPRD DELG61DELE106	LRFN5	PTPRD WT	0.057157224	LRFN
PTPRD R232CR233CIG2	LRFN5	PTPRD WT	0.100375555	LRFN
PTPRD G285EIG3	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD S912FFN7	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD R995CFN7	LRFN5	PTPRD WT	0.384235693	LRFN
PTPRD P249LIG3	LRFN5	PTPRD MUTANT	0.844595347	LRFN

PTPRD R1088CFN8	LRFN5	PTPRD WT	0.631480791	LRFN
PTPRD R561QFN3	LRFN5	PTPRD WT	0.701779109	LRFN
PTPRD E406KFN1	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD P249LIG3	LRFN5	PTPRD WT	0.766294876	LRFN
PTPRD G285EIG3	LRFN5	PTPRD WT	0.72759346	LRFN
PTPRD S912FFN7	LRFN5	PTPRD WT	0.584031267	LRFN
PTPRD G203EK204EIG2	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD R561QFN3	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD E406KFN1	LRFN5	PTPRD WT	0.76320489	LRFN
PTPRD R1088CFN8	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD S431LFN2	LRFN5	PTPRD WT	0.84666801	LRFN
PTPRD S431LFN2	LRFN5	PTPRD MUTANT	0.844595347	LRFN
PTPRD R1088CFN8	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD G285EIG3	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD DELG61DELE106	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD P249LIG3	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD S912FFN7	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD R995CFN7	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD S912FFN7	LRRC4B	PTPRD WT	0.081146473	LRRC
PTPRD R1088CFN8	LRRC4B	PTPRD WT	0.090078329	LRRC
PTPRD R995CFN7	LRRC4B	PTPRD WT	0.041338886	LRRC
PTPRD V892IFN6	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD G285EIG3	LRRC4B	PTPRD WT	0.084741163	LRRC
PTPRD E406KFN1	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD P249LIG3	LRRC4B	PTPRD WT	0.073544789	LRRC
PTPRD R232CR233CIG2	LRRC4B	PTPRD WT	0.044383749	LRRC

PTPRD G203EK204EIG2	LRRC4B	PTPRD WT	0.024765296	LRRC
PTPRD DELG61DELE106	LRRC4B	PTPRD WT	0.039054643	LRRC
PTPRD S431LFN2	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD E406KFN1	LRRC4B	PTPRD WT	0.065698194	LRRC
PTPRD P666SFN4	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD E755KFN5	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD R561QFN3	LRRC4B	PTPRD WT	0.066408314	LRRC
PTPRD R232CR233CIG2	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD S431LFN2	LRRC4B	PTPRD WT	0.068419992	LRRC
PTPRD V892IFN6	LRRC4B	PTPRD WT	0.089097104	LRRC
PTPRD G203EK204EIG2	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD R561QFN3	LRRC4B	PTPRD MUTANT	0.585780347	LRRC
PTPRD P666SFN4	LRRC4B	PTPRD WT	0.073476112	LRRC
PTPRD E755KFN5	LRRC4B	PTPRD WT	0.200511073	LRRC
PTPRD G285EIG3	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD R232CR233CIG2	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD E406KFN1	NTRK3	PTPRD WT	0.221500598	NTRK
PTPRD P249LIG3	NTRK3	PTPRD WT	0.182133642	NTRK
PTPRD P249LIG3	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD DELG61DELE106	NTRK3	PTPRD WT	0.008984574	NTRK
PTPRD G285EIG3	NTRK3	PTPRD WT	0.096383487	NTRK
PTPRD DELG61DELE106	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD R1088CFN8	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD G203EK204EIG2	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD R995CFN7	NTRK3	PTPRD MUTANT	0.630524324	NTRK

PTPRD S912FFN7	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD P666SFN4	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD V892IFN6	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD E755KFN5	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD S431LFN2	NTRK3	PTPRD WT	0.182518859	NTRK
PTPRD E406KFN1	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD R1088CFN8	NTRK3	PTPRD WT	0.181007248	NTRK
PTPRD S912FFN7	NTRK3	PTPRD WT	0.167599851	NTRK
PTPRD R995CFN7	NTRK3	PTPRD WT	0.081117697	NTRK
PTPRD V892IFN6	NTRK3	PTPRD WT	0.203234229	NTRK
PTPRD E755KFN5	NTRK3	PTPRD WT	0.398734177	NTRK
PTPRD R561QFN3	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD S431LFN2	NTRK3	PTPRD MUTANT	0.630524324	NTRK
PTPRD G203EK204EIG2	NTRK3	PTPRD WT	0.012110447	NTRK
PTPRD P666SFN4	NTRK3	PTPRD WT	0.588969823	NTRK
PTPRD R232CR233CIG2	NTRK3	PTPRD WT	0.035020775	NTRK
PTPRD R561QFN3	NTRK3	PTPRD WT	0.140622222	NTRK
PTPRD R1088CFN8	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD V892IFN6	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD S912FFN7	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD R995CFN7	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD R1088CFN8	SLITRK1	PTPRD WT	0.368304804	SLITRK
PTPRD S912FFN7	SLITRK1	PTPRD WT	0.401634776	SLITRK
PTPRD R995CFN7	SLITRK1	PTPRD WT	0.396226415	SLITRK
PTPRD V892IFN6	SLITRK1	PTPRD WT	0.6573988	SLITRK
PTPRD E755KFN5	SLITRK1	PTPRD WT	0.784636256	SLITRK
PTPRD P666SFN4	SLITRK1	PTPRD WT	0.853102503	SLITRK

PTPRD R561QFN3	SLITRK1	PTPRD WT	0.460399113	SLITRK
PTPRD S431LFN2	SLITRK1	PTPRD WT	0.76978183	SLITRK
PTPRD E406KFN1	SLITRK1	PTPRD WT	0.650764007	SLITRK
PTPRD P249LIG3	SLITRK1	PTPRD WT	0.580838323	SLITRK
PTPRD G285EIG3	SLITRK1	PTPRD WT	0.646817599	SLITRK
PTPRD DELG61DELE106	SLITRK1	PTPRD WT	0.034968596	SLITRK
PTPRD R232CR233CIG2	SLITRK1	PTPRD WT	0.01082124	SLITRK
PTPRD G203EK204EIG2	SLITRK1	PTPRD WT	0.011778085	SLITRK
PTPRD P666SFN4	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD R561QFN3	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD S431LFN2	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD E406KFN1	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD P249LIG3	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD G285EIG3	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD DELG61DELE106	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD E755KFN5	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD G203EK204EIG2	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD R232CR233CIG2	SLITRK1	PTPRD MUTANT	0.815953757	SLITRK
PTPRD R1088CFN8	SLITRK2	PTPRD WT	0.00390262	SLITRK
PTPRD S912FFN7	SLITRK2	PTPRD WT	0.003546099	SLITRK
PTPRD V892IFN6	SLITRK2	PTPRD WT	0.016240116	SLITRK
PTPRD E755KFN5	SLITRK2	PTPRD WT	0.009121132	SLITRK
PTPRD R995CFN7	SLITRK2	PTPRD WT	0.01310268	SLITRK
PTPRD P666SFN4	SLITRK2	PTPRD WT	0.031911204	SLITRK
PTPRD R561QFN3	SLITRK2	PTPRD WT	0.008533333	SLITRK
PTPRD R1088CFN8	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK

PTPRD S912FFN7	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD R995CFN7	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD V892IFN6	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD E755KFN5	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD P666SFN4	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD R561QFN3	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD S431LFN2	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD E406KFN1	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD P249LIG3	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD G285EIG3	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD DELG61DELE106	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD R232CR233CIG2	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD G203EK204EIG2	SLITRK2	PTPRD MUTANT	0.441207627	SLITRK
PTPRD G203EK204EIG2	SLITRK2	PTPRD WT	0.006721192	SLITRK
PTPRD E406KFN1	SLITRK2	PTPRD WT	0.005830904	SLITRK
PTPRD P249LIG3	SLITRK2	PTPRD WT	0.000444879	SLITRK
PTPRD S431LFN2	SLITRK2	PTPRD WT	0.006428513	SLITRK
PTPRD DELG61DELE106	SLITRK2	PTPRD WT	0.001867572	SLITRK
PTPRD G285EIG3	SLITRK2	PTPRD WT	0.011447469	SLITRK
PTPRD R232CR233CIG2	SLITRK2	PTPRD WT	0.011956989	SLITRK
PTPRD R1088CFN8	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD S912FFN7	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD E406KFN1	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK

PTPRD P249LIG3	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD G285EIG3	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD DELG61DELE106	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD R232CR233CIG2	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD G203EK204EIG2	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD P666SFN4	SLITRK3	PTPRD WT	0.866758007	SLITRK
PTPRD R561QFN3	SLITRK3	PTPRD WT	0.541560961	SLITRK
PTPRD S431LFN2	SLITRK3	PTPRD WT	0.828796327	SLITRK
PTPRD E406KFN1	SLITRK3	PTPRD WT	0.78892497	SLITRK
PTPRD P249LIG3	SLITRK3	PTPRD WT	0.676036543	SLITRK
PTPRD G285EIG3	SLITRK3	PTPRD WT	0.636642784	SLITRK
PTPRD DELG61DELE106	SLITRK3	PTPRD WT	0.054076962	SLITRK
PTPRD R232CR233CIG2	SLITRK3	PTPRD WT	0.015008904	SLITRK
PTPRD G203EK204EIG2	SLITRK3	PTPRD WT	0.120458582	SLITRK
PTPRD P666SFN4	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD R561QFN3	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD S431LFN2	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD R1088CFN8	SLITRK3	PTPRD WT	0.589776593	SLITRK
PTPRD R995CFN7	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD V892IFN6	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD E755KFN5	SLITRK3	PTPRD MUTANT	0.804393064	SLITRK
PTPRD S912FFN7	SLITRK3	PTPRD WT	0.563981917	SLITRK
PTPRD R995CFN7	SLITRK3	PTPRD WT	0.40254022	SLITRK
PTPRD V892IFN6	SLITRK3	PTPRD WT	0.711614588	SLITRK
PTPRD E755KFN5	SLITRK3	PTPRD WT	0.81799521	SLITRK
PTPRD P249LIG3	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK

PTPRD G285EIG3	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD E406KFN1	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD DELG61DELE106	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD R232CR233CIG2	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD G203EK204EIG2	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD R1088CFN8	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD S912FFN7	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD R995CFN7	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD V892IFN6	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD E755KFN5	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD P666SFN4	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD R561QFN3	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD S431LFN2	SLITRK6	PTPRD MUTANT	0.757773837	SLITRK
PTPRD R1088CFN8	SLITRK6	PTPRD WT	0.752689161	SLITRK
PTPRD S912FFN7	SLITRK6	PTPRD WT	0.722668143	SLITRK
PTPRD R995CFN7	SLITRK6	PTPRD WT	0.615071973	SLITRK
PTPRD V892IFN6	SLITRK6	PTPRD WT	0.816558578	SLITRK
PTPRD E755KFN5	SLITRK6	PTPRD WT	0.835956209	SLITRK
PTPRD P666SFN4	SLITRK6	PTPRD WT	0.859736256	SLITRK
PTPRD R561QFN3	SLITRK6	PTPRD WT	0.641844501	SLITRK
PTPRD S431LFN2	SLITRK6	PTPRD WT	0.841095441	SLITRK
PTPRD E406KFN1	SLITRK6	PTPRD WT	0.811656127	SLITRK
PTPRD P249LIG3	SLITRK6	PTPRD WT	0.790056219	SLITRK
PTPRD G285EIG3	SLITRK6	PTPRD WT	0.773797339	SLITRK
PTPRD DELG61DELE106	SLITRK6	PTPRD WT	0.096626547	SLITRK
PTPRD R232CR233CIG2	SLITRK6	PTPRD WT	0.807512931	SLITRK

PTPRD G203EK204EIG2	SLITRK6	PTPRD WT	0.383336025	SLITRK

Table 10. Cox proportional hazards for survival analysis of CRC patient data

Gene or Signature	Survival Model	Dataset	Stage	N	HR	95% Confidence Interval	P-value	Signif. level
PDPN	*RFS ~ PDPN*	GSE33113	II	85	3.696	2.043 - 6.686	1.55E-05	***
	RFS ~ PDPN	GSE39582	I	37	0.6827	0.06547 - 7.119	7.50E-01	
			II	235	1.286	0.9968 - 1.658	5.30E-02	^
			III	183	0.956	0.7365 - 1.241	7.35E-01	
			IV	56	1.705	1.205 - 2.412	2.60E-03	***
			ALL	511	1.227	1.051 - 1.432	9.48E-03	**
Activated Fibroblasts	*RFS ~ Act. Fib.*	GSE33113	II	85	3.054	1.559 - 5.98	1.13E-03	**
	RFS ~ Act. Fib.	GSE39582	II	235	1.575	1.153 - 2.152	4.36E-03	**
			ALL	511	1.55	1.287 - 1.866	3.83E-06	***
	RFS ~ Act. Fib. + STAGE	GSE39582	ALL	511	1.472	1.2161 - 1.781	7.20E-05	***
FAP Fibroblasts	*RFS ~ FAP Fib.*	GSE33113	II	85	4.055	1.694 - 9.703	1.66E-03	**
	RFS ~ FAP Fib.	GSE39582	II	235	1.618	1.129 - 2.317	8.74E-03	**
			ALL	511	1.612	1.303 - 1.994	1.07E-05	***
	RFS ~ FAP Fib. + STAGE	GSE39582	ALL	511	1.516	1.2207 - 1.882	1.66E-04	***

^p < 0.1, *p < 0.05, **p < 0.01, ***p < 0.0001

Table 11. Genes in activated fibroblast signature

Gene Symbol	EntrezID
ACTA2	59
CALD1	800
CDH11	1009
FAP	2191
LRRC15	131578
PDPN	10630
POSTN	10631
S100A4	6275

Table 12. Genes in FAP$^+$ fibroblast signature and expression levels across sorted cell types

					Average expression				
Gene Symbol	logFC	t	P.Value	adj.P.Val	EpCAM+	CD45+	FAP+	CD31+	All cells
LUM	7.19308115	35.3139128	1.70E-23	3.53E-19	1.40040376	1.60445265	8.71176024	1.55118084	3.31694937
CXCL14	6.03015105	24.0745447	2.27E-19	9.41E-16	2.33522259	2.04403339	8.23664139	2.24021503	3.7140281
AXL	4.51231586	20.4661023	1.17E-17	3.48E-14	2.41667865	2.55913915	6.9251358	2.26264202	3.5408989
VCAN	5.63154046	18.0147843	2.49E-16	4.69E-13	2.07637682	2.50051759	8.115062	2.87367019	3.89140665
SPON2	4.39501999	17.031275	9.37E-16	1.39E-12	2.56757098	2.9999312	7.12604115	2.62556131	3.82977616
FIBIN	4.00037496	16.8895736	1.14E-15	1.48E-12	2.29978418	2.23936459	6.20826318	2.0845159	3.20798196
CYGB	4.42690977	16.7824147	1.32E-15	1.53E-12	2.31706058	2.33546892	6.92222735	2.83342322	3.60204502
PCDH18	3.69897361	16.3403118	2.48E-15	2.70E-12	2.72655021	2.69110957	6.39751091	2.67795214	3.62328071
ISLR	4.9977407	15.095215	1.56E-14	1.41E-11	2.43522776	2.38090673	7.44790411	2.53435575	3.69959859
GPNMB	4.52944591	14.2335775	5.99E-14	4.97E-11	2.75280662	2.96190655	7.33947507	2.71537432	3.94239064
PDGFC	3.82419051	14.1391255	6.97E-14	5.56E-11	1.76362833	2.08393581	5.82924698	2.16760527	2.9611041
MEIS1	3.58955935	13.4291911	2.23E-13	1.60E-10	2.37801633	1.94108428	5.79055452	2.28388493	3.09838501
C4A /// C4B ///	3.31847486	13.0665004	4.13E-13	2.67E-10	2.39568223	2.5945314	5.88802473	2.71843598	3.39916858

LOC100292046									
ASPN	3.98565876	12.6555752	8.40E-13	4.84E-10	2.31628389	2.7249375	6.49181237	2.47723946	3.50256831
COL8A1	4.01803272	12.2920589	1.60E-12	8.28E-10	2.78259124	2.45244548	6.71367016	2.85187559	3.70014562
GREM1	3.88866254	12.1587295	2.03E-12	1.03E-09	1.68427858	1.47290709	5.46626306	1.57561589	2.54976615
MMP3	5.0885164	11.3810798	8.51E-12	3.75E-09	1.89457043	1.69268306	6.92613481	1.92560172	3.1097475
ADAMDEC1	4.70625553	11.0829627	1.50E-11	6.23E-09	1.11891724	1.43324281	5.95461976	1.19293263	2.42492811
MFAP4	3.15346624	10.4150649	5.56E-11	2.26E-08	1.89058524	1.871057	5.06999834	1.98795406	2.70489866
TWIST1	3.02315709	10.3499666	6.33E-11	2.53E-08	2.16581835	2.29543144	5.21756981	2.12198837	2.95020199
WNT2B	2.97709497	10.1845352	8.84E-11	3.34E-08	2.9371018	2.32028399	5.66784363	2.8148602	3.43502241
MXRA8	3.24208188	10.0450901	1.17E-10	4.20E-08	2.74274777	2.65946976	5.88807444	2.53576016	3.45651303
SDK1	3.05852336	10.050661	1.16E-10	4.20E-08	2.66183316	2.21512299	5.52975974	2.53675297	3.23586721
LRRN4CL	3.34797	9.83629266	1.81E-10	6.24E-08	2.10861241	1.5420821	5.19631839	1.89435068	2.6853409
WNT5A	4.19946715	9.60847443	2.91E-10	9.42E-08	1.07377208	1.08282947	5.28309242	1.09427425	2.13349206
FNDC1	3.3485901	9.59987577	2.96E-10	9.44E-08	2.60171628	2.58443732	5.96461573	2.6619233	3.45317316
CHI3L1	4.28455717	9.42977509	4.24E-10	1.31E-07	2.96362673	2.86166315	7.21226167	2.95782361	3.99884379
COL7A1	2.75433407	9.3378982	5.16E-10	1.53E-07	2.82929048	2.6164538	5.45382244	2.65272081	3.38807188
LOXL1	2.81018719	9.08959933	8.80E-10	2.53E-07	2.87091799	2.61912077	5.5218389	2.64491637	3.41419851
PLXDC1	2.91317831	8.58888266	2.65E-09	7.05E-07	2.45173707	2.91564477	5.45213455	2.24948688	3.26725082
COL11A1	3.42467138	8.02728745	9.49E-09	2.19E-06	1.65010987	1.7237981	5.12498818	1.72704242	2.55648464
TBX2	3.01723634	7.8389565	1.47E-08	3.18E-06	2.13947242	2.23206179	5.30973318	2.50595633	3.04680593
NOTCH3	2.36806199	6.16351089	8.75E-07	0.00013547	2.92654284	2.67265753	5.22744073	2.97893585	3.45139424

SLIT3	2.805 58497	5.556 47049	4.15 E-06	0.000 55838	2.167967 54	2.213966 34	5.0007 1286	2.2034 498	2.8965 2413
SFRP4	2.752 06796	4.738 86214	3.49 E-05	0.003 69712	2.673690 52	2.697740 11	5.3324 0291	2.3695 7423	3.2683 5195

Average expression cutoffs were as follows: FAP+ > 5, EpCAM+ < 3, CD31+ < 3, CD45+ < 3.

Table 13. Parameters for phospho-proteomics assay

	Samples	TMT reagents	TMT reporter ions
Bioreplicate 1	DMSO	TMT10-126	126.1277
	Clec 2 min	TMT10-127N	127.1246
	Clec 30 min	TMT10-127C	127.1309
	CD177 2 min	TMT10-128N	128.1281
	CD177 30 min	TMT10-128C	128.1341
Bioreplicate 2	DMSO	TMT10-129N	129.1317
	Clec 2 min	TMT10-129C	129.1376
	Clec 30 min	TMT10-130N	130.1348
	CD177 2 min	TMT10-130C	130.1409
	CD177 30 min	TMT10-131	131.1381

Table 14. IgSF prediction training set

Query (Short Name)	Prey (Short Name)	Class
ALCAM	ALCAM	Positive
ALCAM	CD6	Positive
AMICA1	CXADR	Positive
AMIGO1	AMIGO2	Positive
BTLA	TNFRSF14	Positive
CADM1	CADM1	Positive
CADM1	CADM3	Positive
CADM1	CRTAM	Positive
CADM2	CADM2	Positive
CADM2	CADM3	Positive
CADM2	CADM4	Positive
CADM3	CADM2	Positive
CADM3	CADM3	Positive
CADM3	CADM4	Positive
CD177	PDPN	Positive

CD2	CD58	Positive
CD200	CD200R1	Positive
CD226	PVR	Positive
CD226	PVRL2	Positive
CD274	CD80	Positive
CD274	EPHA3	Positive
CD276	IL20RA	Positive
CD28	CD80	Positive
CD28	CD86	Positive
CD28	ICOSLG	Positive
CD33	CD33	Positive
CD47	SIRPA	Positive
CD47	SIRPG	Positive
CD80	CD28	Positive
CD84	CD84	Positive
CD86	CD28	Positive
CD96	PVR	Positive
CD96	PVRL1	Positive
CEACAM1	CEACAM1	Positive
CEACAM1	CEACAM8	Positive
CLEC1B	PDPN	Positive
CSF1R	CSF1	Positive
DLK1	ACVR2B	Positive
DLK1	ERBB4	Positive
DSCAML1	DSCAML1	Positive
EDAR	EDA	Positive
EFNB2	EPHA1	Positive
EFNB2	EPHA1	Positive
EFNB2	EPHA10	Positive
EFNB2	EPHA2	Positive
EFNB2	EPHA3	Positive
EFNB2	EPHA4	Positive
EFNB2	EPHA7	Positive

EFNB2	EPHA8	Positive
EFNB2	EPHB4	Positive
EPHB6	EPHB1	Positive
EPHB6	EPHB2	Positive
FAS	FASLG	Positive
HHLA2	TMIGD2	Positive
ICOS	ICOSLG	Positive
JAM2	JAM3	Positive
JAM3	JAM2	Positive
JAM3	JAM3	Positive
LRIG1	C10orf54	Positive
MPZL2	MPZL3	Positive
PDCD1	CD274	Positive
PDCD1	PDCD1LG2	Positive
PDCD1LG2	CEACAM4	Positive
PDPN	CD177	Positive
PVR	CD44	Positive
PVR	KIR2DL5A	Positive
PVR	NECTIN3	Positive
PVR	TIGIT	Positive
PVRL1	PVRL1	Positive
PVRL1	NECTIN3	Positive
PVRL2	CD226	Positive
PVRL2	PVRL2	Positive
PVRL2	NECTIN3	Positive
PVRL2	TIGIT	Positive
NECTIN3	PVR	Positive
NECTIN3	NECTIN3	Positive
PVRL4	PVRL1	Positive
PVRL4	PVRL4	Positive
PVRL4	TIGIT	Positive
REG4	EDAR	Positive
SEMA4A	PLXNB1	Positive

SEMA4A	PLXNB2	Positive
SEMA4A	PLXNB3	Positive
SEMA4A	PLXND1	Positive
SIRPA	CD47	Positive
SIRPG	CD47	Positive
TNFRSF18	TNFSF18	Positive
TNFRSF8	TNFSF8	Positive
UNC5A	FLRT1	Positive
UNC5A	FLRT2	Positive
UNC5A	FLRT3	Positive
UNC5B	FLRT1	Positive
UNC5B	FLRT2	Positive
UNC5B	FLRT3	Positive
UNC5D	FLRT1	Positive
UNC5D	FLRT2	Positive
UNC5D	FLRT3	Positive
RTN4R	*	Non-Specific
SIGLEC5	*	Non-Specific
SIGLEC15	*	Non-Specific
SIGLEC6	*	Non-Specific
MAG	*	Non-Specific
ICAM5	*	Non-Specific
SIGLEC9	*	Non-Specific

(*) all queries screened against this prey

Table 15. Gene pairs predicting responsiveness to atezolizumab

Gene pair	First gene	Second gene	Hazard ratio (HR)	p value HR
SIGLEC6_NCR1	SIGLEC6	NCR1	0.681	0.003
BTN3A1_LRRC4B	BTN3A1	LRRC4B	0.704	0.008
CD80_CTLA4	CD80	CTLA4	0.711	0.009
BTN3A3_LRRC4B	BTN3A3	LRRC4B	0.767	0.043
NCR1_SIGLEC8	NCR1	SIGLEC8	0.774	0.051
CNTFR_LILRB4	CNTFR	LILRB4	0.826	0.147
FGFR3_LRRTM2	FGFR3	LRRTM2	0.86	0.25
FGFR4_SIGLEC15	FGFR4	SIGLEC15	0.861	0.255

FGFR1_KL	FGFR1	KL	0.863	0.26
EFNB2_EPHA10	EFNB2	EPHA10	0.632	0.001
CTLA4_PCDHGB4	CTLA4	PCDHGB4	0.694	0.005
KIR2DL4_MOG	KIR2DL4	MOG	0.701	0.007
SIGLEC6_KIR2DL4	SIGLEC6	KIR2DL4	0.703	0.007
SLAMF7_SLAMF7	SLAMF7	SLAMF7	0.703	0.007
CTLA4_FAM200A	CTLA4	FAM200A	0.726	0.015
ILDR2_CLEC12B	ILDR2	CLEC12B	0.734	0.019
CA12_SIGLEC6	CA12	SIGLEC6	0.735	0.019
EFNB1_TRHDE	EFNB1	TRHDE	0.736	0.02
CADM1_CRTAM	CADM1	CRTAM	0.744	0.024
HHLA2_KIR3DL3	HHLA2	KIR3DL3	0.746	0.026
HHLA2_TMIGD2	HHLA2	TMIGD2	0.746	0.026
HHLA2_VSTM2B	HHLA2	VSTM2B	0.746	0.026
CD79B_CD244	CD79B	CD244	0.748	0.027
BTN2A1_FAM187B	BTN2A1	FAM187B	0.749	0.027
EFNB1_ITLN1	EFNB1	ITLN1	0.754	0.032
CTLA4_ICOSLG	CTLA4	ICOSLG	0.761	0.038
CD7_ADAM15	CD7	ADAM15	0.762	0.039
DAG1_EFNB1	DAG1	EFNB1	0.766	0.043
NRCAM_LCTL	NRCAM	LCTL	0.77	0.047
CD3D_CDHR2	CD3D	CDHR2	0.773	0.05
TCTN3_FCRL1	TCTN3	FCRL1	0.776	0.055
PTPRT_PTPRT	PTPRT	PTPRT	0.784	0.065
NRCAM_NFASC	NRCAM	NFASC	0.787	0.069
TNFRSF21_PI16	TNFRSF21	PI16	0.788	0.07
TGOLN2_BTN3A1	TGOLN2	BTN3A1	0.795	0.081
CD244_IYD	CD244	IYD	0.797	0.083
CD5_TNFRSF25	CD5	TNFRSF25	0.803	0.095
KIR3DL1_TREML1	KIR3DL1	TREML1	0.805	0.098
CD80_CD274	CD80	CD274	0.809	0.106
PDCD1_CD274	PDCD1	CD274	0.81	0.109
CR2_ILDR1	CR2	ILDR1	0.811	0.112
TNFSF9_FCRL1	TNFSF9	FCRL1	0.813	0.115
SIGLEC8_SIGLEC8	SIGLEC8	SIGLEC8	0.814	0.117
SIGLEC8_TEX101	SIGLEC8	TEX101	0.814	0.117
SIGLEC8_TREML4	SIGLEC8	TREML4	0.814	0.117
MCAM_CD226	MCAM	CD226	0.816	0.121
CRTAM_ILDR2	CRTAM	ILDR2	0.816	0.122
CADM1_CADM3	CADM1	CADM3	0.817	0.122
ALCAM_CD6	ALCAM	CD6	0.817	0.123
CEACAM6_STAB1	CEACAM6	STAB1	0.82	0.131
TNFRSF9_TNFSF9	TNFRSF9	TNFSF9	0.822	0.135

FGFR3_KL	FGFR3	KL	0.822	0.136
CD4_SIGLEC6	CD4	SIGLEC6	0.826	0.144
CD28_ICOSLG	CD28	ICOSLG	0.826	0.145
CD28_TMEM95	CD28	TMEM95	0.826	0.145
TNFRSF8_TNFSF8	TNFRSF8	TNFSF8	0.827	0.147
NRXN3_FGFRL1	NRXN3	FGFRL1	0.828	0.152
BTN3A1_LRRC4C	BTN3A1	LRRC4C	0.831	0.158
CD28_CD80	CD28	CD80	0.832	0.161
CADM3_CADM2	CADM3	CADM2	0.833	0.165
LSAMP_OPCML	LSAMP	OPCML	0.837	0.174
CD300LF_IGSF5	CD300LF	IGSF5	0.837	0.175
PDCD1_PDCD1LG2	PDCD1	PDCD1LG2	0.84	0.183
CD47_SIRPG	CD47	SIRPG	0.84	0.184
PRLR_CADM3	PRLR	CADM3	0.843	0.194
IGSF21_ILDR2	IGSF21	ILDR2	0.845	0.202
CNTN1_NRCAM	CNTN1	NRCAM	0.847	0.205
FLT3_FLT3LG	FLT3	FLT3LG	0.847	0.205
NTRK3_CRTAM	NTRK3	CRTAM	0.847	0.206
PLXNB1_SEMA4D	PLXNB1	SEMA4D	0.849	0.214
PRLR_KIAA0090	PRLR	KIAA0090	0.851	0.218
PRLR_NCR2	PRLR	NCR2	0.851	0.218
CD48_PDCD1	CD48	PDCD1	0.853	0.224
SLAMF6_SLAMF6	SLAMF6	SLAMF6	0.855	0.233
ADAM20_IL1RAPL1	ADAM20	IL1RAPL1	0.856	0.236
BTN3A1_VSIG8	BTN3A1	VSIG8	0.856	0.236
KIR3DL1_VSIG8	KIR3DL1	VSIG8	0.858	0.245
CSF2RB_ILDR2	CSF2RB	ILDR2	0.862	0.259
TNFRSF11A_PDCD1LG2	TNFRSF11A	PDCD1LG2	0.864	0.265
SEMA7A_UNC5D	SEMA7A	UNC5D	0.865	0.271
SIGLEC8_LRRC4C	SIGLEC8	LRRC4C	0.866	0.272
TNFRSF17_LY9	TNFRSF17	LY9	0.866	0.272
IL1RAP_PTPRS	IL1RAP	PTPRS	0.866	0.273
IL18R1_NETO2	IL18R1	NETO2	0.868	0.28
PLXNB2_SEMA4C	PLXNB2	SEMA4C	0.868	0.28
CD2_NLGN3	CD2	NLGN3	0.869	0.286
PVR_TIGIT	PVR	TIGIT	0.871	0.293
SELL_UNC5D	SELL	UNC5D	0.872	0.297
CD300C_IGSF5	CD300C	IGSF5	0.877	0.315
ADAM21_CRTAM	ADAM21	CRTAM	0.879	0.328
CNTN1_IL23R	CNTN1	IL23R	0.881	0.335
CD59_TNFSF15	CD59	TNFSF15	0.884	0.345
CD86_CTLA4	CD86	CTLA4	0.885	0.35
EFNB2_FCRL1	EFNB2	FCRL1	0.885	0.35

FLT1_CD300LB	FLT1	CD300LB	0.887	0.36
IL1RAP_PTPRF	IL1RAP	PTPRF	0.887	0.363
PTPRD_IL1RAPL1	PTPRD	IL1RAPL1	0.888	0.366
SIGLEC8_LRFN2	SIGLEC8	LRFN2	0.889	0.37
TNFRSF18_TNFSF18	TNFRSF18	TNFSF18	0.89	0.376
ACVR2B_DLK1	ACVR2B	DLK1	0.89	0.378
IMPG2_CADM3	IMPG2	CADM3	0.893	0.387
CD6_SIGLEC8	CD6	SIGLEC8	0.893	0.388
TNFRSF17_CD300E	TNFRSF17	CD300E	0.893	0.389
FGFR4_NRXN3	FGFR4	NRXN3	0.893	0.391
CD4_NCR1	CD4	NCR1	0.894	0.394
FCGR2A_PDCD1	FCGR2A	PDCD1	0.894	0.394
ICAM5_PDCD1LG2	ICAM5	PDCD1LG2	0.895	0.398
NRCAM_CNTN2	NRCAM	CNTN2	0.895	0.398
CD79A_VSIG8	CD79A	VSIG8	0.897	0.407
GPC1_TNFRSF11B	GPC1	TNFRSF11B	0.9	0.42
CD47_PCSK4	CD47	PCSK4	0.9	0.423
CD244_MUC15	CD244	MUC15	0.902	0.431
FCRL4_AMICA1	FCRL4	AMICA1	0.903	0.438
TNFRSF14_BTLA	TNFRSF14	BTLA	0.905	0.444
PRLR_IMPG2	PRLR	IMPG2	0.904	0.445
PTPRS_LRRC4B	PTPRS	LRRC4B	0.906	0.453
PTPRD_SLITRK1	PTPRD	SLITRK1	0.907	0.456
NTRK3_SIGLEC8	NTRK3	SIGLEC8	0.909	0.47
PTPRS_IL1RAPL1	PTPRS	IL1RAPL1	0.91	0.472
FGFR4_MCAM	FGFR4	MCAM	0.912	0.48
CNTN4_AQPEP	CNTN4	AQPEP	0.916	0.504
NTNG1_SIGLEC8	NTNG1	SIGLEC8	0.916	0.505
PILRB_EPHA10	PILRB	EPHA10	0.918	0.516
PTPRS_LRFN5	PTPRS	LRFN5	0.92	0.523
FGFR3_IL1RAPL2	FGFR3	IL1RAPL2	0.92	0.524
RECK_TIGIT	RECK	TIGIT	0.922	0.536
NTM_THSD7A	NTM	THSD7A	0.923	0.541
LRRN2_TMEM123	LRRN2	TMEM123	0.926	0.556
NCAM2_NCAM2	NCAM2	NCAM2	0.928	0.568
FLRT3_UNC5A	FLRT3	UNC5A	0.928	0.569
IL1RAPL1_CNTN5	IL1RAPL1	CNTN5	0.929	0.573
KITLG_LRRN3	KITLG	LRRN3	0.931	0.582
IL4R_SIGLEC8	IL4R	SIGLEC8	0.931	0.583
PTPRD_LRFN5	PTPRD	LRFN5	0.931	0.584
ACE2_TIGIT	ACE2	TIGIT	0.931	0.586
CRTAM_MUC15	CRTAM	MUC15	0.932	0.592
EFNB2_KLRAP1	EFNB2	KLRAP1	0.932	0.592

MFAP3L_PI16	MFAP3L	PI16	0.933	0.595
SIGLEC7_PCDHAC1	SIGLEC7	PCDHAC1	0.933	0.598
FLT4_FCRL1	FLT4	FCRL1	0.937	0.619
TNFRSF17_NEGR1	TNFRSF17	NEGR1	0.938	0.622
LRRN1_LRRC4C	LRRN1	LRRC4C	0.939	0.631
SIRPA_TIGIT	SIRPA	TIGIT	0.941	0.644
PTPRF_LRRC4B	PTPRF	LRRC4B	0.944	0.66
CD47_SCN1B	CD47	SCN1B	0.944	0.661
CD1B_IL6ST	CD1B	IL6ST	0.945	0.668
ROBO3_F11R	ROBO3	F11R	0.947	0.676
FCRL1_VSIG8	FCRL1	VSIG8	0.947	0.68
IGSF11_EPGN	IGSF11	EPGN	0.947	0.68
LRCH4_CADM3	LRCH4	CADM3	0.948	0.683
PTPRS_IL1RAPL2	PTPRS	IL1RAPL2	0.949	0.687
CEACAM6_UXS1	CEACAM6	UXS1	0.948	0.689
TNFRSF11B_SLITRK1	TNFRSF11B	SLITRK1	0.95	0.696
CD47_SIGLEC1	CD47	SIGLEC1	0.95	0.697
EPHA3_LILRA3	EPHA3	LILRA3	0.951	0.701
PVR_CD96	PVR	CD96	0.952	0.704
IL2RG_CADM3	IL2RG	CADM3	0.952	0.706
PRRG4_CADM4	PRRG4	CADM4	0.953	0.713
TNFRSF11B_NRXN3	TNFRSF11B	NRXN3	0.953	0.713
DSCAM_PTPRT	DSCAM	PTPRT	0.953	0.714
RARRES1_NRP2	RARRES1	NRP2	0.954	0.719
NCR1_SIGLEC7	NCR1	SIGLEC7	0.956	0.728
PLXNB2_SEMA4A	PLXNB2	SEMA4A	0.957	0.74
IL20RA_LYPD6	IL20RA	LYPD6	0.959	0.746
PTPRS_SLITRK4	PTPRS	SLITRK4	0.959	0.749
NRXN2_SIGLEC8	NRXN2	SIGLEC8	0.961	0.763
KIR3DL2_LILRA1	KIR3DL2	LILRA1	0.963	0.773
APLP1_CNTN3	APLP1	CNTN3	0.964	0.781
FLT4_ADAM21	FLT4	ADAM21	0.965	0.783
NLGN3_MDGA1	NLGN3	MDGA1	0.965	0.783
EFNB2_EPHB1	EFNB2	EPHB1	0.965	0.785
IL1RAPL2_MILR1	IL1RAPL2	MILR1	0.965	0.788
SDK2_CADM4	SDK2	CADM4	0.966	0.794
NRXN1_VSTM2B	NRXN1	VSTM2B	0.967	0.794
CD2_CD58	CD2	CD58	0.967	0.796
FLT1_GPC3	FLT1	GPC3	0.967	0.799
CD6_DAG1	CD6	DAG1	0.968	0.802
PTPRS_SLITRK6	PTPRS	SLITRK6	0.969	0.808
PTPRD_SIRPG	PTPRD	SIRPG	0.97	0.813
EFNB2_EPHB6	EFNB2	EPHB6	0.971	0.82

CD4_MOG	CD4	MOG	0.971	0.821
SEMA7A_PLXNC1	SEMA7A	PLXNC1	0.971	0.822
LAYN_LY6G6F	LAYN	LY6G6F	0.971	0.823
IGSF21_MUC15	IGSF21	MUC15	0.974	0.842
PTPRS_SLITRK2	PTPRS	SLITRK2	0.976	0.849
CD6_HBEGF	CD6	HBEGF	0.975	0.85
TNFRSF17_NTM	TNFRSF17	NTM	0.976	0.852
FLT1_TREM2	FLT1	TREM2	0.977	0.857
PECAM1_PECAM1	PECAM1	PECAM1	0.977	0.861
TNFRSF11B_NRXN2	TNFRSF11B	NRXN2	0.977	0.862
KIAA0319L_ILDR1	KIAA0319L	ILDR1	0.979	0.874
KIAA0319L_MPZL3	KIAA0319L	MPZL3	0.979	0.874
PTPRD_SLITRK6	PTPRD	SLITRK6	0.981	0.881
GUCY2D_NECTIN3	GUCY2D	NECTIN3	0.985	0.906
GUCY2D_NECTIN4	GUCY2D	NECTIN4	0.985	0.906
MUSK_DLL1	MUSK	DLL1	0.985	0.909
LRFN3_FCRL1	LRFN3	FCRL1	0.985	0.91
CORIN_LRRC4C	CORIN	LRRC4C	0.985	0.911
AGER_CLEC14A	AGER	CLEC14A	0.986	0.914
AXL_VSIG10L	AXL	VSIG10L	0.986	0.917
DSG1_FLT4	DSG1	FLT4	0.989	0.927
CD200_CD200R1	CD200	CD200R1	0.99	0.937
EPHA3_CD274	EPHA3	CD274	0.99	0.938
HAVCR1_IGSF21	HAVCR1	IGSF21	0.991	0.943
CADM4_CADM2	CADM4	CADM2	0.991	0.945
FAS_FASLG	FAS	FASLG	0.994	0.96
PLXNB1_SEMA4A	PLXNB1	SEMA4A	0.994	0.968
CADM3_C12orf63	CADM3	C12orf63	0.996	0.971
CADM3_CADM3	CADM3	CADM3	0.996	0.971
MXRA5_SIGLEC7	MXRA5	SIGLEC7	0.996	0.976
CD40_IL11RA	CD40	IL11RA	0.997	0.983
SEMA6A_PLXNA4	SEMA6A	PLXNA4	0.998	0.991
HHLA2_VSIG8	HHLA2	VSIG8	1	0.997
NCAM1_CLEC14A	NCAM1	CLEC14A	1	0.999

Table 16. Gene pairs predicting lack of responsiveness to atezolizumab

Gene pair	First gene	Second gene	Hazard ratio (HR)	p value HR
EFNB1_EVC2	EFNB1	EVC2	1.609	0
GPC4_FGFRL1	GPC4	FGFRL1	1.737	0
EFNB3_EPHB4	EFNB3	EPHB4	1.492	0.002
PTPRD_LRFN4	PTPRD	LRFN4	1.479	0.003
EFNB1_AQPEP	EFNB1	AQPEP	1.429	0.007

EFNB1_DSG4	EFNB1	DSG4	1.357	0.021
LDLR_LILRB5	LDLR	LILRB5	1.353	0.021
EFNB3_EPHB3	EFNB3	EPHB3	1.344	0.025
PLXNB3_SEMA4G	PLXNB3	SEMA4G	1.34	0.026
EFNB1_EPHB6	EFNB1	EPHB6	1.318	0.036
FLT4_FLRT2	FLT4	FLRT2	1.295	0.05
FLT1_ELFN1	FLT1	ELFN1	1.263	0.076
GPC4_FGFR4	GPC4	FGFR4	1.251	0.089
GPC3_TNFRSF11B	GPC3	TNFRSF11B	1.242	0.099
FGFR4_GPC6	FGFR4	GPC6	1.24	0.103
PLXNB1_SEMA4B	PLXNB1	SEMA4B	1.229	0.115
EDA_EDAR	EDA	EDAR	1.219	0.132
FGFR4_NRXN2	FGFR4	NRXN2	1.174	0.223
SEMA4D_PLXNB2	SEMA4D	PLXNB2	1.151	0.285
FLT4_NRP2	FLT4	NRP2	1.149	0.292
FGFR4_GPC3	FGFR4	GPC3	1.126	0.366
FGFR2_RAMP1	FGFR2	RAMP1	1.117	0.399
EFNB3_EPHA10	EFNB3	EPHA10	1.699	0
NGFR_LRRTM3	NGFR	LRRTM3	1.554	0.001
CD320_IGSF5	CD320	IGSF5	1.472	0.003
CD300LB_LRRC52	CD300LB	LRRC52	1.428	0.007
EFNB2_EPHA8	EFNB2	EPHA8	1.426	0.007
EFNB2_KIR2DS3	EFNB2	KIR2DS3	1.426	0.007
EFNB2_MGC39681	EFNB2	MGC39681	1.426	0.007
EFNB3_EPHB2	EFNB3	EPHB2	1.405	0.01
PTGFRN_TMEM59L	PTGFRN	TMEM59L	1.406	0.01
CD59_STAB1	CD59	STAB1	1.385	0.013
EFNB2_EPHB4	EFNB2	EPHB4	1.388	0.013
ACVR1B_TDGF1	ACVR1B	TDGF1	1.381	0.014
AQPEP_VSIG8	AQPEP	VSIG8	1.381	0.014
CNTN1_FCGRT	CNTN1	FCGRT	1.379	0.015
ENPEP_SLITRK1	ENPEP	SLITRK1	1.368	0.017
FCGRT_SHISA4	FCGRT	SHISA4	1.366	0.018
EFNB2_EPHB3	EFNB2	EPHB3	1.36	0.019
HBEGF_MOG	HBEGF	MOG	1.353	0.022
IL6ST_VSIG10	IL6ST	VSIG10	1.352	0.022
KIRREL_KIRREL	KIRREL	KIRREL	1.353	0.022
EFNB1_EPHA3	EFNB1	EPHA3	1.34	0.026
CNTN3_PTPRG	CNTN3	PTPRG	1.339	0.027
PCDHAC1_MICA	PCDHAC1	MICA	1.334	0.029
PCDHB3_IGSF11	PCDHB3	IGSF11	1.331	0.029
DSCAML1_DSCAML1	DSCAML1	DSCAML1	1.324	0.033
IL20RA_CLEC14A	IL20RA	CLEC14A	1.324	0.033

IZUMO1_LILRA5	IZUMO1	LILRA5	1.314	0.038
EFNB2_EPHA3	EFNB2	EPHA3	1.312	0.039
FCGR3B_EDA2R	FCGR3B	EDA2R	1.311	0.04
IL6R_BTNL9	IL6R	BTNL9	1.308	0.041
NTM_AMIGO2	NTM	AMIGO2	1.308	0.041
TREM1_VSIG8	TREM1	VSIG8	1.309	0.041
AXL_IL1RL1	AXL	IL1RL1	1.304	0.045
TNFRSF11A_MYEOV	TNFRSF11A	MYEOV	1.301	0.045
EGF_TNFRSF11B	EGF	TNFRSF11B	1.301	0.046
IL1RAP_PTPRD	IL1RAP	PTPRD	1.297	0.048
SIGLEC8_PCDHGA7	SIGLEC8	PCDHGA7	1.295	0.049
CD320_TMEM167A	CD320	TMEM167A	1.293	0.051
IL6R_LRTM2	IL6R	LRTM2	1.29	0.053
IGSF11_CLEC2L	IGSF11	CLEC2L	1.289	0.054
FLRT2_UNC5B	FLRT2	UNC5B	1.288	0.055
L1CAM_AQPEP	L1CAM	AQPEP	1.284	0.057
FLT1_NRP1	FLT1	NRP1	1.282	0.058
PTPRS_LRFN4	PTPRS	LRFN4	1.282	0.059
PTGFRN_SGCG	PTGFRN	SGCG	1.28	0.061
EDA_IL1RL1	EDA	IL1RL1	1.276	0.064
NCAM1_ISLR2	NCAM1	ISLR2	1.276	0.064
EFNB3_MGC39681	EFNB3	MGC39681	1.273	0.067
NOTCH4_UNC5B	NOTCH4	UNC5B	1.273	0.067
CEACAM5_LRP8	CEACAM5	LRP8	1.271	0.068
GPC6_FGFRL1	GPC6	FGFRL1	1.272	0.068
FCGRT_CD300E	FCGRT	CD300E	1.269	0.07
PRNP_TNFRSF25	PRNP	TNFRSF25	1.27	0.07
EFNB3_C19orf38	EFNB3	C19orf38	1.266	0.073
LILRA1_LILRA1	LILRA1	LILRA1	1.266	0.073
EFNB3_EPHB1	EFNB3	EPHB1	1.265	0.075
TNFRSF11B_NRP1	TNFRSF11B	NRP1	1.264	0.075
CNTN1_PTPRZ1	CNTN1	PTPRZ1	1.26	0.079
IGDCC4_PLB1	IGDCC4	PLB1	1.26	0.079
STAB1_NTM	STAB1	NTM	1.259	0.08
ADAM20_IL1RAPL2	ADAM20	IL1RAPL2	1.257	0.082
TNFRSF11B_PCDHAC1	TNFRSF11B	PCDHAC1	1.256	0.083
EFNB3_EPHB6	EFNB3	EPHB6	1.256	0.084
PTPRD_TGFA	PTPRD	TGFA	1.256	0.084
PLXNB2_SEMA4G	PLXNB2	SEMA4G	1.254	0.085
EFNB1_FAM187B	EFNB1	FAM187B	1.253	0.087
LILRA1_CD300E	LILRA1	CD300E	1.25	0.09
SEMA4B_PLXNB2	SEMA4B	PLXNB2	1.249	0.091
NRXN2_FGFRL1	NRXN2	FGFRL1	1.246	0.095

FCER1A_PEAR1	FCER1A	PEAR1	1.246	0.096
CHL1_SIRPA	CHL1	SIRPA	1.241	0.101
C10orf54_IGSF11	C10orf54	IGSF11	1.239	0.103
EFNB2_EPHA4	EFNB2	EPHA4	1.236	0.106
EPHB6_FLT1	EPHB6	FLT1	1.236	0.107
EFNB2_C19orf38	EFNB2	C19orf38	1.233	0.112
NCAM1_NPTN	NCAM1	NPTN	1.232	0.112
GLG1_UNC5B	GLG1	UNC5B	1.228	0.118
TREM1_VSTM2B	TREM1	VSTM2B	1.227	0.12
IL6ST_IL11RA	IL6ST	IL11RA	1.226	0.121
CDHR2_KIRREL	CDHR2	KIRREL	1.222	0.127
IL4R_PCDHGB6	IL4R	PCDHGB6	1.221	0.13
UNC5C_FLRT2	UNC5C	FLRT2	1.219	0.133
EFNB3_EPHA4	EFNB3	EPHA4	1.217	0.135
F3_ULBP3	F3	ULBP3	1.216	0.138
LDLR_LRRC4C	LDLR	LRRC4C	1.212	0.143
PCDHGB6_PLXDC1	PCDHGB6	PLXDC1	1.213	0.143
CD59_SIGLEC1	CD59	SIGLEC1	1.206	0.154
CD300C_NTNG1	CD300C	NTNG1	1.205	0.155
CD320_AMICA1	CD320	AMICA1	1.205	0.155
PLXNB3_SEMA4D	PLXNB3	SEMA4D	1.202	0.161
EPHA7_PILRB	EPHA7	PILRB	1.201	0.162
SIGLEC7_CD320	SIGLEC7	CD320	1.202	0.162
NRXN2_IGSF21	NRXN2	IGSF21	1.201	0.164
CNTN1_PCDHB7	CNTN1	PCDHB7	1.2	0.165
CD300A_IGSF5	CD300A	IGSF5	1.197	0.17
KIAA0319L_UNC5A	KIAA0319L	UNC5A	1.196	0.173
CD14_PLXND1	CD14	PLXND1	1.191	0.184
PVR_KIR2DL5A	PVR	KIR2DL5A	1.19	0.184
PVR_NECTIN3	PVR	NECTIN3	1.19	0.184
PVR_NECTIN4	PVR	NECTIN4	1.19	0.184
PTPRG_CNTN6	PTPRG	CNTN6	1.19	0.186
TNFRSF11B_GPC6	TNFRSF11B	GPC6	1.19	0.186
IL1RAPL1_APOO	IL1RAPL1	APOO	1.187	0.19
ST14_BTN3A1	ST14	BTN3A1	1.186	0.192
NEGR1_NEGR1	NEGR1	NEGR1	1.187	0.193
ROR2_CD320	ROR2	CD320	1.186	0.195
CNTN2_CNTN2	CNTN2	CNTN2	1.186	0.197
CD80_NGFR	CD80	NGFR	1.183	0.201
TNFRSF11B_C14orf37	TNFRSF11B	C14orf37	1.183	0.201
CD69_MXRA5	CD69	MXRA5	1.182	0.205
CDH6_PTGFRN	CDH6	PTGFRN	1.181	0.207
CEACAM5_CEACAM6	CEACAM5	CEACAM6	1.178	0.211

ALCAM_ALCAM	ALCAM	ALCAM	1.178	0.214
LRPAP1_CD320	LRPAP1	CD320	1.177	0.214
CEACAM4_FLT4	CEACAM4	FLT4	1.177	0.217
DSC3_CRTAM	DSC3	CRTAM	1.173	0.226
UNC5C_FLRT1	UNC5C	FLRT1	1.173	0.226
EFNB2_EPHB2	EFNB2	EPHB2	1.172	0.227
FLRT2_UNC5A	FLRT2	UNC5A	1.171	0.231
NEO1_HFE2	NEO1	HFE2	1.17	0.232
SIGLEC7_LRP12	SIGLEC7	LRP12	1.169	0.234
LILRB1_LILRA5	LILRB1	LILRA5	1.168	0.236
C10orf54_VSIG8	C10orf54	VSIG8	1.166	0.243
PTPRD_FAM187B	PTPRD	FAM187B	1.166	0.243
PTPRD_LECT1	PTPRD	LECT1	1.166	0.243
PTPRD_LRIT2	PTPRD	LRIT2	1.166	0.243
LILRA6_LCTL	LILRA6	LCTL	1.165	0.246
LILRA6_LY6G6F	LILRA6	LY6G6F	1.165	0.246
PTPRS_LRFN1	PTPRS	LRFN1	1.165	0.247
GPC3_VSIG10L	GPC3	VSIG10L	1.164	0.248
FCAR_VSIG8	FCAR	VSIG8	1.164	0.249
LILRA6_CD300E	LILRA6	CD300E	1.164	0.249
TNFRSF11A_ACE2	TNFRSF11A	ACE2	1.164	0.249
PTPRS_SLITRK1	PTPRS	SLITRK1	1.164	0.251
NCAM1_CLEC2L	NCAM1	CLEC2L	1.162	0.253
NCAM1_NCAM1	NCAM1	NCAM1	1.162	0.253
NTRK1_TIE1	NTRK1	TIE1	1.162	0.254
PTPRG_CNTN4	PTPRG	CNTN4	1.159	0.264
EDA2R_KIR3DL3	EDA2R	KIR3DL3	1.157	0.268
NT5E_FCRL1	NT5E	FCRL1	1.156	0.271
IL1RAPL1_SIGLEC12	IL1RAPL1	SIGLEC12	1.154	0.278
KIT_KITLG	KIT	KITLG	1.153	0.281
LILRB1_EDAR	LILRB1	EDAR	1.152	0.282
PTPRG_IL1RAPL1	PTPRG	IL1RAPL1	1.152	0.282
NRP2_NRG2	NRP2	NRG2	1.15	0.287
MCAM_TMEM132A	MCAM	TMEM132A	1.147	0.296
GPC3_UNC5C	GPC3	UNC5C	1.147	0.297
FLRT3_UNC5B	FLRT3	UNC5B	1.145	0.302
PTPRD_IL1RAPL2	PTPRD	IL1RAPL2	1.145	0.302
TREML2_GPR116	TREML2	GPR116	1.143	0.309
EFNB1_NAALAD2	EFNB1	NAALAD2	1.139	0.32
LRPAP1_SIRPA	LRPAP1	SIRPA	1.137	0.329
CD69_SIRPA	CD69	SIRPA	1.137	0.33
NTM_VSIG8	NTM	VSIG8	1.136	0.33
CEACAM3_CEACAM7	CEACAM3	CEACAM7	1.129	0.355

SIGLEC8_KIAA0319L	SIGLEC8	KIAA0319L	1.129	0.356
UNC5D_SIGLEC15	UNC5D	SIGLEC15	1.129	0.357
NRXN2_VSTM2B	NRXN2	VSTM2B	1.129	0.358
NETO2_FCRL1	NETO2	FCRL1	1.127	0.361
NTM_NEGR1	NTM	NEGR1	1.126	0.366
FLT4_MUC15	FLT4	MUC15	1.125	0.371
CDH13_NCAM2	CDH13	NCAM2	1.124	0.375
APP_FLT1	APP	FLT1	1.123	0.379
NTM_LRRC4C	NTM	LRRC4C	1.122	0.379
CEACAM3_PTPRD	CEACAM3	PTPRD	1.123	0.38
CEACAM5_CEACAM5	CEACAM5	CEACAM5	1.121	0.383
CEACAM5_CEACAM8	CEACAM5	CEACAM8	1.121	0.383
NEO1_RGMA	NEO1	RGMA	1.121	0.383
NRP2_SIGLEC7	NRP2	SIGLEC7	1.121	0.384
LEPR_KIR2DL5A	LEPR	KIR2DL5A	1.121	0.386
CTLA4_WBP1	CTLA4	WBP1	1.12	0.387
FGFR4_KL	FGFR4	KL	1.12	0.389
CEACAM5_CEACAM3	CEACAM5	CEACAM3	1.118	0.397
FLT4_KIR2DS5	FLT4	KIR2DS5	1.116	0.405
FGFRL1_PLVAP	FGFRL1	PLVAP	1.115	0.408
IGSF3_PTGFRN	IGSF3	PTGFRN	1.114	0.409
LRRC4C_UNC5A	LRRC4C	UNC5A	1.113	0.417
LRRC4_PRSS55	LRRC4	PRSS55	1.113	0.418
EFNB2_TCTN2	EFNB2	TCTN2	1.11	0.428
GLG1_MOG	GLG1	MOG	1.109	0.429
NTNG1_LRRC4C	NTNG1	LRRC4C	1.109	0.431
CADM3_PEAR1	CADM3	PEAR1	1.109	0.433
CXADR_AMICA1	CXADR	AMICA1	1.109	0.433
CHL1_TMEM132A	CHL1	TMEM132A	1.106	0.442
BTN3A2_LRRC4B	BTN3A2	LRRC4B	1.105	0.445
GPC4_TNFRSF11B	GPC4	TNFRSF11B	1.104	0.452
TNFRSF14_LRFN5	TNFRSF14	LRFN5	1.103	0.455
TREML2_ANTXR1	TREML2	ANTXR1	1.103	0.456
APP_CNTN4	APP	CNTN4	1.102	0.46
SIGLEC7_LRRC4C	SIGLEC7	LRRC4C	1.1	0.467
IL20RA_CD276	IL20RA	CD276	1.097	0.48
L1CAM_L1CAM	L1CAM	L1CAM	1.096	0.483
IGSF21_IYD	IGSF21	IYD	1.096	0.485
EFNB1_SLAMF9	EFNB1	SLAMF9	1.095	0.492
IL17RC_IGSF8	IL17RC	IGSF8	1.094	0.494
IL1RAPL2_APOO	IL1RAPL2	APOO	1.09	0.508
CLMP_AMICA1	CLMP	AMICA1	1.09	0.515
NRP2_FCRL6	NRP2	FCRL6	1.089	0.519

PVR_CD226	PVR	CD226	1.088	0.519
IGSF9B_NEGR1	IGSF9B	NEGR1	1.089	0.52
ROBO3_LY6G6F	ROBO3	LY6G6F	1.086	0.531
PTPRM_SIGLEC10	PTPRM	SIGLEC10	1.084	0.538
MPZL2_MPZL3	MPZL2	MPZL3	1.083	0.543
CD79B_IGSF21	CD79B	IGSF21	1.082	0.548
CNTN1_MCAM	CNTN1	MCAM	1.08	0.56
IL7R_TNFRSF11B	IL7R	TNFRSF11B	1.077	0.572
NRP2_NFASC	NRP2	NFASC	1.077	0.572
TNFRSF11B_ACE2	TNFRSF11B	ACE2	1.077	0.572
CEACAM5_CEACAM7	CEACAM5	CEACAM7	1.077	0.574
LRRC4C_TMEM53	LRRC4C	TMEM53	1.075	0.58
CEACAM7_CEACAM6	CEACAM7	CEACAM6	1.075	0.582
CSF1R_LY6G6F	CSF1R	LY6G6F	1.071	0.601
CSF1R_MGC39681	CSF1R	MGC39681	1.071	0.601
NAALADL1_CD96	NAALADL1	CD96	1.071	0.601
PLXNB1_SEMA4G	PLXNB1	SEMA4G	1.07	0.604
ROBO3_ESAM	ROBO3	ESAM	1.07	0.605
NTM_LRRN3	NTM	LRRN3	1.069	0.609
F11R_ULBP3	F11R	ULBP3	1.067	0.618
IL20RA_PCDHAC1	IL20RA	PCDHAC1	1.068	0.618
MXRA8_JAM3	MXRA8	JAM3	1.067	0.62
TREM2_LRRC52	TREM2	LRRC52	1.067	0.621
PTPRF_LRFN5	PTPRF	LRFN5	1.067	0.623
SEMA4F_C10orf54	SEMA4F	C10orf54	1.066	0.626
NRP2_IL20RA	NRP2	IL20RA	1.065	0.629
FLT4_ILDR2	FLT4	ILDR2	1.065	0.631
ADAM21_IGSF21	ADAM21	IGSF21	1.063	0.639
CNTN1_CHL1	CNTN1	CHL1	1.064	0.64
NFASC_LINGO4	NFASC	LINGO4	1.061	0.65
CDHR2_UNC5A	CDHR2	UNC5A	1.061	0.651
LRRC4C_LRRTM4	LRRC4C	LRRTM4	1.061	0.653
PLXNB1_SEMA4C	PLXNB1	SEMA4C	1.059	0.662
CORIN_KIRREL	CORIN	KIRREL	1.058	0.668
APP_CNTN3	APP	CNTN3	1.057	0.673
LILRA1_NETO2	LILRA1	NETO2	1.057	0.673
CXADR_KLRAP1	CXADR	KLRAP1	1.057	0.676
FLRT2_UNC5D	FLRT2	UNC5D	1.057	0.679
MERTK_IGSF5	MERTK	IGSF5	1.056	0.682
CADM3_CADM4	CADM3	CADM4	1.056	0.683
CDH6_CNTN1	CDH6	CNTN1	1.053	0.696
EFNB3_EPHA3	EFNB3	EPHA3	1.051	0.706
GPC4_IGDCC4	GPC4	IGDCC4	1.051	0.707

LRRC4B_UNC5D	LRRC4B	UNC5D	1.051	0.71
PTPRO_SIGLEC7	PTPRO	SIGLEC7	1.049	0.715
GFRA1_TREM2	GFRA1	TREM2	1.048	0.719
GPC4_FLT1	GPC4	FLT1	1.046	0.735
APLP1_CNTN4	APLP1	CNTN4	1.045	0.737
ERBB4_DLK1	ERBB4	DLK1	1.045	0.737
NTRK3_PTPRS	NTRK3	PTPRS	1.045	0.741
PTPRD_SLITRK4	PTPRD	SLITRK4	1.045	0.742
CSF3R_IGSF21	CSF3R	IGSF21	1.043	0.746
DSCAM_DSCAM	DSCAM	DSCAM	1.043	0.751
CEACAM4_PDCD1LG2	CEACAM4	PDCD1LG2	1.04	0.765
LILRB1_ILDR1	LILRB1	ILDR1	1.039	0.772
IL1RAPL1_MILR1	IL1RAPL1	MILR1	1.038	0.779
CD22_IGSF21	CD22	IGSF21	1.037	0.784
CNTN2_KREMEN1	CNTN2	KREMEN1	1.037	0.784
BMP5_PTPRD	BMP5	PTPRD	1.033	0.805
IL6R_LILRB1	IL6R	LILRB1	1.033	0.806
PTPRS_SLITRK3	PTPRS	SLITRK3	1.033	0.806
TIE1_LRFN5	TIE1	LRFN5	1.033	0.807
FLT1_CD300LF	FLT1	CD300LF	1.032	0.809
NTRK3_SIGLEC7	NTRK3	SIGLEC7	1.031	0.815
ITGA1_CEACAM6	ITGA1	CEACAM6	1.031	0.817
FCAR_TNFRSF14	FCAR	TNFRSF14	1.028	0.831
FLT4_LILRB1	FLT4	LILRB1	1.026	0.844
CD79B_KREMEN1	CD79B	KREMEN1	1.026	0.846
FLRT3_UNC5D	FLRT3	UNC5D	1.026	0.85
PTPRD_SLITRK3	PTPRD	SLITRK3	1.025	0.852
DAG1_SARAF	DAG1	SARAF	1.025	0.855
IL1RAPL2_CNTN5	IL1RAPL2	CNTN5	1.023	0.862
DDR1_LY6G6F	DDR1	LY6G6F	1.021	0.873
CD79B_NTM	CD79B	NTM	1.019	0.884
CSF1R_TEK	CSF1R	TEK	1.018	0.892
CD47_SIRPA	CD47	SIRPA	1.016	0.9
LRRC4_NETO2	LRRC4	NETO2	1.016	0.902
L1CAM_CHL1	L1CAM	CHL1	1.016	0.905
CHL1_CNTN5	CHL1	CNTN5	1.015	0.909
GP5_LAYN	GP5	LAYN	1.014	0.919
ADAM21_CLEC12B	ADAM21	CLEC12B	1.013	0.924
CD28_CD86	CD28	CD86	1.012	0.927
CSF1R_PRTG	CSF1R	PRTG	1.012	0.927
CNTN1_SGCG	CNTN1	SGCG	1.011	0.935
UNC5C_FLRT3	UNC5C	FLRT3	1.01	0.941
CD33_KIRREL3	CD33	KIRREL3	1.01	0.942

LRRC4C_SIGLEC15	LRRC4C	SIGLEC15	1.008	0.951
NCAM1_PTPRS	NCAM1	PTPRS	1.008	0.952
SIGLEC7_TIMD4	SIGLEC7	TIMD4	1.008	0.954
MUSK_PTPRO	MUSK	PTPRO	1.008	0.955
CSF3R_CD244	CSF3R	CD244	1.006	0.965
PTPRO_CD300C	PTPRO	CD300C	1.005	0.968
GPC3_UNC5D	GPC3	UNC5D	1.005	0.969
CNTN1_NFASC	CNTN1	NFASC	1.004	0.974
LRRN1_LRRC4	LRRN1	LRRC4	1.003	0.985
LSAMP_NEGR1	LSAMP	NEGR1	1.003	0.986
NLGN4X_MDGA1	NLGN4X	MDGA1	1.003	0.986
PTPRM_PTPRM	PTPRM	PTPRM	1.002	0.987
FCGRT_IGFLR1	FCGRT	IGFLR1	1.002	0.989
CD34_NECTIN3	CD34	NECTIN3	1.002	0.992
CD34_NECTIN4	CD34	NECTIN4	1.002	0.992
PTPRO_SIGLEC8	PTPRO	SIGLEC8	1.001	0.996

Table 17. Subset of genes from tagged STM library for PDPN experiment

1110032F04RIK	CILP2	LMLN	PVRL2
A1BG	CRB2	LOC160348	PXDN
ACPP	CRLF2	LOC256223	PXDNL
ADAM12	CTLA4	LOC374383	RAET1E
ADAM19	CXorf68	LOC376666	RAET1G
ADAM28	DAG1	LOC652900	RGMA
ADAM9	DPCR1	LRCH4	RGMB
ANTXR1	DSG1	LRIT3	ROBO4
APCDD1L	DTPQ5903	LRP6	SARAF
APOO	ECSM2	LRPAP1	SCN1B
ATRAID	EPHB1	LRRC33	SCN4B
ATRN	EPHB2	LRRC38	SDC1
AZGP1	ERN2	LRRC55	SECTM1
BUTR1	EVC2	LRRC66	SEMA3A
C10orf26	FAIM3	LYPD5	SEMA3B
C10orf35	FAM171B	LYPD6	SEMA3C
C11orf92	FAM200A	LYSMD4	SEMA3D
C12orf53	FCAMR	MERTK	SEMA3E
C12orf59	FCGR1C	MFI2	SEMA3F
C14orf180	FCRLA	MMP16	SEMA3G
C15orf24	FCRLB	MUC1	SERTM1
C16orf54	FLT1	MXRA5	SHISA2
C16orf91	FNDC3A	MXRA7	SHISA3
C16orf92	FRRS1L	MYEOV	SHISA5
C17orf80	FSTL4	NCAN	SIRPD
C18orf1	FSTL5	NOMO1	SKINTL

C19orf24	GLIPR1L2	NOTCH1	SMAGP
C19orf38	GPR116	NPR2	SPATA9
C19orf63	GPR124	NRXN3	SPINT1
C19orf75	GPR125	OSMR	TCP11
C1orf101	HAPLN2	P2RX2	TEX29
C1orf130	HAPLN3	PAPLN	TMEM108
C1orf85	HAPLN4	PCSK4	TMEM119
C2orf82	HEPH	PCSK7	TMEM130
C2orf89	HEPHL1	PDCD1LG2	TMEM156
C3orf18	IGFBP7	PDGFRL	TMEM158
C3orf35	IGFBPL1	Phospholipase Inhibi	TMEM167A
C3orf45	IGLON5	PLB1	TMEM167B
C4orf32	IGSF1	PLXNA1	TMEM183B
C4orf34	IGSF21	PRRG2	TMEM213
C5orf15	IL12B	PRSS55	TMEM240
C6orf25	IL18BP	PRSS8	TMEM59L
C6orf72	IL1R1	PSG1	TNFRSF11B
C9orf11	IMPG2	PSG2	TNFRSF1A
CACHD1	ISLR	PSG3	TNFRSF6B
CAV3	IZUMO2	PSG4	TREML4
CD163	KAZALD1	PSG5	VNN3
CD1A	KCNE4	PSG6	VPREB1
CD47	KIAA0090	PSG7	VPREB3
CD48	KIAA0319L	PSG8	VSTM2A
CD8B	KIAA1024	PSG9	VSTM2B
CDH10	KIAA1644	PTGFRN	VSTM2L
CDH13	KIR3DP1	PTPRC	WFIKKN1
CDH9	KIR3DX1	PTPRE	WFIKKN2
CEACAM16	KLB	PTPRF	ZP3
CEACAM18	KLRAP1	PTPRN2	ZPBP
CEACAM6	LAIR2	PTPRO	ZPBP2
CILP	LILRA3	PTPRR	

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, the descriptions and examples should not be construed as limiting the scope of the invention. The disclosures of all patent and scientific literature cited herein are expressly incorporated in their entirety by reference.

WHAT IS CLAIMED IS:

1. A method of identifying an individual having a cancer who may benefit from a treatment comprising a PD-L1 axis binding antagonist, the method comprising determining an expression level of a first member and a second member of at least one of the gene pairs of Table 15 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment comprising a PD-L1 axis binding antagonist.

2. A method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of a first member and a second member at least one of the gene pairs of Table 15 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment comprising a PD-L1 axis binding antagonist.

3. The method of claim 1 or 2, wherein the individual has an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level and the method further comprises administering to the individual an effective amount of a PD-L1 axis binding antagonist.

4. A method of treating an individual having a cancer, the method comprising:

(a) determining an expression level of a first member and a second member at least one of the gene pairs of Table 15 in a sample from the individual, wherein the expression level of the first member of the gene pair is above a first reference expression level and the expression level of the second member of the gene pair is above a second reference expression level; and

(b) administering an effective amount of a PD-L1 axis binding antagonist to the individual.

5. A method of treating an individual having a cancer, the method comprising administering a PD-L1 axis binding antagonist to an individual who has been determined to have an expression level of a first member of a gene pair of Table 15 that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level.

6. A method of identifying an individual having a cancer who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist, the method comprising determining an expression level of a first member and a second member of at least one of the gene pairs of Table 16 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist.

7. A method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of a first member and a second member at least one of the gene pairs of Table 16 in a sample from the individual, wherein an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level identifies the individual as one who may benefit from a treatment other than or in addition to a PD-L1 axis binding antagonist.

8. The method of claim 6 or 7, wherein the individual has an expression level of the first member of the gene pair that is above a first reference expression level and an expression level of the second member of the gene pair that is above a second reference expression level and the method comprises administering to the individual an effective amount of a treatment other than or in addition to a PD-L1 axis binding antagonist.

9. The method of any one of claims 1-8, wherein the first reference expression level is a pre-assigned expression level and the second reference expression level is a pre-assigned reference expression level.

10. The method of any one of claims 1-9, wherein the sample from the individual is obtained from the individual prior to administration of an anti-cancer therapy.

11. The method of any one of claims 1-9, wherein the sample from the individual is obtained from the individual after administration of an anti-cancer therapy.

12. The method of any one of claims 1-11, wherein the sample from the individual is a tumor tissue sample or a tumor fluid sample.

13. The method of claim 12, wherein the sample is a formalin-fixed and paraffin-embedded (FFPE) sample, an archival sample, a fresh sample, or a frozen sample.

14. The method of claim 13, wherein the tumor tissue sample is a FFPE sample.

15. The method of any one of claims 12-14, wherein:

(a) the expression level of the first member and the second member of the gene pair in the sample is a protein expression level; or

(b) the expression level of the first member and the second member of the gene pair in the sample is an mRNA expression level.

16. The method of claim 15, wherein the expression level of the first member and the second member of the gene pair in the sample is a mRNA expression level of the first member and the second member of the gene pair, respectively.

17. The method of claim 16, wherein the mRNA expression level of the first member and the second member of the gene pair is determined by *in situ* hybridization (ISH), RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, FISH, or a combination thereof.

18. The method of claim 16 or 17, wherein the first reference expression level is between about 0.25 to about 0.5 counts per million (CPM) and the second reference expression level is between about 0.25 to about 0.5 CPM.

19. The method of claim 18, wherein the first reference expression level is 0.25 CPM and the second reference expression level is 0.25 CPM.

20. The method of any one of claims 1-19, wherein the first reference expression level and the second reference expression level are expression levels of the first member and the second member of the gene pair, respectively, in a reference population of individuals having a cancer.

21. The method of any one of claims 1-20, wherein the cancer is a urinary tract cancer.

22. The method of claim 21, wherein the urinary tract cancer is a urinary tract carcinoma.

23. The method of claim 22, wherein the urinary tract carcinoma is a locally advanced urothelial carcinoma.

24. The method of claim 22, wherein the urinary tract carcinoma is a metastatic urothelial carcinoma (mUC).

25. The method of any one of claims 1-3 and 6-24, wherein the benefit comprises an extension in the individual's overall survival (OS) as compared to treatment without the PD-L1 axis binding antagonist.

26. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is SIGLEC6 and the second member of the gene pair is NCR1.

27. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is BTN3A1 and the second member of the gene pair is LRRC4B.

28. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is CD80 and the second member of the gene pair is CTLA4.

29. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is BTN3A3 and the second member of the gene pair is LRRC4B.

30. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is EFNB1 and the second member of the gene pair is TRHDE.

31. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is CTLA4 and the second member of the gene pair is PCDHGB4.

32. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is CTLA4 and the second member of the gene pair is FAM200A.

33. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is CA12 and the second member of the gene pair is SIGLEC6.

34. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is ILDR2 and the second member of the gene pair is CLEC12B.

35. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is EFNB1 and the second member of the gene pair is ITLN1.

36. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is CADM1 and the second member of the gene pair is CRTAM.

37. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is CD79B and the second member of the gene pair is CD244.

38. The method of any one of claims 1-5 and 9-25, wherein the first member of the gene pair is DAG1 and the second member of the gene pair is EFNB1.

39. The method of any one of claims 6-25, wherein the first member of the gene pair is EFNB1 and the second member of the gene pair is EVC2.

40. The method of any one of claims 6-25, wherein the first member of the gene pair is GPC4 and the second member of the gene pair is FGFRL1.

41. The method of any one of claims 6-25, wherein the first member of the gene pair is EFNB3 and the second member of the gene pair is EPHB4.

42. The method of any one of claims 6-25, wherein the first member of the gene pair is PTPRD and the second member of the gene pair is LRFN4.

43. The method of any one of claims 6-25, wherein the first member of the gene pair is EFNB1 and the second member of the gene pair is AQPEP.

44. The method of any one of claims 6-25, wherein the first member of the gene pair is EFNB1 and the second member of the gene pair is DSG4.

45. The method of any one of claims 6-25, wherein the first member of the gene pair is LDLR and the second member of the gene pair is LILRB5.

46. The method of any one of claims 6-25, wherein the first member of the gene pair is EFNB3 and the second member of the gene pair is EPHB3.

47. The method of any one of claims 6-25, wherein the first member of the gene pair is PLXNB3 and the second member of the gene pair is SEMA4G.

48. The method of any one of claims 6-25, wherein the first member of the gene pair is EFNB1 and the second member of the gene pair is EPHB6.

49. The method of any one of claims 6-25, wherein the first member of the gene pair is FLT4 and the second member of the gene pair is FLRT2.

50. The method of any one of claims 6-25, wherein the first member of the gene pair is AXL1 and the second member of the gene pair is IL1RL1.

51. The method of any one of claims 6-25, wherein the first member of the gene pair is CD320 and the second member of the gene pair is IGSF5.

52. The method of any one of claims 6-25, wherein the first member of the gene pair is CD59 and the second member of the gene pair is STAB1.

53. The method of any one of claims 6-25, wherein the first member of the gene pair is CNTN3 and the second member of the gene pair is PTPRG.

54. The method of any one of claims 6-25, wherein the first member of the gene pair is EFNB1 and the second member of the gene pair is EPHA3.

55. The method of any one of claims 6-25, wherein the first member of the gene pair is EFNB3 and the second member of the gene pair is EPHB2.

56. The method of any one of claims 6-25, wherein the first member of the gene pair is EGF and the second member of the gene pair is TNFRSF11B.

57. The method of any one of claims 6-25, wherein the first member of the gene pair is ENPEP and the second member of the gene pair is SLITRK1.

58. The method of any one of claims 6-25, wherein the first member of the gene pair is FCGR3B and the second member of the gene pair is EDA2R.

59. The method of any one of claims 6-25, wherein the first member of the gene pair is IL20RA and the second member of the gene pair is CLEC14A.

60. The method of any one of claims 6-25, wherein the first member of the gene pair is IL6R and the second member of the gene pair is BTNL9.

61. The method of any one of claims 6-25, wherein the first member of the gene pair is IZUMO1 and the second member of the gene pair is LILRA5.

62. The method of any one of claims 6-25, wherein the first member of the gene pair is NGFR and the second member of the gene pair is LRRTM3.

63. The method of any one of claims 6-25, wherein the first member of the gene pair is NTM and the second member of the gene pair is AMIGO2.

64. The method of any one of claims 6-25, wherein the first member of the gene pair is PCDHB3 and the second member of the gene pair is IGSF11.

65. The method of any one of claims 6-25, wherein the first member of the gene pair is PTGFRN and the second member of the gene pair is TMEM59L.

66. The method of any one of claims 6-25, wherein the first member of the gene pair is TREM1 and the second member of the gene pair is VSIG8.

67. The method of any one of claims 1-66, wherein the PD-L1 axis binding antagonist is selected from the group consisting of a PD-L1 binding antagonist, a PD-1 binding antagonist, and a PD-L2 binding antagonist.

68. The method of claim 67, wherein the PD-L1 axis binding antagonist is a PD-L1 binding antagonist.

69. The method of claim 68, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to one or more of its ligand binding partners.

70. The method of claim 68, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1.

71. The method of claim 68, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to B7-1.

72. The method of claim 68, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to both PD-1 and B7-1.

73. The method of any one of claims 68-72, wherein the PD-L1 binding antagonist is an antibody or antigen-binding fragment thereof.

74. The method of claim 73, wherein the antibody is selected from the group consisting of atezolizumab, MDX-1105, MEDI4736 (durvalumab), and MSB0010718C (avelumab).

75. The method of claim 74, wherein the anti-PD-L1 antibody comprises the following hypervariable regions:

(a) an HVR-H1 sequence of GFTFSDSWIH (SEQ ID NO: 19);

(b) an HVR-H2 sequence of AWISPYGGSTYYADSVKG (SEQ ID NO: 20);

(c) an HVR-H3 sequence of RHWPGGFDY (SEQ ID NO: 21);

(d) an HVR-L1 sequence of RASQDVSTAVA (SEQ ID NO: 22);

(e) an HVR-L2 sequence of SASFLYS (SEQ ID NO: 23); and

(f) an HVR-L3 sequence of QQYLYHPAT (SEQ ID NO: 24).

76. The method of claim 74 or 75, wherein the anti-PD-L1 antibody comprises:

(a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 3;

(b) a light chain variable (VL) domain comprising an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 4; or

(c) a VH domain as in (a) and a VL domain as in (b).

77. The method of claim 76, wherein the anti-PD-L1 antibody comprises:

(a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 3;

(b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 4; or

(c) a VH domain as in (a) and a VL domain as in (b).

78. The method of claim 77, wherein the anti-PD-L1 antibody comprises:

(a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 96% sequence identity to the amino acid sequence of SEQ ID NO: 3;

(b) a light chain variable (VL) domain comprising an amino acid sequence having at least 96% sequence identity to the amino acid sequence of SEQ ID NO: 4; or

(c) a VH domain as in (a) and a VL domain as in (b).

79. The method of claim 78, wherein the anti-PD-L1 antibody comprises:

(a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 97% sequence identity to the amino acid sequence of SEQ ID NO: 3;

(b) a light chain variable (VL) domain comprising an amino acid sequence having at least 97% sequence identity to the amino acid sequence of SEQ ID NO: 4; or

(c) a VH domain as in (a) and a VL domain as in (b).

80. The method of claim 79, wherein the anti-PD-L1 antibody comprises:

(a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 98% sequence identity to the amino acid sequence of SEQ ID NO: 3;

(b) a light chain variable (VL) domain comprising an amino acid sequence having at least 98% sequence identity to the amino acid sequence of SEQ ID NO: 4; or

(c) a VH domain as in (a) and a VL domain as in (b).

81. The method of claim 80, wherein the anti-PD-L1 antibody comprises:

(a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 3;

(b) a light chain variable (VL) domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 4; or

(c) a VH domain as in (a) and a VL domain as in (b).

82. The method of claim 81, wherein the anti-PD-L1 antibody comprises:

(a) a VH domain comprising the amino acid sequence of SEQ ID NO: 3; and

(b) a VL domain comprising the amino acid sequence of SEQ ID NO: 4.

83. The method of claim 82, wherein the anti-PD-L1 antibody is atezolizumab (MPDL3280A).

84. The method of claim 67, wherein the PD-L1 axis binding antagonist is a PD-1 binding antagonist.

85. The method of claim 84, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to one or more of its ligand binding partners.

86. The method of claim 85, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1.

87. The method of claim 85, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L2.

88. The method of claim 85, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to both PD-L1 and PD-L2.

89. The method of any one of claims 85-88, wherein the PD-1 binding antagonist is an antibody or antigen-binding fragment thereof.

90. The method of claim 89, wherein the antibody is selected from the group consisting of: MDX-1106 (nivolumab), MK-3475 (pembrolizumab), MEDI-0680 (AMP-514), PDR001, REGN2810, and BGB-108.

91. The method of any one of claims 85-88, wherein the PD-1 binding antagonist is an Fc-fusion protein.

92. A method of treating an individual having a cancer comprising administering to the individual an effective amount of an agonist of CD177 activity.

93. A method of identifying an individual having a cancer who may benefit from a treatment comprising an agonist of CD177 activity, the method comprising determining an expression level of podoplanin (PDPN) in a sample from the individual, wherein an expression level of PDPN in the sample that is above a reference PDPN expression level identifies the individual as one who may benefit from a treatment comprising an agonist of CD177 activity.

94. A method of selecting a therapy for an individual having a cancer, the method comprising determining an expression level of PDPN in a sample from the individual, wherein an expression level of PDPN in the sample that is above a reference PDPN expression level identifies the individual as one who may benefit from a treatment comprising an agonist of CD177 activity.

95. The method of claim 93 or 94, wherein the individual has an expression level of PDPN in the sample that is above a reference PDPN expression level and the method further comprises administering to the individual an effective amount of an agonist of CD177 activity.

96. A method of treating an individual having a cancer, the method comprising:

(a) determining an expression level of PDPN in a sample from the individual, wherein the expression level of PDPN in the sample is above a reference PDPN expression level; and

(b) administering to the individual an effective amount of an agonist of CD177 activity.

97. A method of treating an individual having a cancer, the method comprising administering to the individual an effective amount of an agonist of CD177 activity, wherein the expression level of PDPN in a sample from the individual has been determined to be above a reference PDPN expression level.

98. The method of any one of claims 92-97, wherein the CD177 activity is inhibition of PDPN.

99. The method of any one of claims 93-98, wherein the sample from the individual is a tumor tissue sample or a tumor fluid sample.

100. The method of claim 99, wherein the tumor tissue sample is a formalin-fixed and paraffin-embedded (FFPE) sample, an archival sample, a fresh sample, or a frozen sample.

101. The method of any one of claims 93-100, wherein the expression level of PDPN in the sample is a protein expression level of PDPN or an RNA expression level of PDPN.

102. The method of claim 101, wherein the expression level of PDPN in the sample is an RNA expression level of PDPN.

103. The method of claim 102, wherein the RNA expression level of PDPN is determined by *in situ* hybridization (ISH), RNA-seq, RT-qPCR, qPCR, multiplex qPCR or RT-qPCR, microarray analysis, SAGE, MassARRAY technique, FISH, or a combination thereof.

104. The method of any one of claims 93-103, wherein the reference PDPN expression level is an expression level of PDPN in a population of individuals having a cancer.

105. The method of claim 104, wherein the cancer is a colorectal cancer (CRC), a squamous cell carcinoma of the head and neck, or a glioma.

106. The method of claim 104 or 105, wherein the reference PDPN expression level is the 50th percentile of expression levels in the population.

107. The method of claim 104 or 105, wherein the reference PDPN expression level is the 66th percentile of expression levels in the population.

108. The method of any one of claims 93-107, wherein the reference PDPN expression level is a pre-assigned PDPN expression level.

109. The method of any one of claims 92-108, wherein the cancer is a CRC, a squamous cell carcinoma of the head and neck, or a glioma.

110. The method of claim 109, wherein the cancer is a CRC.

111. The method of claim 110, wherein the CRC is a stage II CRC.

112. The method of claim 110, wherein the CRC is a stage IV CRC.

113. The method of any one of claims 93-95 and 98-112, wherein the benefit comprises an extension in the individual's recurrence-free survival (RFS) as compared to treatment without the agonist of CD177 activity.

114. The method of any one of claims 92-113, wherein the agonist of CD177 activity results in an increase in the binding of PDPN and CD177 relative to binding of the two proteins in the absence of the agonist.

115. The method of any one of claims 92-114, wherein the agonist of CD177 activity results in a change in a downstream activity of PDPN relative to the downstream activity in the absence of the agonist of CD177 activity.

116. The method of claim 115, wherein the change in the downstream activity is a decrease in tumor growth.

117. The method of claim 115, wherein the change in the downstream activity is a decrease in cancer-associated fibroblast (CAF) contractility.

118. The method of any one of claims 92-117, wherein the agonist of CD177 activity is a small molecule, an antibody or antigen-binding fragment thereof, a peptide, or a mimic.

119. The method of claim 118, wherein the agonist of CD177 activity is a peptide.

120. The method of claim 119, wherein the peptide is a CD177 peptide.

121. The method of claim 120, wherein the CD177 peptide is an extracellular domain of CD177.

122. The method of claim 121, wherein the peptide is multimerized.

123. The method of claim 122, wherein the peptide is tetramerized.

124. The method of claim 123, wherein the peptide is tetramerized using streptavidin.

125. The method of claim 118, wherein the agonist of CD177 activity is an antibody or antigen-binding fragment thereof.

126. The method of claim 125, wherein the antibody or antigen-binding fragment thereof binds PDPN.

127. The method of claim 126, wherein the antibody or antigen-binding fragment thereof is an antagonist antibody or antigen-binding fragment thereof.

128. The method of claim 125, wherein the antibody or antigen-binding fragment thereof binds CD177.

129. The method of claim 128, wherein the antibody or antigen-binding fragment thereof is an agonist antibody or antigen-binding fragment thereof.

130. The method of any one of claims 118 and 125-129, wherein the antigen-binding fragment is a bis-Fab, an Fv, a Fab, a Fab'-SH, a $F(ab')_2$, a diabody, a linear antibody, an scFv, an ScFab, a VH domain, or a VHH domain.

131. The method of any one of claims 1-130, wherein the individual is a human.

132. A collection of polypeptides, wherein each polypeptide comprises an extracellular domain, a tag, and an anchor, and wherein the collection of polypeptides comprises the extracellular domains of at least 81% of the proteins of Table 7.

133. The method of claim 132, wherein the collection of polypeptides comprises the extracellular domains of at least 85% of the proteins of Table 7.

134. The method of claim 133, wherein the collection of polypeptides comprises the extracellular domains of at least 90% of the proteins of Table 7.

135. The method of claim 134, wherein the collection of polypeptides comprises the extracellular domains of at least 95% of the proteins of Table 7.

136. The method of claim 135, wherein the collection of polypeptides comprises the extracellular domains of all of the proteins of Table 7.

137. The collection of polypeptides of any one of claims 132-136, wherein the anchor is capable of tethering the extracellular domain to the surface of a plasma membrane of a cell.

138. The collection of polypeptides of any one of claims 132-137, wherein the anchor is a glycosylphosphatidyl-inositol (GPI) polypeptide.

139. The collection of polypeptides of any one of claims 132-138, wherein the tag can be directly or indirectly visualized.

140. The collection of polypeptides of claim 139, wherein the tag comprises a moiety that can be detected using an antibody or an antibody fragment.

141. The collection of polypeptides of claim 139 or 140, wherein the tag is a glycoprotein D (gD) polypeptide.

142. The collection of polypeptides of claim 139, wherein the tag comprises a fluorescent protein.

143. The collection of polypeptides of any one of claims 132-142, wherein the extracellular domain has a native conformation.

144. The collection of polypeptides of any one of claims 132-143, wherein the extracellular domain comprises a native post-translational modification.

145. The collection of polypeptides of any one of claims 137-144, wherein the cell is a mammalian cell.

146. The collection of polypeptides of claim 145, wherein the cell is a COS7 cell.

147. The collection of polypeptides of any one of claims 137-146, wherein the cell has been transiently transfected with a plasmid encoding the polypeptide.

148. A collection of vectors encoding the collection of polypeptides of any one of claims 132-147.

149. A collection of cells comprising the collection of vectors of claim 148.

150. The collection of cells of claim 149, wherein a plurality of the cells are capable of expressing at least one polypeptide of any one of claims 132-147, optionally wherein different cells express different polypeptides.

151. The collection of polypeptides of any one of claims 132-147, wherein each of the one or more of said polypeptides is immobilized to a distinct location on one or more solid surfaces.

152. A method for identifying a protein-protein interaction, the method comprising:

(a) providing the collection of polypeptides of any one of claims 132-147, optionally wherein said polypeptides are immobilized on one or more solid surfaces;

(b) contacting the collection of step (a) with a multimerized query protein under conditions permitting the binding of the multimerized query protein and at least one of the extracellular domains of the polypeptides; and

(c) detecting an interaction between the multimerized query protein and the at least one extracellular domain, thereby identifying a protein-protein interaction.

153. The method of claim 152, wherein one or more of said polypeptides each is immobilized to a distinct location on said one or more solid surfaces.

154. The method of claim 152 or 153, wherein the distinct location comprises a cell that displays the polypeptide.

155. The method of claim 154, wherein the cells are mammalian cells.

156. The method of any one of claims 152-155, wherein the contacting step is semi-automated.

157. The method of any one of claims 152-156, wherein detecting an interaction comprises detecting a signal, optionally a fluorescent signal, at a location on the solid surface that is above a threshold level.

158. The method of claim 157, wherein the detecting is automated.

159. The method of any one of claims 152-158, wherein the interaction is a transient interaction.

160. The method of any one of claims 152-159, wherein the interaction is a low-affinity interaction.

161. The method of claim 160, wherein the low-affinity interaction is a micromolar-affinity interaction.

162. The method of any one of claims 152-161, wherein the multimerized query protein is a dimerized, trimerized, tetramerized, or pentamerized query protein.

163. The method of claim 162, wherein the multimerized query protein is a tetramerized query protein.

164. The method of any one of claims 152-163, wherein the multimerized query protein comprises an isolated extracellular domain of the query protein.

165. The method of claim 164, wherein the isolated extracellular domain of the query protein has been biotinylated and conjugated to a fluorescent streptavidin to tetramerize the query protein.

166. A method of identifying a modulator of the interaction between a protein of Table 1 and a protein of Table 2, the method comprising:

(a) providing a candidate modulator;

(b) contacting a protein of Table 1 with a protein of Table 2 in the presence or absence of the candidate modulator under conditions permitting the binding of the protein of Table 1 to the protein of Table 2, wherein the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and

(c) measuring the binding of the protein of Table 1 to the protein of Table 2, wherein an increase or decrease in binding in the presence of the candidate modulator relative to binding in the absence of the candidate modulator identifies the candidate modulator as a modulator of the interaction between the protein of Table 1 and the protein of Table 2.

167. A method of identifying a modulator of a downstream activity of a protein of Table 1, the method comprising:

(a) providing a candidate modulator;

(b) contacting the protein of Table 1 with a protein of Table 2 in the presence or absence of the candidate modulator under conditions permitting the binding of the protein of Table 1 to the protein of Table 2, wherein the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and

(c) measuring a downstream activity of the protein of Table 1, wherein a change in the downstream activity in the presence of the candidate modulator relative to the downstream activity in the absence of the candidate modulator identifies the candidate modulator as a modulator of the downstream activity of the protein of Table 1.

168. A method of identifying a modulator of a downstream activity of a protein of Table 2, the method comprising:

(a) providing a candidate modulator;

(b) contacting the protein of Table 2 with a protein of Table 1 in the presence or absence of the candidate modulator under conditions permitting the binding of the protein of Table 2 to the protein of Table 1, wherein the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and

(c) measuring a downstream activity of the protein of Table 2, wherein a change in the downstream activity in the presence of the candidate modulator relative to the downstream activity in the absence of the candidate modulator identifies the candidate modulator as a modulator of the downstream activity of the protein of Table 2.

169. The method of claim 166, wherein the increase or decrease in binding is at least 70%, as measured by surface plasmon resonance, biolayer interferometry, or an enzyme-linked immunosorbent assay (ELISA).

170. The method of claim 167 or 168, wherein the modulator is an inhibitor of the downstream activity of the protein of Table 1 or Table 2.

171. The method of claim 167 or 168, wherein the modulator is an activator of the downstream activity of the protein of Table 1 or Table 2.

172. The method of claim 167 or 168, wherein the change in the downstream activity is a decrease in the amount, strength, or duration of the downstream activity.

173. The method of claim 167 or 168, wherein the change in the downstream activity is an increase in the amount, strength, or duration of the downstream activity.

174. The method any one of claims 166-168, wherein the modulator is a small molecule, an antibody or antigen-binding fragment thereof, a peptide, a mimic, an antisense oligonucleotide, or a small interfering RNA (siRNA).

175. The method of claim 174, wherein the antigen-binding fragment is a bis-Fab, an Fv, a Fab, a Fab'-SH, a $F(ab')_2$, a diabody, a linear antibody, an scFv, an ScFab, a VH domain, or a VHH domain.

176. The method of claim 174, wherein the antibody or antigen-binding fragment thereof binds the protein of Table 1.

177. The method of claim 174, wherein the antibody or antigen-binding fragment thereof binds the protein of Table 2.

178. The method of any one of claims 166-168, wherein the protein of Table 1 is podoplanin (PDPN).

179. The method of claim 178, wherein the protein of Table 2 is CD177.

180. The method of claim 178 or 179, wherein the downstream activity is cancer-associated fibroblast (CAF) contractility.

181. The method of claim 180, wherein CAF contractility is decreased in the presence of the modulator.

182. The method of claim 181, wherein CAF contractility is decreased by at least 20%, as measured in a gel contraction assay.

183. The method of claim 182, wherein CAF contractility is decreased by at least 20%, as measured in a 3D gel elongation assay.

184. The method of claim 178 or 179, wherein the downstream activity is tumor growth.

185. The method of claim 184, wherein tumor growth is decreased in the presence of the modulator.

186. The method of claim 185, wherein tumor growth is decreased by at least 20%, as measured in a tumor growth assay.

187. The method of any one of claims 178-186, wherein the modulator is an antibody or antigen-binding fragment thereof targeting PDPN.

188. The method of any one of claims 178-186, wherein the modulator is an antibody or antigen-binding fragment thereof targeting CD177.

189. The method of any one of claims 166-168, wherein the protein of Table 1 is PD-L1 (CD274).

190. The method of claim 189, wherein the protein of Table 2 is EPHA3.

191. The method of any one of claims 166-168, wherein the protein of Table 1 is PD-L2 (PDCD1LG2).

192. The method of claim 191, wherein the protein of Table 2 is CEACAM4, ICAM5, NECTIN3, PSG9, or TNFRSF11A.

193. The method of claim 192, wherein the protein of Table 2 is CEACAM4.

194. The method of any one of claims 189-193, wherein the downstream activity is immune checkpoint inhibition.

195. The method of claim 194, wherein immune checkpoint inhibition is decreased in the presence of the modulator.

196. The method of claim 195, wherein immune checkpoint inhibition is decreased by at least 30%, as measured in a cell-based assay.

197. The method of any one of claims 166-168, wherein the protein of Table 1 is PTPRD.

198. The method of claim 197, wherein the PTPRD comprises a G203E and K204E; R232C and R233C; P249L; G285E; E406K; S431L; R561Q; P666S; E755K; V892I; S912F; R995C; or R1088C amino acid substitution mutation or a ΔG61 ΔE106 amino acid deletion mutation.

199. The method of claim 197 or 198, wherein the protein of Table 2 is BMP5, CEACAM3, IL1RAP, IL1RAPL2, LECT1, LRFN5, SIRPG, SLITRK3, SLITRK4, SLITRK6, or TGFA.

200. The method of any one of claims 197-199, wherein the downstream activity is suppression of cell proliferation.

201. The method of claim 200, wherein suppression of cell proliferation is increased in the presence of the modulator.

202. The method of claim 201, wherein suppression of cell proliferation is increased by at least 30%, as measured in a colony formation assay.

203. The method of any one of claims 197-199, wherein the downstream activity is suppression of STAT3 phosphorylation.

204. The method of claim 203, wherein suppression of STAT3 phosphorylation is increased in the presence of the modulator.

205. The method of claim 204, wherein suppression of STAT3 phosphorylation is increased by at least 30%, as measured in a Western blot for phosphorylated STAT3.

206. The method of any one of claims 166-168, wherein the protein of Table 1 is PTPRS.

207. The method of claim 206, wherein the protein of Table 2 is C6orf25, IL1RAP, IL1RAPL1, IL1RAPL2, LRFN1, LRFN5, LRRC4B, NCAM1, SLITRK1, SLITRK2, SLITRK3, SLITRK4, or SLITRK6.

208. The method of any one of claims 166-168, wherein the protein of Table 1 is PTPRF.

209. The method of claim 208, wherein the protein of Table 2 is CD177, IL1RAP, or LRFN5.

210. The method of any one of claims 206-209, wherein the downstream activity is inhibition of cell migration.

211. The method of claim 210, wherein inhibition of cell migration is increased in the presence of the modulator.

212. The method of claim 211, wherein inhibition of cell migration is increased by at least 20%.

213. The method of any one of claims 206-209, wherein the downstream activity is phosphorylation of EGFR.

214. The method of claim 213, wherein phosphorylation of EGFR is decreased in the presence of the modulator.

215. The method of claim 214, wherein phosphorylation of EGFR is decreased by at least 30%, as measured in an assay for phosphorylation of EGFR.

216. The method of any one of claims 166-168, wherein the protein of Table 1 is CHL1.

217. The method of claim 216, wherein the protein of Table 2 is CNTN1, CNTN5, SIRPA, L1CAM, or TMEM132A.

218. The method of claim 216 or 217, wherein the downstream activity is suppression of tumor formation.

219. The method of claim 218, wherein suppression of tumor formation is increased in the presence of the modulator.

220. The method of claim 219, wherein suppression of tumor formation is increased by at least 20%.

221. The method of any one of claims 166-168, wherein the protein of Table 1 is CNTN1.

222. The method of claim 221, wherein the protein of Table 2 is CDH6, CHL1, FCGRT, PCDHB7, or SGCG.

223. The method of claim 221 or 222, wherein the downstream activity is cell proliferation or cell invasion.

224. The method of claim 223, wherein cell proliferation or cell invasion is decreased in the presence of the modulator.

225. The method of claim 224, wherein cell proliferation is decreased by at least 20%, as measured in a colony formation assay.

226. The method of claim 224, wherein cell invasion is decreased by at least 20%, as measured in a gel invasion assay.

227. The method of any one of claims 166-168, wherein the protein of Table 1 is LILRB1.

228. The method of claim 227, wherein the protein of Table 2 is CLEC6A, CXADR, EDAR, FLT4, IL6R, ILDR1, or LILRA5.

229. The method of claim 227 or 228, wherein the downstream activity is suppression of phagocytosis.

230. The method of claim 229, wherein suppression of phagocytosis is decreased in the presence of the modulator.

231. The method of claim 230, wherein suppression of phagocytosis is decreased by at least 20%.

232. The method of any one of claims 166-168, wherein the protein of Table 1 is LILRB2.

233. The method of claim 232, wherein the protein of Table 2 is IGSF8 or MOG.

234. The method of any one of claims 166-168, wherein the protein of Table 1 is LILRB3.

235. The method of claim 234, wherein the protein of Table 2 is LRRC15 or LY6G6F.

236. The method of any one of claims 166-168, wherein the protein of Table 1 is LILRB4.

237. The method of claim 236, wherein the protein of Table 2 is CNTFR.

238. The method of any one of claims 166-168, wherein the protein of Table 1 is LILRB5.

239. The method of claim 238, wherein the protein of Table 2 is APLP2, CD177, CLEC10A, CLECSF13, LDLR, PILRA, or UNC5C.

240. The method of claim 239, wherein the protein of Table 2 is LDLR.

241. The method of any one of claims 227, 228, and 234-240, wherein the downstream activity is osteoclast differentiation.

242. The method of claim 241, wherein osteoclast differentiation is decreased by at least 20% in the presence of the modulator.

243. The method of claim 242, wherein osteoclast differentiation is measured in an assay for TRAP+ multinucleated cells.

244. The method of any one of claims 166-168, wherein the protein of Table 1 is AXL.

245. The method of claim 244, wherein the protein of Table 2 is IL1RL1 or VSIG10L.

246. The method of claim 244 or 245, wherein the downstream activity is activation of the RAS/RAF/MAPK/ERK1/2 pathway, activation of the JAK/STAT pathway, activation of the PI3K signaling pathway, cell migration, formation of filopodia, or phosphorylation of AXL.

247. The method of claim 246, wherein cell migration is decreased by at least 20% as measured in a gel invasion assay.

248. The method of any one of claims 166-168, wherein the protein of Table 1 is LRRC4B.

249. The method of claim 248, wherein the protein of Table 2 is BTN3A1 or BTN3A3

250. The method of any one of claims 166-249, wherein expression of the protein of Table 1 or the protein of Table 2 is upregulated or downregulated in tumor tissue relative to healthy tissue.

251. An isolated modulator of the interaction between a protein of Table 1 and a protein of Table 2, wherein:

i. the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and

ii. the modulator causes an increase or decrease in the binding of the protein of Table 1 to the protein of Table 2 relative to binding in the absence of the modulator.

252. An isolated modulator of the downstream activity of a protein of Table 1 or a protein of Table 2, wherein:

i. the protein of Table 1 and the protein of Table 2 are reported to interact in Table 3; and

ii. the modulator causes a change in the downstream activity of the protein of Table 1 or the protein of Table 2 relative to downstream activity in the absence of the modulator.

253. The modulator of claim 251, wherein the increase or decrease in binding is at least 70%, as measured by surface plasmon resonance, biolayer interferometry, or an enzyme-linked immunosorbent assay (ELISA).

254. The modulator of claim 251 or 252, wherein the modulator is an inhibitor of the downstream activity of the protein of Table 1 or Table 2.

255. The modulator of claim 251 or 252, wherein the modulator is an activator of the downstream activity of the protein of Table 1 or Table 2.

256. The modulator of claim 252, wherein the change in the downstream activity is a decrease in the amount, strength, or duration of the downstream activity.

257. The modulator of claim 252, wherein the change in the downstream activity is an increase in the amount, strength, or duration of the downstream activity.

258. The modulator of any one of claims 251-257, wherein the modulator is a small molecule, an antibody or antigen-binding fragment thereof, a peptide, or a mimic.

259. The modulator of claim 258, wherein the antigen-binding fragment is a bis-Fab, an Fv, a Fab, a Fab'-SH, a $F(ab')_2$, a diabody, a linear antibody, an scFv, an ScFab, a VH domain, or a VHH domain.

260. The modulator of claim 259, wherein the antibody or antigen-binding fragment thereof binds the protein of Table 1.

261. The modulator of claim 259, wherein the antibody or antigen-binding fragment thereof binds the protein of Table 2.