

COMPOSITIONS AND METHODS FOR TARGETED DELIVERY OF THERAPEUTIC AGENTS

SEQUENCE LISTING

5 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 June 6, 2022, is named 51666-002WO2_Sequence_Listing_6_6_22_ST25 and is 276,968 bytes in size.

BACKGROUND OF THE INVENTION

10 Undesirable off-target effects are a problem for otherwise desirable therapeutic targets that are present in healthy as well as diseased tissues.

SUMMARY OF THE INVENTION

The present disclosure describes, in part, macromolecule compositions and related methods that effect targeted delivery of therapeutic agents to effector targets in a desired cell, tissue and/or organ of interest while minimizing or avoiding undesirable delivery to other cells, tissues or organs. Generally, compositions described herein comprise macromolecules, such as an ANDbody™, that include an effector target binding domain specific for an effector target, and an address binding domain specific for an address target. The address target is generally sufficiently restricted in the subject to target the macromolecule to the desired cell, tissue or organ. In some embodiments, the effector target binding domain does not influence an effector target in the absence of an address target binding domain. Moreover, the address target binding domain does not influence signaling upon binding the address target. However, localization of the effector target binding domain by the address target binding domain enables the effector target binding domain to bind the effector target sufficiently to elicit an influence on signaling by the effector target in the target cell or tissue. The compositions described herein can be used, e.g., to specifically deliver a therapeutic agent to a desired location, e.g., a cell, tissue or organ, in a subject, while avoiding undesirable off-target effects.

In one aspect, the present disclosure provides a method of localizing a macromolecule at a target tissue or cell of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in the subject, and (b) the second binding site is specific for an address target expressed in the target tissue or cell in the subject; wherein: (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and allowing the macromolecule to localize at the target tissue or cell of the subject.

In some embodiments, at least 25% of the macromolecule detectable in the subject is detected at the target tissue or cell at a time point between 1 and 7 days following administration of

the macromolecule to the subject.

In some embodiments, the potency of the first binding site at the target tissue or cell is substantially increased relative to a reference macromolecule lacking the second binding site.

In some embodiments, the first binding site has a low affinity for the effector target.

In some embodiments, the first binding site has a low avidity for the effector target.

In some embodiments, the affinity of the first binding site for the effector target is lower than the affinity of the second binding site for the address target.

In some embodiments, the avidity of the first binding site for the effector target is lower than the avidity of the second binding site for the address target.

In some embodiments, effector target signaling by the macromolecule in a non-target tissue or cell of the subject is substantially decreased relative to a reference macromolecule lacking the second binding site.

In some embodiments, the address target is regionally expressed in the subject. In some embodiments, the address target is locally expressed in the subject. In some embodiments, the expression of the address target is restricted to a cell type in the subject.

In some embodiments, the address target is expressed only by a cell in the subject when in a specific cell state.

5 In some embodiments, the address target is expressed only by a cell in the subject in a disease state.

In some embodiments, the first binding site or the second binding site comprises a polypeptide.

In some embodiments, the polypeptide is an antibody or antigen-binding fragment thereof.

In some embodiments, the macromolecule is an antibody comprising a first binding site that is specific for the effector target in the subject and a second binding site that is specific for the address target.

In some embodiments, the polypeptide is a ligand of the effector target or a ligand of the address target.

In some embodiments, (a) the first binding site comprises an antibody or antigen-binding fragment thereof and the second binding site comprises a ligand of the address target; or (b) the first binding site comprises a ligand of the effector target and the second binding site comprises an antibody or antigen-binding fragment thereof.

In some embodiments, the target tissue is skin and the second binding site is specific for desmoglein-1 (DSG-1).

In some embodiments, the target tissue is lung tissue and the second binding site is specific for RAGE.

In some embodiments, the target tissue is kidney tissue and the second binding site is specific for cadherin 16 (CDH16).

In some embodiments, the target tissue is intestine tissue and the second binding site is specific for cadherin 17 (CDH17).

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein: (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site.

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and wherein localization of the macromolecule to a non-target tissue or cell is substantially reduced relative to localization of a reference macromolecule lacking the second binding site.

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and wherein localization of the macromolecule to a target tissue or cell is substantially increased relative to localization of a reference macromolecule lacking the second binding site.

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and wherein at least **25%** of the macromolecule administered to a subject is detected at the target tissue or cell at a time point between 1 and 7 days following administration.

In another aspect, the present disclosure provides a macromolecule comprising a first binding

site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and wherein the affinity of the first binding site for the effector target is lower than the affinity of the second binding site for the address target.

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and wherein the avidity of the first binding site for the effector target is lower than the avidity of the second binding site for the address target.

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and wherein the potency of the first binding site at the target tissue or cell is substantially increased relative to a reference macromolecule lacking the second binding site.

In some embodiments, the first binding site has a low affinity for the effector target.

In some embodiments, the first binding site has a low avidity for the effector target.

In some embodiments, the affinity of the first binding site for the effector target is lower than the affinity of the second binding site for the address target.

In some embodiments, the avidity of the first binding site for the effector target is lower than the avidity of the second binding site for the address target.

In some embodiments, (a) the K_d of the first binding site for the effector target is higher than the K_d of the second binding site for the address target; (b) the EC_{50} of the first binding site for the effector target is higher than the EC_{50} of the second binding site for the address target; or (c) the IC_{50} of the first binding site for the effector target is higher than the IC_{50} of the second binding site for the address target.

In some embodiments, the first binding site has an affinity to the effector target of at least

about 2 times, at least about 5 times, or at least about 10 times less than the affinity of the second binding site to the address target.

In some embodiments, the affinity of the second binding site to the address target has a K_d of greater than about 1 nM, greater than about 2 nM, or greater than about 50 nM.

In some embodiments, the effector target is a protein, lipid, or sugar.

In some embodiments, the effector target is a cell membrane-associated target.

In some embodiments, the effector target is a protein. In some embodiments, the effector target is a secreted protein.

In some embodiments, the effector target is encoded by a gene selected from the group consisting of the genes recited in Table 1.

In some embodiments, the macromolecule agonizes the effector target.

In some embodiments, the macromolecule antagonizes the effector target.

In some embodiments, the address target is a protein, lipid, or sugar.

In some embodiments, the address target is a protein.

In some embodiments, expression of the effector target or the address target is expression of an RNA sequence encoding the effector target or the address target.

In some embodiments, the expression level of the effector target or the address target is assessed by using a RNA sequence dataset.

In some embodiments, the RNA sequence dataset is a Genotype-Tissue Expression (GTEx) dataset or a Human Protein Atlas (HPA) dataset.

In some embodiments, expression of the effector target or the address target is protein expression.

In some embodiments, the effector target is systemically expressed in the subject.

In some embodiments, the effector target is regionally expressed in the subject.

In some embodiments, the effector target is locally expressed in the subject.

In some embodiments, the address target is regionally expressed in the subject.

In some embodiments, the address target is locally expressed in the subject.

In some embodiments, the expression of the address target is restricted to a cell type in the subject.

In some embodiments, the address target is a soluble protein or an extracellular matrix (ECM)-associated protein and is not present in detectable amounts on the cell surface.

In some embodiments, the address target is expressed in the ECM and is not present in detectable amounts elsewhere in the subject.

In some embodiments, the address target is expressed only by a cell in the subject when in a specific cell state.

In some embodiments, the address target is expressed only by a cell in the subject when in a disease state.

In some embodiments, the address target is not expressed in a tissue in which binding of the second binding site to the effector target is deleterious to the subject.

In some embodiments, the binding site for the address target does not bind in detectable amounts to the binding site of a natural ligand of the address target.

In some embodiments, expression of the effector target or address target includes expression in one or more of minor salivary gland, thyroid, lung, breast, mammary tissue, pancreas, adrenal gland, liver, kidney, kidney cortex, kidney medulla, adipose-visceral tissue, omentum, small intestine, terminal ileum, fallopian tube, ovary, uterus, skin, skin not sun exposed, suprapubic skin, cervix, endocervix, ectocervix, vagina, skin sun exposed, lower leg skin, eneanterior cingulate cortex, Brodmann area 24 (BA24), basal ganglia, caudate nucleus, putamen, nucleus acumbens, hypothalamus, amygdala, hippocampus, cerebellum, cerebellar hemisphere, substantia nigra, pituitary gland, spinal cord, cervical spinal cord, artery, aorta, heart, atrial appendage, coronary artery, left ventricle, esophagus, esophagus mucosa, esophagus muscularis, gastroesophageal junction, spleen, stomach, colon, transverse colon, sigmoid colon, testis, whole blood cells, EBV-transformed lymphocytes, artery-tibial, or nerve-tibial tissues.

In some embodiments, expression of the effector target or address target includes expression in skin tissue, lung tissue, kidney tissue, or intestine tissue. In some embodiments, expression of the address target is substantially higher in skin tissue, lung tissue, kidney tissue, or intestine tissue than in any other tissue.

In some embodiments, the effector target and/or the address target is expressed on a structural tissue in the subject.

In some embodiments, the effector target and address target are on the same cell.

In some embodiments, the effector target and address target are on different cells.

In some embodiments, the effector target and address target are on different cells of the same cell type.

In some embodiments, the effector target and address target are on different cells of different cell types.

In some embodiments, the effector target and address target are on different cells in the same tissue.

In some embodiments, (a) the effector target is on a circulating cell and the address target is on a tissue-restricted cell; or (b) the effector target is on a tissue-restricted cell and the address target is on a circulating cell.

In some embodiments, the effector target and address target are on different cells located within 100 nm of each other in the subject.

In some embodiments, either the effector target or the address target is present on a cell surface.

In some embodiments, the macromolecule is a DNA polynucleotide.

In some embodiments, the macromolecule comprises an RNA or RNA-polypeptide conjugate.

In some embodiments, the macromolecule comprises a polypeptide. In some embodiments, the macromolecule is a polypeptide.

In some embodiments, the polypeptide is an antibody or antigen-binding fragment thereof.

In some embodiments, the first binding site and the second binding site each comprise a VH and/or a VL.

In some embodiments, the macromolecule is an antibody comprising a first binding site that is specific for the effector target in the subject and a second binding site that is specific for the address target.

In some embodiments, the macromolecule is an asymmetric antibody or a symmetric antibody.

- 5 In some embodiments, the antibody or antigen-binding fragment thereof comprises an scFv, BslgG, a BsAb fragment, a BiTE, a dual-affinity re-targeting protein (DART), a tandem diabody (TandAb), a diabody, an Fab2, a di-scFv, chemically linked F(ab')₂, an Ig molecule with 2, 3 or 4 different antigen binding sites, a DVI-IgG four-in-one, an ImmTac, an HSAbody, an IgG-IgG, a Cov-X-Body, an scFv1-PEG-scFv₂, an appended IgG, an DVD-IgG, an affibody, an affilin, an affimer, an affitin, an alphabody, an anticalin, an avimer, a DARPin, a Fynomer, a monobody, a nanoCLAMP, a
10 bis-Fab, an Fv, a Fab, a Fab'-SH, a linear antibody, an scFv, an antibody with only a heavy chain (Humabody), an ScFab, an IgG antibody fragment, a single-chain variable region antibody, a single-domain heavy chain antibody, a bispecific triplebody, a BIKE, a CrossMAb, a dsDb, an scDb, tandem a dAb / VHH, a triple dAb VHH, a tetravalent dAb / VHH, a Fab-scFv, a Fab-Fv, or a DART-Fc,
15 an adnectin, a Kunitz-type inhibitor, or a receptor decoy.

In some embodiments, the polypeptide is a ligand of the effector target or a ligand of the address target.

In some embodiments, the ligand is a natural ligand, a modified ligand, or a synthetic ligand.

In some embodiments, the effector target or address target is a receptor and the polypeptide is a ligand thereof.

- 20 In some embodiments, the first binding site comprises an antibody or antigen-binding fragment thereof and the second binding site comprises a ligand of the address target.

In some embodiments, the first binding site comprises a ligand of the effector target and the second binding site comprises an antibody or antigen-binding fragment thereof.

- 25 In some embodiments, the amino acid sequences of the first and second binding sites are at least about 10% identical, at least about 20% identical, at least about 30% identical, at least about 40% identical, at least about 50% identical, at least about 60% identical, or at least about 70% identical.

In some embodiments, the address target has a Gini coefficient higher than about 0.4, about 0.5, about 0.57, about 0.65, about 0.7, about 0.85, about 0.90, or about 0.95.

In some embodiments, the address target has a Tau coefficient higher than about 0.67, about 0.75, about 0.8, about 0.85, about 0.90, or about 0.95.

In some embodiments, the effector target has a Gini coefficient lower than about 0.25, about 0.20, or about 0.15.

In some embodiments, the effector target has a Tau coefficient lower than about 0.25, about 0.20, or about 0.15.

In some embodiments, the macromolecule further comprises a third binding site. In some embodiments, the third binding site is the same as the first binding site. In some embodiments, the third binding site is the same as the second binding site.

In some embodiments, the first binding site and second binding site are directly joined to each other in the macromolecule.

In some embodiments, the first binding site and the second binding site in the macromolecule are joined by a stable domain.

In some embodiments, the effector target is Notch2 and the address target is RAGE.

In some embodiments, RAGE signaling is not influenced by the second site binding the RAGE address target.

5 In some embodiments, the effector target is Notch2 and the address target is uromodulin (UMOD).

In some embodiments, UMOD signaling is not influenced by the second site binding the UMOD address target.

10 In some embodiments, the effector target is Notch2 and the address target is meprin A subunit beta (MEP1B).

In some embodiments, MEP1B signaling is not influenced by the second site binding the MEP1B address target.

In some embodiments, the effector target is IL11Ra and the address target is RAGE. In some embodiments, RAGE signaling is not influenced by the second site binding the RAGE address target.

15 In some embodiments, the effector target is IL 11Ra and the address target is UMOD. In some embodiments, UMOD signaling is not influenced by the second site binding the UMOD address target.

In some embodiments, the subject is a human.

In another aspect, the present disclosure provides a method of delivering a moiety to a target tissue or cell in a subject, comprising administering to the subject a macromolecule of any one of claims 1-86, wherein the target tissue comprises the address target.

In some embodiments, the moiety is a molecule.

In some embodiments, the moiety is not a toxin.

In some embodiments, the moiety is a cell.

In some embodiments, the moiety is not a T cell or an NK cell.

In some embodiments, the target tissue is not a tumor.

In another aspect, the present disclosure provides a method of modulating an effector target in a target tissue, comprising administering to the tissue a macromolecule of any one of claims 1-86, wherein the target tissue comprises the address target and the effector target.

In another aspect, the present disclosure provides a method of biasing a binding agent away from binding an effector target when the effector target is found in the heart or lungs, comprising administering the macromolecule of any one of claims 1-86, wherein the address target is not substantially expressed in the heart or lungs.

In another aspect, the present disclosure provides a method of modulating a target tissue in a subject, comprising administering to the subject a macromolecule of any one of claims 1-86, wherein the target tissue comprises the address target and the effector target.

In another aspect, the present disclosure provides a method of treating a subject having a disease or condition associated with an effector target, comprising administering to the subject a macromolecule of any one of claims 1-86, wherein the first binding site of the macromolecule binds the effector target.

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell, wherein the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site, and wherein the second binding site does not bind to the binding site of the natural ligand of the address target.

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell, wherein the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site, and wherein the first binding site and second binding site are directly joined to each other in the macromolecule.

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell, wherein the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site, and wherein the first binding site and second binding are joined to each other by a stable domain.

In another aspect, the present disclosure provides a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell, wherein the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site, and wherein the effector target and/or the address target is expressed on a structural tissue in a host.

In another aspect, the present disclosure provides a pharmaceutical composition comprising the macromolecule of any one of the above embodiments.

In another aspect, the present disclosure provides a pharmaceutical composition comprising a macromolecule and one or more pharmaceutically acceptable excipients, wherein the macromolecule comprises a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell, and wherein the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site.

In some embodiments, the pharmaceutical composition is an RNA pharmaceutical composition.

In some embodiments, the pharmaceutical composition further comprises a carrier.

In some embodiments, the carrier is a lipid nanoparticle.

In some embodiments, the carrier is a viral vector.

In some embodiments, the carrier is a membrane-based carrier.

In some embodiments, the membrane-based carrier is a cell.

In some embodiments, the membrane-based carrier is a vesicle.

5 In another aspect, the present disclosure provides a method for modulating activity of an effector target in the skin of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in the subject, and (b) the second binding site is specific for desmoglein-1 (DSG-1).

In another aspect, the present disclosure provides a method for modulating activity of an effector target in the lung of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in the subject, and (b) the second binding site is specific for RAGE.

In another aspect, the present disclosure provides a method for modulating activity of an effector target in the kidney of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in the subject, and (b) the second binding site is specific for cadherin 16 (CDH16).

In another aspect, the present disclosure provides a method for modulating activity of an effector target in the intestine of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in the subject, and (b) the second binding site is specific for cadherin 17 (CDH17).

In another aspect, the present disclosure provides a method of localizing a macromolecule at

a target tissue or cell of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in the subject, and (b) the second binding site is specific for an address target expressed in the target tissue or cell in the subject; wherein: (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and allowing the macromolecule to localize at the target tissue or cell of the subject.

In another aspect, the present disclosure provides a method of concentrating a macromolecule in a target tissue or cell in a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein (a) the first binding site is specific for an effector target in a subject, and (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell; (ii) the second binding site does not substantially influence signaling upon binding the address target; and (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; and allowing the macromolecule to concentrate at the target tissue or cell of the subject, wherein at least 25% of the macromolecule detectable in the subject is detected at the target tissue or cell at a time point between 1 and 7 days following administration of the macromolecule to the subject.

In some embodiments, the potency of the first binding site at the target tissue or cell is substantially increased relative to a reference macromolecule lacking the second binding site.

In some embodiments, effector target signaling by the macromolecule in a non-target tissue or cell of the subject is substantially decreased relative to a reference macromolecule lacking the second binding site.

In some embodiments, the macromolecule is a macromolecule of any one of the above embodiments.

The details of one or more embodiments of the invention are set forth in the description below. Other features or advantages of the present invention will be apparent from the following drawings and detailed description of several embodiments, and also from the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic illustrating exemplary ANDbody™ molecules and their use as logic-gated medicines. FIG. 1 shows broad distribution of a therapeutic target (right side), such as an effector target, in a human subject with no address targeting, and a localized and restricted distribution with address targeting (left side), which is provided by an address target binding domain. FIG. 1 also provides a representative bipartite structure of an ANDbody with an address target binding domain linked to an effector target binding domain, which includes a functional moiety, e.g., a moiety

that modulates, e.g., agonizes or antagonizes, a target effector in an address targeted cell or tissue. The address target binding domain directs the ANDbody to a desired location, such as a targeted cell or tissue, allowing for the effector target binding domain to engage the therapeutic effector target in the localized and restricted distribution area. In some embodiments, high affinity of the effector domain for the target effector may not be required; localization of the effector target binding domain by the address target binding domain enables the effector target binding domain to bind the effector target sufficiently to elicit an influence on signaling by the effector target in the target cell or tissue despite low affinity of the effector domain for the effector target. The address target binding domain can alternatively be used to transport molecular or cellular cargos to a desired address.

FIG. 2 is a schematic map showing activity of exemplary effector targets that can be restricted to tissues or cells of interest by developing ANDbody therapeutics comprised of an effector targeting domain and an address targeting domain. These ANDbody biologics represent potent, address-restricted medicines according to the present technology.

FIG. 3 provides exemplary structures of ANDbody biologics that can be engineered according to the present technology, including (but not limited to): an asymmetric antibody, an dual-affinity re-targeting protein (DART), a tandem diabody (TandAb), a diabody, an Fab2, IgG(L,H)-Fv or a BiTE.

FIG. 4 demonstrates an EC₅₀ curve of an exemplary single effector targeting domain (dashed line), such as a monospecific biologic (for example scFv) having a single binding domain to an effector target compared to an EC₅₀ of an exemplary bispecific ANDbody biologic (for example di-scFc) with an address target binding domain and an effector target binding domain (solid line), such that single effector targeting domain (usually broadly expressed) is targeted/restricted to local, address target-specific tissues and/or cells, thus effectively increasing affinity of the effector target binding domain for the effector target binding site, as evidenced by a shift of the curve to the left (lower EC₅₀, higher affinity).

FIG. 5A is a bar graph showing the level of fluorescence intensity detected in the indicated tissues in mice treated with the anti-DSG1 antibody PRO003 conjugated to IRDYE® 800CW. Data are shown as average of three mice. To control for differences in labeling efficiency, values are shown with the strongest signal set to 1.

FIG. 5B is a bar graph showing the level of fluorescence intensity detected in the indicated tissues in mice treated with the anti-DSG1 antibody PRO004 conjugated to IRDYE® 800CW or with a vehicle control (untreated). Data are shown as average of three mice. To control for differences in labeling efficiency, values are shown with the strongest signal set to 1.

FIG. 6A is a bar graph showing the level of fluorescence intensity detected in the indicated tissues in mice treated with the anti-RAGE antibody PRO001 conjugated to IRDYE® 800CW or with a vehicle control. Data are shown as average of three mice. To control for differences in labeling efficiency, values are shown with the strongest signal set to 1.

FIG. 6B is a bar graph showing the level of fluorescence intensity detected in the indicated tissues in mice treated with the anti-RAGE antibody PRO002 conjugated to IRDYE® 800CW or with a vehicle control. Data are shown as average of three mice. To control for differences in labeling

efficiency, values are shown with the strongest signal set to 1.

FIG. 7 is a pair of photomicrographs showing representative IHC staining of an anti-human secondary antibody conjugated to horseradish peroxidase in lung tissue of Balb/C mice that were treated by tail vein injection with 3 mg/kg of the anti-RAGE antibody PRO002 (left panel) as compared to untreated mice (right panel). PRO002 comprises a human IgG1 backbone.

FIG. 8 is a bar graph showing the level of fluorescence intensity detected in the indicated tissues in mice treated with the anti-CDH16 antibody PRO056 conjugated to IRDYE® 800CW or with a vehicle control. Data are shown as average of three mice. To control for differences in labeling efficiency, values are shown with the strongest signal set to 1.

FIG. 9 is a bar graph showing the level of fluorescence intensity detected in the indicated tissues in mice treated with the anti-CDH17 antibody PRO061 conjugated to IRDYE® 800CW or with a vehicle control. Data are shown as average of three mice. To control for differences in labeling efficiency, values are shown with the strongest signal set to 1.

FIG. 10 is a set of photomicrographs showing staining for the Notch2 antagonistic mAbs PRO034, PRO035, and PRO036 and the corresponding RAGE-targeting ANDbodies PRO051, PRO052, and PRO053 on fresh frozen healthy mouse tissue microarray (FF TMA) sections. Lung sections are indicated by boxes.

FIG. 11 is a plot showing the concentration of PRO052, a control antibody that binds RAGE and respiratory syncytial virus (RSV) glycoprotein F (RAGE XT-4/Motavizumab), and a control antibody that binds Notch2 and RSV glycoprotein F (Notch2-2/Motavizumab), as detected by sandwich ELISA. Points show the average of three mice. Error bars show the standard deviation.

FIG. 12 is a set of schematic diagrams showing the design of the PRO023, PRO025, PRO024, PRO027, and PRO026 IL-10/DSG1 ANDbodies.

FIG. 13A is a bar graph showing the level of tumor necrosis factor alpha (TNFα) in peripheral blood mononuclear cell (PBMC) cell culture after pre-stimulation with hrIL-10 followed by treatment with lipopolysaccharide (LPS) for the indicated lengths of time.

FIG. 13B is a bar graph showing the level of TNFα in PBMC cell culture after pre-stimulation with an anti-DSG1 monoclonal antibody (mAb) followed by treatment with LPS for the indicated lengths of time.

FIG. 13C is a bar graph showing the level of TNFα in PBMC cell culture after pre-stimulation with the IL-10/DSG1 ANDbody PRO024 followed by treatment with LPS for the indicated lengths of time.

FIG. 13D is a bar graph showing the level of TNFα in PBMC cell culture after pre-stimulation with the IL-10/DSG1 ANDbody PRO026 followed by treatment with LPS for the indicated lengths of time.

FIG. 13E is a bar graph showing the level of TNFα in PBMC cell culture after pre-stimulation with the IL-10/DSG1 ANDbody PRO023 followed by treatment with LPS for the indicated lengths of time.

FIG. 13F is a bar graph showing the level of TNFα in PBMC cell culture after pre-stimulation

with the IL-10/DSG1 ANDbody PRO025 followed by treatment with LPS for the indicated lengths of time.

FIG. 13G is a bar graph showing the level of TNF α in PBMC cell culture after pre-stimulation with the IL-10/DSG1 ANDbody PRO027 followed by treatment with LPS for the indicated lengths of time.

FIG. 14A is a bar graph showing the level of TNF α in primary macrophage cell culture cell culture after pre-stimulation with hrIL-10 followed by treatment with LPS for the indicated lengths of time.

FIG. 14B is a bar graph showing the level of TNF α in primary macrophage cell culture after pre-stimulation with the anti-DSG1 monoclonal antibody (mAb) PRO003 followed by treatment with LPS for the indicated lengths of time.

FIG. 14C is a bar graph showing the level of TNF α in primary macrophage cell culture after pre-stimulation with the IL-10/DSG1 ANDbody PRO024 followed by treatment with LPS for the indicated lengths of time.

FIG. 14D is a bar graph showing the level of TNF α in primary macrophage cell culture after pre-stimulation with the IL-10/DSG1 ANDbody PRO026 followed by treatment with LPS for the indicated lengths of time.

FIG. 14E is a bar graph showing the level of TNF α in primary macrophage cell culture after pre-stimulation with the IL-10/DSG1 ANDbody PRO023 followed by treatment with LPS for the indicated lengths of time.

FIG. 14F is a bar graph showing the level of TNF α in primary macrophage cell culture after pre-stimulation with the IL-10/DSG1 ANDbody PRO025 followed by treatment with LPS for the indicated lengths of time.

FIG. 14G is a bar graph showing the level of TNF α in primary macrophage cell culture after pre-stimulation with the IL-10/DSG1 ANDbody PRO027 followed by treatment with LPS for the indicated lengths of time.

FIG. 15 is a plot showing the level of IL-10 signaling detected in parental HEK-BLUE™ IL-10 cells or HEK-BLUE™ IL-10 cells stably expressing DSG1 (+ DSG1 expression) that were treated overnight with the IL-10/DSG1 ANDbody PRO058 (functionally equivalent to PRO026) or a control antibody that comprises IL-10 and binds RSV glycoprotein F (IL-10/Motavizumab) at the indicated concentrations. IL-10 was measured using a colorimetric assay to detect expression of secreted embryonic alkaline phosphatase (SEAP). OD630: optical density at 630 nm. Curve fitting was performed using GraphPad Prism 9 to fit a 4-parameter log(agonist) vs. response.

FIG. 16A is a plot showing the concentration (ng/mL) of PRO003, PRO024, and PRO058 over time in serum samples from BALB/c mice dosed by tail vein injection with 3 mg/kg of the indicated antibody or ANDbody. The concentration of circulating molecules was measured by ELISA. Average concentration and standard deviation are shown. N=3.

FIG. 16B is a plot showing the concentration (ng of target protein per mg of total protein) of PRO003, PRO024, and PRO058 (functionally equivalent to PRO026) over time in skin tissue samples

from BALB/c mice dosed by tail vein injection with 3 mg/kg of the indicated antibody or ANDbody. Skin samples were collected at the indicated time points and homogenized to extract proteins. Concentration was measured by ELISA. Average concentration and standard deviation are shown. N=3.

5 FIG. 17 is a set of schematic diagrams showing the design of the PRO070, PRO074, PRO075, and PRO077 TNF α -blocking anti-DSG1 ANDbodies.

FIG. 18A is a plot showing the level of IL-10 signaling detected in parental HEK-BLUE™ IL-10 cells that were treated overnight with PRO003, recombinant human IL-10 (rhIL-10), or recombinant human IL-10 fused to a human Fc domain (IL-10-Fc). IL-10 was measured using a colorimetric assay to detect expression of SEAP. OD630: optical density at 630 nm. Curve fitting was performed using GraphPad Prism 9 to fit a 4-parameter log(agonist) vs. response.

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FIG. 18B is a plot showing the level of IL-10 signaling detected in parental HEK-BLUE™ IL-10 cells that were treated overnight with the IL-10/DSG1 ANDbodies PRO023, PRO024, PRO025, PRO026, and PRO027. IL-10 was measured using a colorimetric assay to detect expression of SEAP. OD630: optical density at 630 nm. Curve fitting was performed using GraphPad Prism 9 to fit a 4-parameter log(agonist) vs. response.

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DETAILED DESCRIPTION OF THE INVENTION

Provided herein are ANDbody™ molecules that include a therapeutic effector target binding domain and an address target binding domain. The therapeutic effector target on the ANDbody molecule productively engages its therapeutic effector target only if the address target binding domain also engages an address target on a target tissue or cell to localize the effector target to the targeted cell or tissue, e.g., to form an AND-gate type of logic gate. For example, in some embodiments, an ANDbody is a macromolecule comprising at least (a) a first binding site specific for a therapeutic effector target that is expressed, e.g., broadly expressed, on a mammalian subject, e.g., on a cell surface; and (b) a second binding site specific for an address target. In embodiments, expression of the address target is restricted *in vivo* in a subject. In some embodiments, the binding of a first binding site to a therapeutic effector target is weaker than the binding of the second binding site to the address marker. The effector and address targets may be on the same cell, or in different cells or compartments within the same tissue.

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In some embodiments, at least 25% of the macromolecule (e.g., ANDbody) detectable in the subject is detected at the target tissue or cell at a time point between 1 and 7 days (e.g., at 1 day, 2 days, 3 days, 4 days, 5, days, 6 days, and/or 7 days) following administration of the macromolecule (e.g., ANDbody) to the subject. For example, in some embodiments, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 100% (e.g., 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%, or 95-100%) of the macromolecule detectable in the subject is detected at the target

tissue or cell at a time point between 1 and 7 days following administration of the macromolecule the subject.

Effector Target

An ANDbody™ of the invention comprises an effector that modulates a therapeutic effector target in a subject, e.g., a mammalian subject such as a human, in need thereof. As used herein, an "effector target" is a discrete structure (e.g., a cell surface protein, a transmembrane protein, a receptor) of a cell or tissue of a subject, to which a therapeutic effector binding domain of an ANDbody can bind and exert a modulating effect, such as a therapeutic effect, on the subject. The ANDbody described herein has a binding site specific for an effector target. Upon binding of the effector binding domain to the effector target, the effector modulates the target cell or tissue to produce a biological response, such as a therapeutic effect, on the subject. However, in some embodiments, the effector target binding domain provided herein may not elicit a biological effect unless it is provided in conjunction with an address targeting domain to localize the effector to the desired target address in a targeted cell or tissue. In some embodiments, such therapeutic signaling may require the binding of multiple effector targets by multiple macromolecules according to the invention.

In some embodiments, an effector target binding domain may produce a small/weak biological effect when provided alone and provide a larger/stronger biological effect when provided in conjunction with an address targeting domain that localizes and concentrates/focuses the effector to the desired target address in a targeted cell or tissue. In some embodiments, an effector target binding domain may produce an acceptable biological effect when provided alone and provide an even larger/stronger biological effect when provided in conjunction with an address targeting domain to localize the effector target binding domain to a targeted cell or tissue. In some embodiments, an effector target binding domain may produce a strong biological effect when provided alone and provide a strong, or stronger, targeted effect when provided in conjunction with an address targeting domain to localize the effector target binding domain to a targeted cell or tissue. In some embodiments, an effector target binding domain may produce a biological effect with undesirable off target biological effects when provided alone, but can be targeted, concentrated, and focused to desired addresses in a targeted cell or tissue when provided in conjunction with an address targeting domain in order to decrease or eliminate undesirable off-target biological effects. Accordingly, effector target binding domains of the present technology provide superior therapeutic agents that provide stronger, targeted biological effects with less side effects, including less unintended off-target biological effects, when provided in conjunction with address target binding domains as described herein.

Examples of such therapeutic signaling effects include, but are not limited to:

- (i) blocking a signal transduction pathway that promotes or maintains a disease state;
- (ii) activating a signal transduction pathway that reduces or prevents a disease state;

- (iii) promoting antibody-dependent cellular cytotoxicity (ADCC);
- (iv) inducing complement activation on the target cell or tissue;
- (v) promoting phagocytosis;
- (vi) blocking or activating a signal transduction pathway that promotes differentiation of a cell;
- (vii) inducing tissue remodeling to reduce or prevent fibrosis.

In some embodiments, the therapeutic effector target is more broadly expressed than the address target in the subject. In some embodiments, the therapeutic effector target is expressed systemically, regionally, or locally in the organism. "Systemic expression" of a therapeutic effector target means that the therapeutic effector target is expressed at substantially the same levels in most parts of a subject organism body. Systemic expression involves a plurality of tissues. "Regional expression" of a therapeutic effector target means that the therapeutic target is expressed in an area less than systemic expression but more than local expression. Regional expression is not limited to a single tissue but can occur in a plurality of different tissues. "Local expression" of a therapeutic effector target means that the therapeutic target is expressed in single or few tissue areas. Local expression is not limited to a single tissue but can occur in a plurality of different tissues.

In some embodiments, the effector target binding domain has a low affinity for the effector target. For example, a low affinity may be an affinity of greater than 10 nM (e.g., an affinity between 10 nM-1 μ M, e.g., an affinity between 10 nM and 100 nM).

In some embodiments, the effector target binding domain has a low avidity for the effector target. Non-limiting examples of therapeutic effector targets that can be targeted with ANDbodies disclosed herein are listed in Table 1, along with the exemplary function for the effector targets.

Table 1: Exemplary Effector Targets

Target	Sequence Accession number	Exemplary effector function for therapeutic effect
Notch 2	Q04721	Blocking Notch2 signaling, e.g., to treat COPD, cancer
IL11RA	Q14626	Blocking IL11RA signaling, e.g., to treat fibrosis
Endothelin Receptor A	P25101	Blocking Endothelin Receptor A, e.g., to treat IPF
b3 adrenergic receptor	P13945	Agonizing b3AR, e.g., to treat obesity
FASR	P25445	agonize FASR mediated apoptotic signaling cascades eg. To treat cancer
Integrin alpha4		Blocking Integrin alpha 4 to treat IBD
GLP1R	P43220	Agonizing GLP1R to treat T2D or obesity
LeptinR (peptide)	P48357	block leptin signaling to suppress appetite, eg. To treat weight gain
PTHR (GPCR)	U6CS43	Activate PTH with intermittent agonizing peptide. Eg. exposure to activating peptide to stimulate bone growth in

		osteoporosis
A4b7 (Integrin B7)	P26010	Antagonize its interactions with MAdCAM to prevent inflammation associated with gut disease (eg. IBD)

Address Target

An ANDbody of the invention also comprises an address target binder that binds to an address target to provide targeted delivery of the effector. As used herein, an “address target” is a structure on a cell or tissue whose expression is sufficiently restricted in an organism to allow it to identify an organ, tissue, cell, or cell state of interest in an organism. The address target can be, e.g., a cell surface protein, or a structure localizing to the extracellular matrix. As used herein, “restricted” expression of an address target means that the address target has a differential, e.g., less broad, *in vivo* expression, as opposed to systemic expression. In certain embodiments, the address target is expressed, for example, in a single cell type, tissue or cell state in a mammalian subject, such as a human subject.

In some embodiments, the currently provided address target binding domains do not substantially influence biological signaling upon binding to the address target, e.g., does not modulate a signal transduction pathway or other biological response in the target cell or tissue. For example, the address target binder can be inert or inactive, in which it lacks any additional activity (other than binding), including lacking catalytic activity, after binding to the address target. For example, the address target binder binds a non-signaling site or motif of the address target. “Signal” is used herein to indicate a conformational, enzymatic, and/or electrical consequence occurs as a result of target binding. Accordingly, as described herein, address target binding domains do not signal upon address target binding. A domain that does not “substantially” influence biological signaling, as used herein, is a domain that modulates a signal transduction pathway or other biological response in the target cell or tissue to which it binds by no more than 25% relative to a control condition, e.g., relative to signaling in the absence of the domain. For example, the domain may modulate (e.g., increase or decrease) the signal transduction pathway or other biological response by less than 20%, less than 15%, less than 10%, less than 5%, less than 2%, or less than 1% (e.g., 20-25%, 15-20%, 10-15%, 5-10%, 2-5%, or 1-2%).

Similarly, an effector target binding domain may not substantially signal, or may not signal at all, when it is not localized by an address target binding domain. In embodiments, an effector target binding domain signals with higher potency (e.g., has higher avidity) when it is localized by an address target binding domain compared to the signal when it is not localized by an address target binding domain. When an effector target binding domain is localized to a targeted cell or tissue by an address target binding domain as part of the same macromolecule, effector target signaling can be influenced as discussed above.

In some embodiments, the address target is used for organ-specific addressing, tissue-specific addressing, or cell-specific addressing.

The specificity of address target binding domains for a cell or tissue can be detected using

methods known in the art. In one embodiment, a Gini coefficient (GC) score, which is a method for assessing the expression variation of a particular gene in a data set, is used. (See O'Hagan et al., GeneGini: assessment via the Gini coefficient of reference "housekeeping" genes and diverse human transporter expression profiles. *Cell systems* 6, 230–244, <https://doi.org/10.1016/j.cels.2018.01.003> (2018); Wright Muelas et al., The role and robustness of the Gini coefficient as an unbiased tool for the selection of Gini genes for normalising expression profiling data. *Sci Rep* 9, 17960 (2019). <https://doi.org/10.1038/s41598-019-54288-7>). Address target binders can be identified using cell expression data generated for address target binders as described herein (Table 2A and 2B). In some embodiments, address target markers exhibit Gini scores of greater than 0.4, such as between 0.74 and 1.00. Conversely, non-address markers that are expressed more systemically exhibit Gini Scores of between 0.15 to 0.19.

In one embodiment, a Tau score, which represents the expression variation of a particular gene in a data set, is used. Calculating Tau uses the information of expression of a gene in each tissue and its maximal expression over all tissues while also taking into account the number of tissues where expression is measured (see Itai Yanai, *et al.*, Genome-wide midrange transcription profiles reveal expression level relationships in human tissue specification, *Bioinformatics*, Volume 21, Issue 5, 1 March 2005, Pages 650–659; Kryuchkova-Mostacci N, Robinson-Rechavi M. A benchmark of gene expression tissue-specificity metrics. *Brief Bioinform.* 2017 Mar 1;18(2):205-214. doi: 10.1093/bib/bbw008). In some embodiments, address target markers exhibit Tau scores of greater than 0.6, such as between 0.74 and 1.00. Conversely, non-address markers that are expressed more systemically exhibit Tau Scores of below 0.3, such as 0.15 to 0.19.

In some embodiments, specificity of address target binding domains for a particular cell or tissue, such as that indicated by an appropriate Gini and/or Tau score, is determined with a tissue based analysis that does not include tissues having a natural biological separation barrier (i.e., blood-brain barrier). For example, in some embodiments, Gini and/or Tau scores may be calculated without data from tissues such as (but not limited to): central nervous system, brain, eye, and/or testis tissues. In some embodiments, an address target as provided herein identifies a cell state. As used herein a "cell state" refers to a given physiological condition of a cell. A cell state may be, e.g., a disease state (relative to a non-disease state or normal state of a cell or tissue); or an activated state (relative to a non-activated state of a cell). Exemplary disease states include inflammation, infection (e.g., bacterial, viral, or fungal infection), and states relating to cancer (e.g., precancerous or cancerous cell states). In some aspects, cell state reflects the fact that cells of a particular type can exhibit variability with regard to one or more features and/or can exist in a variety of different conditions, while retaining the features of their particular cell type and not gain features that would cause them to be classified as a different cell type. The different states or conditions in which a cell can exist may be characteristic of a particular cell type (e.g., may involve properties or characteristics exhibited only by that cell type and/or involve functions performed only or primarily by that cell type) or may occur in multiple different cell types. In some embodiments, a cell state reflects the capability of a cell to respond to a particular stimulus or environmental condition (e.g., whether or not the cell will

- respond, or the type of response that will be elicited) or is a condition of the cell brought about by a stimulus or environmental condition. Cells in different cell states may be distinguished from one another in a variety of ways. For example, they may express, produce, or secrete one or more different genes, proteins, or other molecules ("markers", such as the address targets provided herein),
- 5 exhibit differences in protein modifications such as phosphorylation, acetylation, etc., or may exhibit differences in appearance. Thus a cell state may be a condition of the cell in which the cell expresses, produces, or secretes one or more markers, exhibits particular protein modification(s), has a particular appearance, and/or will or will not exhibit one or more biological response(s) to a stimulus or environmental condition. Exemplary address targets of the present technology are provided in Tables
- 10 2A (HPA database analysis) and 2B (Gtex database analysis), below.

Table 2A: Exemplary Address Targets (HPA database analysis)

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
AADACL4	ENSG00000204518	Q5VUY2	0.9194	0.7852	epididymis
AATK	ENSG00000181409	Q6ZMQ8	0.7783	0.546	cerebral cortex
ABCA10	ENSG00000154263	Q8WWZ4	0.6792	0.4586	ovary
ABCA12	ENSG00000144452	Q86UK0	0.9539	0.8965	skin
ABCA13	ENSG00000179869	Q86UQ4	0.9202	0.6745	bone marrow
ABCA4	ENSG00000198691	P78363	0.8841	0.7214	epididymis
ABCB11	ENSG00000073734	O95342	0.9914	0.9671	liver
ABCB4	ENSG00000005471	P21439	0.8274	0.5034	liver
ABCB5	ENSG00000004846	Q2M3G0	0.9258	0.7265	epididymis
ABCC11	ENSG00000121270	Q96J66	0.9664	0.8631	breast
ABCC12	ENSG00000140798	Q96J65	0.974	0.97	breast
ABCC2	ENSG00000023839	Q92887	0.8356	0.6441	liver
ABCC6	ENSG00000091262	O95255	0.7146	0.4741	liver
ABCC8	ENSG00000006071	Q09428	0.8101	0.6626	cerebral cortex
ABCG4	ENSG00000172350	Q9H172	0.8977	0.6697	cerebral cortex
ABCG5	ENSG00000138075	Q9H222	0.9457	0.929	small intestine
ABCG8	ENSG00000143921	Q9H221	0.9273	0.8325	small intestine
ABHD16A	ENSG00000204427	Q95870	0.875	0.7778	gallbladder
ACKR4	ENSG00000129048	Q9NPB9	0.6411	0.4466	duodenum
ACP4	ENSG00000142513	Q9BZG2	0.9708	0.9329	skin
ACVR1C	ENSG00000123612	Q8NER5	0.8594	0.5953	adipose tissue
ADAM11	ENSG00000073670	O75078	0.9234	0.7693	cerebral cortex
ADAM12	ENSG00000148848	O43184	0.8419	0.6349	placenta
ADAM2	ENSG00000104755	Q99965	1	1	breast
ADAM20	ENSG00000134007	O43506	0.9268	0.9268	cerebral cortex
ADAM21	ENSG00000139985	Q9UKJ8	0.9202	0.7532	cerebral cortex
ADAM22	ENSG00000008277	Q9P0K1	0.7283	0.4446	cerebral cortex
ADAM23	ENSG00000114948	O75077	0.7735	0.4184	parathyroid gland
ADAM29	ENSG00000168594	Q9UKF5	0.9508	0.919	endometrium
ADAM32	ENSG00000197140	Q8TC27	0.6516	0.4608	skin
ADAM33	ENSG00000149451	Q9BZ11	0.5621	0.4	endometrium
ADAM7	ENSG00000069206	Q9H2U9	0.99	0.9835	epididymis
ADCY1	ENSG00000164742	Q08828	0.8168	0.516	cerebral cortex
ADCY2	ENSG00000078295	Q08462	0.8139	0.5967	cerebral cortex

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
ADCY4	ENSG00000129467	Q8NFM4	0.6858	0.406	placenta
ADCY8	ENSG00000155897	P40145	0.9347	0.8854	epididymis
ADCYAP1R1	ENSG00000078549	P41586	0.8129	0.5539	cerebral cortex
ADGRA1	ENSG00000197177	Q86SQ6	0.9659	0.9383	cerebral cortex
ADGRB1	ENSG00000181790	O14514	0.9121	0.6453	cerebral cortex
ADGRB2	ENSG00000121753	O60241	0.8582	0.5438	cerebral cortex
ADGRB3	ENSG00000135298	O60242	0.8675	0.5458	cerebral cortex
ADGRD1	ENSG00000111452	Q6QNK2	0.6088	0.4	placenta
ADGRE1	ENSG00000174837	Q14246	0.8457	0.6051	granulocytes
ADGRE2	ENSG00000127507	Q9UHX3	0.7344	0.4061	monocytes
ADGRE3	ENSG00000131355	Q9BY15	0.8976	0.6734	granulocytes
ADGRF1	ENSG00000153292	Q5T601	0.837	0.7738	urinary bladder
ADGRF3	ENSG00000173567	Q8IZF5	0.7837	0.534	kidney
ADGRF4	ENSG00000153294	Q8IZF3	0.9132	0.7968	skin
ADGRG2	ENSG00000173698	Q8IZP9	0.8866	0.6442	epididymis
ADGRG3	ENSG00000182885	Q86Y34	0.8231	0.634	granulocytes
ADGRG4	ENSG00000156920	Q8IZF6	0.9554	0.9216	duodenum
ADGRG5	ENSG00000159618	Q8IZF4	0.8129	0.6296	granulocytes
ADGRG7	ENSG00000144820	Q96K78	0.9117	0.8692	small intestine
ADGRL3	ENSG00000150471	Q9HAR2	0.7403	0.4781	cerebral cortex
ADGRV1	ENSG00000164199	Q8WXG9	0.8353	0.5653	adrenal gland
ADIG	ENSG00000182035	Q0VDE8	0.9659	0.9504	epididymis
ADORA1	ENSG00000163485	P30542	0.7977	0.5357	cerebral cortex
ADORA2B	ENSG00000170425	P29275	0.7032	0.5341	granulocytes
ADRA1A	ENSG00000120907	P35348	0.7744	0.5909	liver
ADRA1B	ENSG00000170214	P35368	0.7861	0.5465	spleen
ADRA1D	ENSG00000171873	P25100	0.8478	0.733	prostate
ADRA2A	ENSG00000150594	P08913	0.5927	0.4122	cervix, uterine
ADRA2C	ENSG00000184160	P18825	0.769	0.5862	seminal vesicle
ADRB3	ENSG00000188778	P13945	0.9072	0.7684	ovary
ADTRP	ENSG00000111863	Q96IZ2	0.6807	0.4974	small intestine
AGER (RAGE)	ENSG00000204305	Q15109	0.942	0.6711	lung
AGTR1	ENSG00000144891	P30556	0.7202	0.4443	placenta
AGTR2	ENSG00000180772	P50052	0.8982	0.8656	smooth muscle
AJAP1	ENSG00000196581	Q9UKB5	0.8534	0.6208	cerebral cortex
ALK	ENSG00000171094	Q9UM73	0.9357	0.7784	cerebral cortex
ALPP	ENSG00000163283	P05187	0.9534	0.8933	placenta
AMHR2	ENSG00000135409	Q16671	0.9219	0.8097	ovary
AMN	ENSG00000166126	Q9BXJ7	0.8765	0.7804	small intestine
ANKAR	ENSG00000151687	Q7Z5J8	0.7159	0.4233	parathyroid gland
ANO2	ENSG00000047617	Q9NQ90	0.6832	0.4454	placenta
ANO3	ENSG00000134343	Q9BYT9	0.9296	0.7809	epididymis
ANO4	ENSG00000151572	Q32M45	0.8429	0.7696	adrenal gland
ANO5	ENSG00000171714	Q75V66	0.7448	0.4641	parathyroid gland
ANO7	ENSG00000146205	Q6IWH7	0.8989	0.7931	prostate
ANO9	ENSG00000185101	A1A5B4	0.6923	0.4909	duodenum
APCDD1L	ENSG00000198768	Q8NCL9	0.8607	0.6756	salivary gland
APLNR	ENSG00000134817	P35414	0.6624	0.4032	spleen
APLP1	ENSG00000105290	P51693	0.8158	0.4277	cerebral cortex
AQP10	ENSG00000143595	Q96PS8	0.9493	0.8894	duodenum

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
AQP11	ENSG00000178301	Q8NBQ7	0.7626	0.4971	duodenum
AQP12A	ENSG00000184945	Q8IXF9	0.9956	0.9894	pancreas
AQP12B	ENSG00000185176	A6NM10	0.9956	0.9904	pancreas
AQP2	ENSG00000167580	P41181	0.9629	0.9304	kidney
AQP4	ENSG00000171885	P55087	0.9052	0.7745	cerebral cortex
AQP5	ENSG00000161798	P55064	0.8702	0.7198	salivary gland
AQP7	ENSG00000165269	O14520	0.7575	0.4682	adipose tissue
AQP9	ENSG00000103569	O43315	0.762	0.5304	granulocytes
AREG	ENSG00000109321	P15514	0.6962	0.4279	placenta
ARMCX4	ENSG00000196440	Q5H9R4	0.6554	0.4114	parathyroid gland
ARSH	ENSG00000205667	Q5FYA8	0.9463	0.9109	epididymis
ASAH2	ENSG00000188611	Q9NR71	0.8775	0.558	duodenum
ASGR1	ENSG00000141505	P07306	0.8114	0.461	liver
ASGR2	ENSG00000161944	P07307	0.8595	0.6116	liver
ASIC1	ENSG00000110881	P78348	0.8174	0.4887	cerebral cortex
ASIC2	ENSG00000108684	Q16515	0.9146	0.8482	cerebral cortex
ASIC3	ENSG00000213199	Q9UHC3	0.7375	0.4063	cerebral cortex
ASIC4	ENSG00000072182	Q96FT7	0.9852	0.9606	cerebral cortex
ASPHD1	ENSG00000174939	Q5U4P2	0.8855	0.6676	cerebral cortex
ASPRV1	ENSG00000244617	Q53RT3	0.8511	0.4144	skin
ASTN1	ENSG00000152092	O14525	0.8921	0.6976	cerebral cortex
ATP12A	ENSG00000075673	P54707	0.8957	0.8698	tonsil
ATP13A4	ENSG00000127249	Q4VNC1	0.7862	0.6789	parathyroid gland
ATP13A5	ENSG00000187527	Q4VNC0	0.9243	0.7622	breast
ATP1A2	ENSG00000018625	P50993	0.7206	0.4823	cerebral cortex
ATP1A3	ENSG00000105409	P13637	0.9301	0.78	cerebral cortex
ATP1A4	ENSG00000132681	Q13733	0.8721	0.7453	placenta
ATP1B2	ENSG00000129244	P14415	0.7556	0.4022	cerebral cortex
ATP2B2	ENSG00000157087	Q01814	0.9158	0.8334	cerebral cortex
ATP2B3	ENSG00000067842	Q16720	0.9545	0.9245	cerebral cortex
ATP2C2	ENSG00000064270	O75185	0.699	0.5908	rectum
ATP4A	ENSG00000105675	P20648	0.9883	0.958	stomach
ATP4B	ENSG00000186009	P51164	0.9822	0.9467	stomach
ATP6AP1L	ENSG00000205464	Q52LC2	0.7776	0.5805	skin
ATP6V0A4	ENSG00000105929	Q9HBG4	0.8975	0.7973	kidney
ATP8A2	ENSG00000132932	Q9NTI2	0.9234	0.6846	cerebral cortex
ATP8B4	ENSG00000104043	Q8TF62	0.7421	0.4466	bone marrow
ATRNL1	ENSG00000107518	Q5VV63	0.7727	0.572	cerebral cortex
AVPR1A	ENSG00000166148	P37288	0.7499	0.4988	adrenal gland
AVPR1B	ENSG00000198049	P47901	0.938	0.86	stomach
AVPR2	ENSG00000126895	P30518	0.7322	0.4842	adipose tissue
B3GAT1	ENSG00000109956	Q9P2W7	0.8956	0.6452	cerebral cortex
BAMBI	ENSG00000095739	Q13145	0.6256	0.4095	ovary
BDKRB1	ENSG00000100739	P46663	0.8144	0.6334	gallbladder
BDKRB2	ENSG00000168398	P30411	0.619	0.458	gallbladder
BEAN1	ENSG00000166546	Q3B7T3	0.7434	0.407	cerebral cortex
BEST2	ENSG00000039987	Q8NFU1	0.7958	0.4578	colon
BEST3	ENSG00000127325	Q8N1M1	0.88	0.6157	cerebral cortex
BEST4	ENSG00000142959	Q8NFU0	0.8121	0.5532	colon
BMPR1B	ENSG00000138696	O00238	0.7647	0.6117	cervix, uterine
BRS3	ENSG00000102239	P32247	0.9899	0.9704	epididymis
BSND	ENSG00000162399	Q8WZ55	0.9777	0.9343	kidney

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BTBD11	ENSG00000151136	A6QL63	0.789	0.4599	parathyroid gland
BTC	ENSG00000174808	P35070	0.5619	0.4328	skin
BTLA	ENSG00000186265	Q7Z6A9	0.8055	0.5853	b-cells
BTN1A1	ENSG00000124557	Q13410	0.9711	0.8582	breast
BTNL2	ENSG00000204290	Q9UIR0	0.949	0.9175	prostate
BTNL3	ENSG00000168903	Q6UXE8	0.9075	0.8702	duodenum
BTNL8	ENSG00000113303	Q6UX41	0.8409	0.7188	granulocytes
BVES	ENSG00000112276	Q8NE79	0.6818	0.4488	smooth muscle
C10orf105	ENSG00000214688	Q8TEF2	0.8618	0.664	spleen
C11orf87	ENSG00000185742	Q6NUJ2	0.9758	0.9342	cerebral cortex
C14orf132	ENSG00000227051	Q9NPU4	0.6557	0.4353	cerebral cortex
C16orf54	ENSG00000185905	Q6UWD8	0.7006	0.4573	granulocytes
C1orf185	ENSG00000204006	Q5T7R7	0.9512	0.9512	adipose tissue
C1orf210	ENSG00000253313	Q8IVY1	0.5899	0.4638	duodenum
C20orf141	ENSG00000258713	Q9NUB4	0.9552	0.9318	placenta
C3orf20	ENSG00000131379	Q8ND61	0.8184	0.6937	lymph node
C3orf80	ENSG00000180044	F5H4A9	0.8604	0.6126	cerebral cortex
C5AR2	ENSG00000134830	Q9P296	0.7691	0.4073	granulocytes
C8A	ENSG00000157131	P07357	0.9864	0.9694	liver
C9	ENSG00000113600	P02748	0.9899	0.9808	liver
C9orf135	ENSG00000204711	Q5VTT2	0.9477	0.8632	fallopian tube
C9orf57	ENSG00000204669	Q5W0N0	1	1	parathyroid gland
CA12	ENSG00000074410	Q43570	0.6732	0.4937	kidney
CA14	ENSG00000118298	Q9ULX7	0.8243	0.5757	seminal vesicle
CA9	ENSG00000107159	Q16790	0.9256	0.856	stomach
CABP7	ENSG00000100314	Q86V35	0.9258	0.8336	cerebral cortex
CACNA1A	ENSG00000141837	Q00555	0.8763	0.5395	cerebral cortex
CACNA1B	ENSG00000148408	Q00975	0.9309	0.8096	cerebral cortex
CACNA1C	ENSG00000151067	Q13936	0.7159	0.4702	smooth muscle
CACNA1D	ENSG00000157388	Q01668	0.6777	0.4827	fallopian tube
CACNA1E	ENSG00000198216	Q15878	0.9383	0.8194	cerebral cortex
CACNA1G	ENSG00000006283	Q43497	0.8372	0.5872	cerebral cortex
CACNA1H	ENSG00000196557	Q95180	0.6199	0.4231	ovary
CACNA1I	ENSG00000100346	Q9P0X4	0.901	0.8161	cerebral cortex
CACNA1S	ENSG00000081248	Q13698	0.9826	0.953	skeletal muscle
CACNA2D3	ENSG00000157445	Q8IZS8	0.8617	0.6321	cerebral cortex
CACNA2D4	ENSG00000151062	Q7Z3S7	0.9147	0.8188	t-cells
CACNG1	ENSG00000108878	Q06432	0.9779	0.9486	skeletal muscle
CACNG2	ENSG00000166862	Q9Y698	0.9906	0.9792	cerebral cortex
CACNG3	ENSG00000006116	Q60359	0.9935	0.9887	cerebral cortex
CACNG4	ENSG00000075461	Q9UBN1	0.8845	0.7714	cerebral cortex
CACNG5	ENSG00000075429	Q9UF02	0.9665	0.946	cerebral cortex
CACNG6	ENSG00000130433	Q9BXT2	0.9353	0.8716	skeletal muscle
CACNG7	ENSG00000105605	P62955	0.9961	0.9904	cerebral cortex
CADM2	ENSG00000175161	Q8N3J6	0.9024	0.6175	cerebral cortex
CADM3	ENSG00000162706	Q8N126	0.6988	0.4311	cerebral cortex
CALCR	ENSG00000004948	P30988	0.9218	0.7574	kidney
CALHM1	ENSG00000185933	Q8IU99	0.9283	0.7211	cerebral cortex
CALHM3	ENSG00000183128	Q86XJ0	0.9119	0.8789	dendritic cells
CALHM4	ENSG00000164451	Q5JW98	0.9932	0.9669	placenta
CALHM5	ENSG00000178033	Q8N5C1	0.6974	0.4378	placenta
CALN1	ENSG00000183166	Q9BXU9	0.9455	0.8658	cerebral cortex

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CALY	ENSG00000130643	Q9NYX4	0.9377	0.8051	cerebral cortex
CASR	ENSG00000036828	P41180	0.9558	0.7864	parathyroid gland
CATSPER1	ENSG00000175294	Q8NEC5	0.9399	0.8835	granulocytes
CATSPERE	ENSG00000179397	Q5SY80	0.7595	0.5126	epididymis
CATSPERG	ENSG00000099338	Q6ZRH7	0.6892	0.4463	skin
CBARP	ENSG00000099625	Q8N350	0.9515	0.8475	cerebral cortex
CCDC188	ENSG00000234409	H7C350	0.7238	0.5424	spleen
CKAR	ENSG00000163394	P32238	0.9647	0.9456	gallbladder
CCKBR	ENSG00000110148	P32239	0.9403	0.9019	stomach
CCR10	ENSG00000184451	P46092	0.8477	0.5315	t-cells
CCR3	ENSG00000183625	P51677	0.9375	0.6845	granulocytes
CCR4	ENSG00000183813	P51679	0.8177	0.4888	t-cells
CCR6	ENSG00000112486	P51684	0.7454	0.4983	t-cells
CCR7	ENSG00000126353	P32248	0.7939	0.5403	t-cells
CCR8	ENSG00000179934	P51685	0.9344	0.7641	t-cells
CCR9	ENSG00000173585	P51686	0.9086	0.7792	b-cells
CD101	ENSG00000134256	Q93033	0.7972	0.506	granulocytes
CD163L1	ENSG00000177675	Q9NR16	0.6974	0.4893	spleen
CD164L2	ENSG00000174950	Q6UWJ8	0.9023	0.7942	fallopian tube
CD180	ENSG00000134061	Q99467	0.7324	0.4903	b-cells
CD19	ENSG00000177455	P15391	0.8386	0.67	b-cells
CD1A	ENSG00000158477	P06126	0.8649	0.7269	skin
CD1B	ENSG00000158485	P29016	0.8813	0.7032	dendritic cells
CD1D	ENSG00000158473	P15813	0.7375	0.4226	dendritic cells
CD200R1L	ENSG00000206531	Q6Q8B3	0.9983	0.9937	granulocytes
CD207	ENSG00000116031	Q9UJ71	0.8544	0.5934	skin
CD209	ENSG00000090659	Q9NNX6	0.628	0.4093	adipose tissue
CD22	ENSG00000012124	P20273	0.6788	0.4436	lymph node
CD244	ENSG00000122223	Q9BZW8	0.809	0.5361	granulocytes
CD27	ENSG00000139193	P26842	0.6947	0.4212	t-cells
CD28	ENSG00000178562	P10747	0.7684	0.4953	t-cells
CD300C	ENSG00000167850	Q08708	0.7864	0.4942	monocytes
CD300E	ENSG00000186407	Q496F6	0.7976	0.5542	monocytes
CD300LB	ENSG00000178789	A8K4G0	0.8274	0.5806	granulocytes
CD300LD	ENSG00000204345	Q6UXZ3	0.8802	0.5851	granulocytes
CD300LF	ENSG00000186074	Q8TDQ1	0.7616	0.5162	granulocytes
CD300LG	ENSG00000161649	Q6UXG3	0.7808	0.4994	adipose tissue
CD3G	ENSG00000160654	P09693	0.804	0.4154	t-cells
CD40LG	ENSG00000102245	P29965	0.8186	0.5313	t-cells
CD5	ENSG00000110448	P06127	0.7439	0.4332	t-cells
CD6	ENSG00000013725	P30203	0.7028	0.4657	lymph node
CD7	ENSG00000173762	P09564	0.7469	0.4697	nk-cells
CD70	ENSG00000125726	P32970	0.867	0.6187	t-cells
CD72	ENSG00000137101	P21854	0.7585	0.4113	b-cells
CD79A	ENSG00000105369	P11912	0.6686	0.4153	b-cells
CD79B	ENSG00000007312	P40259	0.7013	0.4123	b-cells
CD80	ENSG00000121594	P33681	0.7816	0.6058	appendix
CDH10	ENSG00000040731	Q9Y6N8	0.9679	0.9117	cerebral cortex
CDH12	ENSG00000154162	P55289	0.8881	0.8058	cervix, uterine
CDH15	ENSG00000129910	P55291	0.9719	0.9079	skeletal muscle
CDH16	ENSG00000166589	O75309	0.9351	0.8659	kidney
CDH17	ENSG00000079112	Q12864	0.7727	0.5189	duodenum

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CDH18	ENSG00000145526	Q13634	0.968	0.9189	cerebral cortex
CDH19	ENSG00000071991	Q9H159	0.6206	0.4289	heart muscle
CDH2	ENSG00000170558	P19022	0.7051	0.5105	parathyroid gland
CDH20	ENSG00000101542	Q9HBT6	0.9554	0.8643	cerebral cortex
CDH22	ENSG00000149654	Q9UJ99	0.9283	0.8231	cerebral cortex
CDH26	ENSG00000124215	Q8IXH8	0.8039	0.4825	prostate
CDH3	ENSG00000062038	P22223	0.6662	0.523	skin
CDH4	ENSG00000179242	P55283	0.9085	0.7865	cerebral cortex
CDH6	ENSG00000113361	P55285	0.6697	0.4549	kidney
CDH7	ENSG00000081138	Q9ULB5	0.9643	0.9296	cerebral cortex
CDH8	ENSG00000150394	P55286	0.9384	0.7675	cerebral cortex
CDH9	ENSG00000113100	Q9ULB4	0.8018	0.4357	cerebral cortex
CDHR1	ENSG00000148600	Q96JP9	0.8326	0.6175	skin
CDHR2	ENSG00000074276	Q9BYE9	0.8837	0.8041	duodenum
CDHR3	ENSG00000128536	Q6ZTQ4	0.838	0.4979	fallopian tube
CDHR4	ENSG00000187492	A6H8M9	0.9317	0.7328	fallopian tube
CDHR5	ENSG00000099834	Q9HBB8	0.8542	0.806	duodenum
CDON	ENSG00000064309	Q4KMG0	0.6369	0.4068	thyroid gland
CEACAM3	ENSG00000170956	P40198	0.9229	0.8046	granulocytes
CEACAM4	ENSG00000105352	O75871	0.8559	0.6729	granulocytes
CELSR1	ENSG00000075275	Q9NYQ6	0.6755	0.4933	fallopian tube
CELSR2	ENSG00000143126	Q9HCU4	0.7034	0.4656	cerebral cortex
CELSR3	ENSG00000008300	Q9NYQ7	0.9027	0.5699	cerebral cortex
CEND1	ENSG00000184524	Q8N111	0.9462	0.764	cerebral cortex
CFAP65	ENSG00000181378	Q6ZU64	0.9513	0.841	fallopian tube
CFTR	ENSG00000001626	P13569	0.7716	0.6409	gallbladder
CHODL	ENSG00000154645	Q9H9P2	0.778	0.4593	spleen
CHRFAM7A	ENSG00000166664	Q494W8	0.7671	0.4566	parathyroid gland
CHRM1	ENSG00000168539	P11229	0.8881	0.7732	prostate
CHRM2	ENSG00000181072	P08172	0.8564	0.7383	heart muscle
CHRM3	ENSG00000133019	P20309	0.7266	0.4916	cerebral cortex
CHRM4	ENSG00000180720	P08173	0.9191	0.8248	spleen
CHRM5	ENSG00000184984	P08912	0.8419	0.5754	cerebral cortex
CHRNA1	ENSG00000138435	P02708	0.8978	0.7471	skeletal muscle
CHRNA10	ENSG00000129749	Q9GZZ6	0.9216	0.4942	skeletal muscle
CHRNA2	ENSG00000120903	Q15822	0.9722	0.868	prostate
CHRNA3	ENSG00000080644	P32297	0.9161	0.7668	adrenal gland
CHRNA4	ENSG00000101204	P43681	0.9421	0.9079	parathyroid gland
CHRNA6	ENSG00000147434	Q15825	0.8564	0.764	t-cells
CHRNA7	ENSG00000175344	P36544	0.7674	0.5196	small intestine
CHRNA9	ENSG00000174343	Q9UGM1	0.9653	0.926	fallopian tube
CHRN2	ENSG00000160716	P17787	0.9776	0.8975	cerebral cortex
CHRN3	ENSG00000147432	Q05901	0.9675	0.9478	cerebral cortex
CHRN4	ENSG00000117971	P30926	0.8944	0.6441	adrenal gland
CHRN5	ENSG00000135902	Q07001	0.992	0.9835	skeletal muscle
CHRNA	ENSG00000108556	Q04844	0.9206	0.5626	heart muscle
CHRNA	ENSG00000196811	P07510	0.9922	0.9772	skeletal muscle
CHST9	ENSG00000154080	Q7L1S5	0.7933	0.6416	fallopian tube
CLCA2	ENSG00000137975	Q9UQC9	0.9003	0.8079	esophagus
CLCA4	ENSG00000016602	Q14CN2	0.8632	0.7863	esophagus
CLCN1	ENSG00000188037	P35523	0.9641	0.8257	skeletal muscle
CLCNKA	ENSG00000186510	P51800	0.9169	0.7845	kidney

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CLCNKB	ENSG00000184908	P51801	0.9068	0.7137	kidney
CLDN1	ENSG00000163347	O95832	0.6574	0.4902	skin
CLDN10	ENSG00000134873	P78369	0.7168	0.5876	kidney
CLDN11	ENSG00000013297	O75508	0.8002	0.5644	cerebral cortex
CLDN14	ENSG00000159261	O95500	0.9525	0.8433	liver
CLDN17	ENSG00000156282	P56750	0.9872	0.9773	esophagus
CLDN18	ENSG00000066405	P56856	0.9317	0.7657	stomach
CLDN19	ENSG00000164007	Q8N6F1	0.9528	0.9125	kidney
CLDN2	ENSG00000165376	P57739	0.8305	0.7468	kidney
CLDN20	ENSG00000171217	P56880	0.8244	0.7053	skin
CLDN22	ENSG00000177300	Q8N7P3	0.9869	0.9699	fallopian tube
CLDN23	ENSG00000253958	Q96B33	0.6963	0.4432	stomach
CLDN24	ENSG00000185758	A6NM45	0.9842	0.952	kidney
CLDN3	ENSG00000165215	O15551	0.7346	0.585	small intestine
CLDN4	ENSG00000189143	O14493	0.5271	0.4219	colon
CLDN6	ENSG00000184697	P56747	0.9285	0.7482	placenta
CLDN8	ENSG00000156284	P56748	0.8092	0.7417	breast
CLDN9	ENSG00000213937	O95484	0.8802	0.7045	parathyroid gland
CLEC12A	ENSG00000172322	Q5QGZ9	0.7177	0.4406	granulocytes
CLEC12B	ENSG00000256660	Q2HXU8	0.9188	0.7737	skin
CLEC17A	ENSG00000187912	Q6ZS10	0.8431	0.6669	b-cells
CLEC1B	ENSG00000165682	Q9P126	0.9127	0.7923	liver
CLEC2A	ENSG00000188393	Q6UVW9	0.9857	0.9748	skin
CLEC2L	ENSG00000236279	P0C7M8	0.9206	0.7872	cerebral cortex
CLEC4C	ENSG00000198178	Q8WTT0	0.9151	0.6812	dendritic cells
CLEC4D	ENSG00000166527	Q8WXI8	0.8592	0.7041	granulocytes
CLEC4E	ENSG00000166523	Q9ULY5	0.7384	0.4538	granulocytes
CLEC4F	ENSG00000152672	Q8N1N0	0.6906	0.4672	small intestine
CLEC4G	ENSG00000182566	Q6UXB4	0.7874	0.5732	liver
CLEC4M	ENSG00000104938	Q9H2X3	0.9053	0.8054	liver
CLEC5A	ENSG00000258227	Q9NY25	0.8159	0.5412	bone marrow
CLEC6A	ENSG00000205846	Q6EIG7	0.9216	0.8336	monocytes
CLEC9A	ENSG00000197992	Q6UXN8	0.8203	0.5195	dendritic cells
CLECL1	ENSG00000184293	Q8IZS7	0.7301	0.4551	b-cells
CLIC3	ENSG00000169583	O95833	0.8114	0.5761	dendritic cells
CLIC5	ENSG00000112782	Q9NZA1	0.6392	0.4525	lung
CLIC6	ENSG00000159212	Q96NY7	0.7244	0.5014	stomach
CLRN1	ENSG00000163646	P58418	0.9812	0.9558	adrenal gland
CLRN2	ENSG00000249581	A0PK11	1	1	kidney
CLRN3	ENSG00000180745	Q8NCR9	0.8423	0.8068	small intestine
CLSTN2	ENSG00000158258	Q9H4D0	0.7843	0.5489	ovary
CLTRN	ENSG00000147003	Q9HBJ8	0.869	0.5739	kidney
CMTM2	ENSG00000140932	Q8TAZ6	0.8479	0.7435	granulocytes
CMTM5	ENSG00000166091	Q96DZ9	0.8645	0.4956	cerebral cortex
CNGA1	ENSG00000198515	P29973	0.6269	0.4383	liver
CNGA3	ENSG00000144191	Q16281	0.8049	0.7604	esophagus
CNGA4	ENSG00000132259	Q8IV77	0.9381	0.6384	fallopian tube
CNGB1	ENSG00000070729	Q14028	0.8773	0.6916	adrenal gland
CNGB3	ENSG00000170289	Q9NQW8	0.8828	0.703	bone marrow
CNIH2	ENSG00000174871	Q6PI25	0.9444	0.762	cerebral cortex
CNIH3	ENSG00000143786	Q8TBE1	0.8792	0.538	cerebral cortex
CNMD	ENSG00000136110	O75829	0.9375	0.9018	thyroid gland

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CNNM1	ENSG00000119946	Q9NRU3	0.852	0.6167	cerebral cortex
CNR1	ENSG00000118432	P21554	0.7306	0.4309	cerebral cortex
CNR2	ENSG00000188822	P34972	0.851	0.7168	granulocytes
CNTNAP2	ENSG00000174469	Q9UHC6	0.9154	0.7375	cerebral cortex
CNTNAP3	ENSG00000106714	Q9BZ76	0.6749	0.452	esophagus
CNTNAP4	ENSG00000152910	Q9C0A0	0.9864	0.9545	cerebral cortex
CNTNAP5	ENSG00000155052	Q8WYK1	0.9775	0.9582	cerebral cortex
COL13A1	ENSG00000197467	Q5TAT6	0.7004	0.4352	epididymis
COL17A1	ENSG00000065618	Q9UMD9	0.7774	0.5608	skin
COL23A1	ENSG00000050767	Q86Y22	0.7673	0.4674	thyroid gland
COL25A1	ENSG00000188517	Q9BXS0	0.7203	0.5199	adipose tissue
COLEC12	ENSG00000158270	Q5KU26	0.6676	0.4039	placenta
CORIN	ENSG00000145244	Q9Y5Q5	0.8754	0.7183	heart muscle
CPT1C	ENSG00000169169	Q8TCG5	0.7878	0.5129	cerebral cortex
CR2	ENSG00000117322	P20023	0.8222	0.6599	lymph node
CRB1	ENSG00000134376	P82279	0.9456	0.7913	cerebral cortex
CRB2	ENSG00000148204	Q5IJ48	0.9209	0.7644	cerebral cortex
CRHR1	ENSG00000120088	P34998	0.9543	0.8524	cerebral cortex
CRHR2	ENSG00000106113	Q13324	0.8712	0.663	seminal vesicle
CRLF2	ENSG00000205755	Q9HC73	0.8401	0.6627	appendix
CRTAM	ENSG00000109943	Q95727	0.8311	0.5369	nk-cells
CSF3R	ENSG00000119535	Q99062	0.7128	0.4267	granulocytes
CSMD1	ENSG00000183117	Q96PZ7	0.943	0.8207	cerebral cortex
CSMD2	ENSG00000121904	Q7Z408	0.9081	0.7275	cerebral cortex
CSMD3	ENSG00000164796	Q7Z407	0.98	0.9399	cerebral cortex
CSPG4	ENSG00000173546	Q6UVK1	0.6146	0.4138	adipose tissue
CSPG5	ENSG00000114646	Q95196	0.9551	0.7032	cerebral cortex
CT83	ENSG00000204019	Q5H943	0.9896	0.9743	salivary gland
CTLA4	ENSG00000163599	P16410	0.7876	0.58	t-cells
CTXN1	ENSG00000178531	P60606	0.844	0.624	cerebral cortex
CTXN2	ENSG00000233932	P0C2S0	0.9893	0.9669	cerebral cortex
CTXN3	ENSG00000205279	Q4LDR2	0.9775	0.9544	kidney
CWH43	ENSG00000109182	Q9H720	0.8095	0.7094	prostate
CXCR1	ENSG00000163464	P25024	0.8736	0.6096	granulocytes
CXCR2	ENSG00000180871	P25025	0.8166	0.4876	granulocytes
CXCR3	ENSG00000186810	P49682	0.8056	0.565	dendritic cells
CXCR5	ENSG00000160683	P32302	0.8476	0.6776	b-cells
CXorf66	ENSG00000203933	Q5JRM2	1	1	liver
CYP26C1	ENSG00000187553	Q6V0L0	0.9617	0.9404	spleen
CYP46A1	ENSG00000036530	Q9Y6A2	0.8925	0.5676	cerebral cortex
DBH	ENSG00000123454	P09172	0.9353	0.7033	adrenal gland
DCC	ENSG00000187323	P43146	0.9127	0.7725	cerebral cortex
DCHS2	ENSG00000197410	Q6V1P9	0.8847	0.7649	endometrium
DCST1	ENSG00000163357	Q5T197	0.9423	0.7328	skin
DCST2	ENSG00000163354	Q5T1A1	0.8439	0.5085	skin
DCSTAMP	ENSG00000164935	Q9H295	0.9527	0.8384	lung
DIO2	ENSG00000211448	Q92813	0.7722	0.5472	thyroid gland
DIO3	ENSG00000197406	P55073	0.8138	0.6283	cervix, uterine
DISP2	ENSG00000140323	A7MBM2	0.8604	0.5382	cerebral cortex
DLK1	ENSG00000185559	P80370	0.8856	0.6954	placenta
DLK2	ENSG00000171462	Q6UY11	0.779	0.506	skin
DLL3	ENSG00000090932	Q9NYJ7	0.9855	0.9576	cerebral cortex

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DNAJC22	ENSG00000178401	Q8N4W6	0.6981	0.5753	thyroid gland
DNER	ENSG00000187957	Q8NFT8	0.8426	0.6116	cerebral cortex
DPP10	ENSG00000175497	Q8N608	0.9034	0.763	cerebral cortex
DPP6	ENSG00000130226	P42658	0.8432	0.6837	cerebral cortex
DPY19L2	ENSG00000177990	Q6NUT2	0.5998	0.4219	parathyroid gland
DRD1	ENSG00000184845	P21728	0.9075	0.686	cerebral cortex
DRD2	ENSG00000149295	P14416	0.9091	0.7389	adrenal gland
DRD4	ENSG00000069696	P21917	0.9664	0.9315	dendritic cells
DRD5	ENSG00000169676	P21918	0.9548	0.9264	stomach
DSC1	ENSG00000134765	Q08554	0.9557	0.883	skin
DSC3	ENSG00000134762	Q14574	0.8758	0.719	skin
DSCAM	ENSG00000171587	Q60469	0.9788	0.947	cerebral cortex
DSCAML1	ENSG00000177103	Q8TD84	0.834	0.4943	cerebral cortex
DSG1	ENSG00000134760	Q02413	0.9463	0.8739	skin
DSG3	ENSG00000134757	P32926	0.9166	0.8278	esophagus
DSG4	ENSG00000175065	Q86SJ6	0.9484	0.9276	duodenum
DUOX1	ENSG00000137857	Q9NRD9	0.7017	0.5701	skin
DUOX2	ENSG00000140279	Q9NRD8	0.8314	0.6573	gallbladder
DUOXA1	ENSG00000140254	Q1HG43	0.7335	0.5998	esophagus
ECEL1	ENSG00000171551	Q95672	0.9213	0.7051	ovary
EDA2R	ENSG00000131080	Q9HAV5	0.5572	0.4466	thyroid gland
EDAR	ENSG00000135960	Q9UNE0	0.8266	0.6016	t-cells
EDNRA	ENSG00000151617	P25101	0.6316	0.4122	seminal vesicle
EFNB3	ENSG00000108947	Q15768	0.8052	0.5291	cerebral cortex
EGF	ENSG00000138798	P01133	0.8815	0.7105	kidney
ELFN1	ENSG00000225968	P0C7U0	0.8076	0.614	liver
ELFN2	ENSG00000166897	Q5R3F8	0.9753	0.9224	cerebral cortex
ENPEP	ENSG00000138792	Q07075	0.742	0.5254	small intestine
ENPP3	ENSG00000154269	Q14638	0.7351	0.5526	small intestine
ENTPD2	ENSG00000054179	Q9Y5L3	0.6289	0.4853	duodenum
ENTPD8	ENSG00000188833	Q5MY95	0.837	0.7208	small intestine
EPCAM	ENSG00000119888	P16422	0.5686	0.4487	small intestine
EPGN	ENSG00000182585	Q6UW88	0.9242	0.7649	esophagus
EPHA1	ENSG00000146904	P21709	0.8606	0.5333	parathyroid gland
EPHA10	ENSG00000183317	Q5JZY3	0.7811	0.6473	colon
EPHA3	ENSG00000044524	P29320	0.6787	0.4576	prostate
EPHA5	ENSG00000145242	P54756	0.9169	0.7947	cerebral cortex
EPHA6	ENSG00000080224	Q9UF33	0.8422	0.6941	ovary
EPHA7	ENSG00000135333	Q15375	0.8538	0.5811	parathyroid gland
EPHA8	ENSG00000070886	P29322	0.955	0.9321	adrenal gland
EPHB1	ENSG00000154928	P54762	0.7204	0.4531	cerebral cortex
EPHB2	ENSG00000133216	P29323	0.6051	0.431	rectum
EPHB3	ENSG00000182580	P54753	0.6416	0.4106	skin
EPHX4	ENSG00000172031	Q8IUS5	0.8357	0.5897	cerebral cortex
ERBB4	ENSG00000178568	Q15303	0.8478	0.7284	fallopian tube
EREG	ENSG00000124882	Q14944	0.8495	0.6461	bone marrow
ERVFRD-1	ENSG00000244476	P60508	0.9243	0.6874	placenta
ERVMER34-1	ENSG00000226887	Q9H9K5	0.8898	0.603	parathyroid gland
ERVW-1	ENSG00000242950	Q9UQF0	0.9025	0.4919	placenta
ESR1	ENSG00000091831	P03372	0.7662	0.5445	endometrium
ESYT3	ENSG00000158220	A0FGR9	0.8418	0.724	thyroid gland

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EVC2	ENSG00000173040	Q86UK5	0.6373	0.4229	ovary
F2RL2	ENSG00000164220	O00254	0.7398	0.459	gallbladder
FAIM2	ENSG00000135472	Q9BWQ8	0.7616	0.4478	cerebral cortex
FAM151A	ENSG00000162391	Q8WW52	0.9047	0.7183	kidney
FAM155A	ENSG00000204442	B1AL88	0.8962	0.6476	cerebral cortex
FAM155B	ENSG00000130054	O75949	0.8664	0.6844	thyroid gland
FAM162B	ENSG00000183807	Q5T6X4	0.7169	0.4473	placenta
FAM163A	ENSG00000143340	Q96GL9	0.8844	0.6974	adrenal gland
FAM163B	ENSG00000196990	P0C2L3	0.9408	0.8145	cerebral cortex
FAM171A2	ENSG00000161682	A8MVW0	0.8564	0.6362	cerebral cortex
FAM171B	ENSG00000144369	Q6P995	0.7462	0.4187	cerebral cortex
FAM187B	ENSG00000177558	Q17R55	0.9745	0.9626	spleen
FAM189A1	ENSG00000104059	Q60320	0.9036	0.8075	cerebral cortex
FAM189A2	ENSG00000135063	Q15884	0.6824	0.4629	thyroid gland
FAM205A	ENSG00000205108	Q6ZU69	1	1	skin
FAM209A	ENSG00000124103	Q5JX71	0.8871	0.5849	bone marrow
FAM209B	ENSG00000213714	Q5JX69	0.8429	0.4616	bone marrow
FAP	ENSG00000078098	Q12884	0.6894	0.5067	endometrium
FASLG	ENSG00000117560	P48023	0.8422	0.5348	t-cells
FAT2	ENSG00000086570	Q9NYQ8	0.8973	0.7615	skin
FAT3	ENSG00000165323	Q8TDW7	0.9323	0.8573	cerebral cortex
FAXC	ENSG00000146267	Q5TGI0	0.695	0.5034	cerebral cortex
FCAR	ENSG00000186431	P24071	0.9731	0.9395	bone marrow
FCER2	ENSG00000104921	P06734	0.8403	0.6096	b-cells
FCGR1A	ENSG00000150337	P12314	0.635	0.4073	epididymis
FCGR1B	ENSG00000198019	Q92637	0.7229	0.4751	epididymis
FCMR	ENSG00000162894	Q60667	0.679	0.403	b-cells
FCRL1	ENSG00000163534	Q96LA6	0.8784	0.7758	b-cells
FCRL2	ENSG00000132704	Q96LA5	0.8088	0.675	lymph node
FCRL3	ENSG00000160856	Q96P31	0.8183	0.6984	lymph node
FCRL4	ENSG00000163518	Q96PJ5	0.9465	0.9099	tonsil
FCRL5	ENSG00000143297	Q96RD9	0.7691	0.622	tonsil
FCRL6	ENSG00000181036	Q6DN72	0.8083	0.4367	t-cells
FER1L6	ENSG00000214814	Q2WVGJ9	0.919	0.8418	stomach
FFAR1	ENSG00000126266	O14842	0.8923	0.7677	bone marrow
FFAR2	ENSG00000126262	O15552	0.8519	0.5841	granulocytes
FFAR3	ENSG00000185897	O14843	0.8565	0.6858	appendix
FFAR4	ENSG00000186188	Q5NUL3	0.8454	0.6118	rectum
FGFR3	ENSG00000068078	P22607	0.7475	0.4729	skin
FGFR4	ENSG00000160867	P22455	0.6746	0.4789	lung
FIBCD1	ENSG00000130720	Q8N539	0.8997	0.7961	parathyroid gland
FLRT3	ENSG00000125848	Q9NZU0	0.6166	0.4585	lung
FLT3	ENSG00000122025	P36888	0.848	0.5553	dendritic cells
FMR1NB	ENSG00000176988	Q8N0W7	1	1	epididymis
FNDC10	ENSG00000228594	F2Z333	0.6928	0.4154	adrenal gland
FNDC4	ENSG00000115226	Q9H6D8	0.6724	0.4405	adrenal gland
FNDC5	ENSG00000160097	Q8NAU1	0.7674	0.5168	skeletal muscle
FNDL9	ENSG00000172568	Q8TBE3	0.9628	0.889	cerebral cortex
FOLH1	ENSG00000086205	Q04609	0.7895	0.5517	duodenum
FPR1	ENSG00000171051	P21462	0.7182	0.4011	granulocytes
FPR2	ENSG00000171049	P25090	0.8206	0.5174	granulocytes
FRAS1	ENSG00000138759	Q86XX4	0.7806	0.5116	thyroid gland

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FRMD5	ENSG00000171877	Q7Z6J6	0.888	0.6285	heart muscle
FUT6	ENSG00000156413	P51993	0.7662	0.6658	esophagus
FXYD2	ENSG00000137731	P54710	0.806	0.4767	kidney
FXYD3	ENSG00000089356	Q14802	0.6079	0.4579	rectum
FXYD4	ENSG00000150201	P59646	0.9563	0.8703	kidney
FXYD7	ENSG00000221946	P58549	0.8706	0.6034	cerebral cortex
FZD10	ENSG00000111432	Q9ULW2	0.7846	0.6284	cervix, uterine
FZD8	ENSG00000177283	Q9H461	0.6885	0.4081	spleen
FZD9	ENSG00000188763	O00144	0.8597	0.7432	skeletal muscle
GABBR1	ENSG00000204681	Q9UBS5	0.717	0.4883	cerebral cortex
GABBR2	ENSG00000136928	O75899	0.964	0.8549	cerebral cortex
GABRA1	ENSG00000022355	P14867	0.99	0.9732	cerebral cortex
GABRA2	ENSG00000151834	P47869	0.8797	0.6296	cerebral cortex
GABRA3	ENSG00000011677	P34903	0.9595	0.868	cerebral cortex
GABRA4	ENSG00000109158	P48169	0.983	0.9548	cerebral cortex
GABRA5	ENSG00000186297	P31644	0.9786	0.9144	cerebral cortex
GABRA6	ENSG00000145863	Q16445	1	1	cerebral cortex
GABRB1	ENSG00000163288	P18505	0.9774	0.901	cerebral cortex
GABRB2	ENSG00000145864	P47870	0.9149	0.703	cerebral cortex
GABRB3	ENSG00000166206	P28472	0.8101	0.5443	cerebral cortex
GABRD	ENSG00000187730	O14764	0.9652	0.8236	cerebral cortex
GABRE	ENSG00000102287	P78334	0.798	0.578	adipose tissue
GABRG1	ENSG00000163285	Q8N1C3	0.9864	0.9539	cerebral cortex
GABRG2	ENSG00000113327	P18507	0.8558	0.4767	cerebral cortex
GABRG3	ENSG00000182256	Q99928	0.9072	0.7995	prostate
GABRR1	ENSG00000146276	P24046	0.9557	0.9056	placenta
GABRR2	ENSG00000111886	P28476	0.8049	0.8049	adrenal gland
GALR1	ENSG00000166573	P47211	0.8884	0.5863	adrenal gland
GALR2	ENSG00000182687	O43603	0.9673	0.9038	smooth muscle
GALR3	ENSG00000128310	O60755	0.9872	0.9833	cerebral cortex
GAPT	ENSG00000175857	Q8N292	0.7573	0.4356	granulocytes
GCGR	ENSG00000215644	P47871	0.929	0.8826	liver
GDPD2	ENSG00000130055	Q9HCC8	0.8694	0.7595	spleen
GDPD4	ENSG00000178795	Q6W3E5	0.9476	0.9104	placenta
GGT6	ENSG00000167741	Q6P531	0.6224	0.5347	colon
GHRHR	ENSG00000106128	Q02643	0.974	0.9693	adrenal gland
GHSR	ENSG00000121853	Q92847	0.9672	0.9543	nk-cells
GJA3	ENSG00000121743	Q9Y6H8	0.9227	0.8719	parathyroid gland
GJA8	ENSG00000121634	P48165	0.9756	0.9756	kidney
GJB1	ENSG00000169562	P08034	0.7185	0.5841	liver
GJB2	ENSG00000165474	P29033	0.7914	0.5439	esophagus
GJB3	ENSG00000188910	O75712	0.8277	0.6428	skin
GJB4	ENSG00000189433	Q9NTQ9	0.9322	0.8421	skin
GJB5	ENSG00000189280	O95377	0.8712	0.7508	skin
GJB6	ENSG00000121742	O95452	0.8647	0.7504	esophagus
GJB7	ENSG00000164411	Q6PEY0	0.9611	0.8877	fallopian tube
GJC2	ENSG00000198835	Q5T442	0.7813	0.4853	cerebral cortex
GJC3	ENSG00000176402	Q8NFK1	0.8521	0.6084	breast
GJD2	ENSG00000159248	Q9UKL4	0.9694	0.9223	adrenal gland
GJD3	ENSG00000183153	Q8N144	0.7774	0.537	spleen
GJD4	ENSG00000177291	Q96KN9	0.8018	0.5009	cerebral cortex
GLDN	ENSG00000186417	Q6ZMI3	0.7713	0.5463	cerebral cortex

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GLP1R	ENSG00000112164	P43220	0.8591	0.8071	cerebral cortex
GLP2R	ENSG00000065325	O95838	0.8001	0.6416	gallbladder
GLRA1	ENSG00000145888	P23415	0.9931	0.9892	adrenal gland
GLRA2	ENSG00000101958	P23416	0.9522	0.898	cerebral cortex
GLRA3	ENSG00000145451	O75311	0.9665	0.9115	cerebral cortex
GLRB	ENSG00000109738	P48167	0.7101	0.4729	parathyroid gland
GLT6D1	ENSG00000204007	Q7Z4J2	1	1	epididymis
GNRHR	ENSG00000109163	P30968	0.9173	0.818	adrenal gland
GP1BA	ENSG00000185245	P07359	0.832	0.5932	lymph node
GP1BB	ENSG00000203618	P13224	0.9402	0.8534	granulocytes
GP5	ENSG00000178732	P40197	0.8588	0.7206	lymph node
GP6	ENSG00000088053	Q9HCN6	0.8762	0.7097	skin
GP9	ENSG00000169704	P14770	0.9436	0.8717	granulocytes
GPA33	ENSG00000143167	Q99795	0.8312	0.7357	rectum
GPBAR1	ENSG00000179921	Q8TDU6	0.859	0.5696	monocytes
GPM6A	ENSG00000150625	P51674	0.7844	0.4163	cerebral cortex
GPR1	ENSG00000183671	P46091	0.8154	0.5967	placenta
GPR101	ENSG00000165370	Q96P66	1	1	cerebral cortex
GPR119	ENSG00000147262	Q8TDV5	0.91	0.8962	pancreas
GPR12	ENSG00000132975	P47775	0.9499	0.8619	cerebral cortex
GPR135	ENSG00000181619	Q8IZ08	0.6903	0.4918	fallopian tube
GPR139	ENSG00000180269	Q6DWJ6	0.9911	0.987	endometrium
GPR141	ENSG00000187037	Q7Z602	0.7095	0.4316	bone marrow
GPR142	ENSG00000257008	Q7Z601	1	1	appendix
GPR143	ENSG00000101850	P51810	0.6504	0.4686	skin
GPR148	ENSG00000173302	Q8TDV2	1	1	stomach
GPR149	ENSG00000174948	Q86SP6	0.9983	0.9968	seminal vesicle
GPR15	ENSG00000154165	P49685	0.7845	0.6345	rectum
GPR150	ENSG00000178015	Q8NGU9	0.8726	0.6653	parathyroid gland
GPR152	ENSG00000175514	Q8TDT2	1	1	spleen
GPR156	ENSG00000175697	Q8NFN8	0.8933	0.7445	fallopian tube
GPR158	ENSG00000151025	Q5T848	0.9772	0.8937	cerebral cortex
GPR161	ENSG00000143147	Q8N6U8	0.6565	0.4207	smooth muscle
GPR17	ENSG00000144230	Q13304	0.7134	0.5483	spleen
GPR171	ENSG00000174946	O14626	0.7299	0.4017	t-cells
GPR174	ENSG00000147138	Q9BXC1	0.7059	0.4536	lymph node
GPR18	ENSG00000125245	Q14330	0.7504	0.5883	nk-cells
GPR182	ENSG00000166856	O15218	0.9283	0.7541	spleen
GPR19	ENSG00000183150	Q15760	0.8279	0.5477	cerebral cortex
GPR20	ENSG00000204882	Q99678	0.8085	0.5781	monocytes
GPR21	ENSG00000188394	Q99679	0.816	0.5364	cerebral cortex
GPR22	ENSG00000172209	Q99680	0.9266	0.9104	heart muscle
GPR25	ENSG00000170128	O00155	0.9611	0.8981	t-cells
GPR26	ENSG00000154478	Q8NDV2	1	1	cerebral cortex
GPR27	ENSG00000170837	Q9NS67	0.6935	0.4211	parathyroid gland
GPR3	ENSG00000181773	P46089	0.8521	0.572	cerebral cortex
GPR31	ENSG00000120436	O00270	0.9285	0.8677	lymph node
GPR32	ENSG00000142511	O75388	0.9944	0.9909	parathyroid gland
GPR35	ENSG00000178623	Q9HC97	0.6515	0.4276	small intestine
GPR37	ENSG00000170775	O15354	0.8774	0.6418	cerebral cortex
GPR37L1	ENSG00000170075	O60883	0.9761	0.8041	cerebral cortex
GPR39	ENSG00000183840	O43194	0.7671	0.572	parathyroid gland

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GPR4	ENSG00000177464	P46093	0.67	0.405	adipose tissue
GPR42	ENSG00000126251	O15529	0.8996	0.8869	appendix
GPR45	ENSG00000135973	Q9Y5Y3	0.9977	0.9959	cerebral cortex
GPR50	ENSG00000102195	Q13585	0.9662	0.9264	placenta
GPR52	ENSG00000203737	Q9Y2T5	0.9877	0.9595	cerebral cortex
GPR55	ENSG00000135898	Q9Y2T6	0.7792	0.5548	spleen
GPR6	ENSG00000146360	P46095	1	1	cerebral cortex
GPR61	ENSG00000156097	Q9BZJ8	0.9662	0.9266	cerebral cortex
GPR62	ENSG00000180929	Q9BZJ7	0.974	0.8468	cerebral cortex
GPR65	ENSG00000140030	Q8IYL9	0.6899	0.427	t-cells
GPR75	ENSG00000119737	O95800	0.7644	0.4088	cerebral cortex
GPR82	ENSG00000171657	Q96P67	0.8403	0.5502	granulocytes
GPR83	ENSG00000123901	Q9NYM4	0.8845	0.5479	thyroid gland
GPR84	ENSG00000139572	Q9NQS5	0.7767	0.6001	bone marrow
GPR87	ENSG00000138271	Q9BY21	0.8488	0.7889	skin
GPR88	ENSG00000181656	Q9GZN0	0.8875	0.7724	spleen
GPRC5A	ENSG00000013588	Q8NFI5	0.6952	0.4713	lung
GPRC5D	ENSG00000111291	Q9NZD1	0.8103	0.5153	b-cells
GPRC6A	ENSG00000173612	Q5T6X5	0.9604	0.9422	kidney
GRAMD2A	ENSG00000175318	Q8IUJ3	0.8197	0.6383	placenta
GREB1	ENSG00000196208	Q4ZG55	0.7766	0.5349	ovary
GREB1L	ENSG00000141449	Q9C091	0.7258	0.5669	thyroid gland
GRIA1	ENSG00000155511	P42261	0.9521	0.8156	cerebral cortex
GRIA2	ENSG00000120251	P42262	0.8926	0.7656	cerebral cortex
GRIA3	ENSG00000125675	P42263	0.8277	0.5568	cerebral cortex
GRIA4	ENSG00000152578	P48058	0.9046	0.7143	cerebral cortex
GRID1	ENSG00000182771	Q9ULK0	0.8491	0.6075	cerebral cortex
GRID2	ENSG00000152208	O43424	0.9422	0.8808	cerebral cortex
GRIK1	ENSG00000171189	P39086	0.9038	0.7519	adrenal gland
GRIK2	ENSG00000164418	Q13002	0.821	0.4661	cerebral cortex
GRIK3	ENSG00000163873	Q13003	0.8602	0.5852	cerebral cortex
GRIK4	ENSG00000149403	Q16099	0.9149	0.7465	cerebral cortex
GRIK5	ENSG00000105737	Q16478	0.7345	0.4966	cerebral cortex
GRIN1	ENSG00000176884	Q05586	0.9873	0.9287	cerebral cortex
GRIN2A	ENSG00000183454	Q12879	0.9232	0.7076	cerebral cortex
GRIN2B	ENSG00000273079	Q13224	0.9866	0.954	cerebral cortex
GRIN2C	ENSG00000161509	Q14957	0.8804	0.6899	thyroid gland
GRIN2D	ENSG00000105464	Q15399	0.8795	0.7124	cerebral cortex
GRIN3A	ENSG00000198785	Q8TCU5	0.9175	0.6785	cerebral cortex
GRIN3B	ENSG00000116032	O60391	0.9215	0.801	fallopian tube
GRM1	ENSG00000152822	Q13255	0.976	0.951	cerebral cortex
GRM2	ENSG00000164082	Q14416	0.9852	0.9288	cerebral cortex
GRM3	ENSG00000198822	Q14832	0.9833	0.9132	cerebral cortex
GRM4	ENSG00000124493	Q14833	0.9815	0.9072	cerebral cortex
GRM5	ENSG00000168959	P41594	0.9941	0.9737	cerebral cortex
GRM6	ENSG00000113262	Q15303	0.8325	0.6712	cerebral cortex
GRM7	ENSG00000196277	Q14831	0.9033	0.8068	cerebral cortex
GRM8	ENSG00000179603	O00222	0.8539	0.7253	cerebral cortex
GRPR	ENSG00000126010	P30550	0.8554	0.6632	pancreas
GSDMA	ENSG00000167914	Q96QA5	0.8564	0.536	skin
GSDMB	ENSG00000073605	Q8TAX9	0.631	0.4023	small intestine
GSDMC	ENSG00000147697	Q9BYG8	0.9207	0.8956	skin

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GSG1L	ENSG00000169181	Q6UXU4	0.8902	0.6614	cerebral cortex
GSG1L2	ENSG00000214978	A8MUP6	1	1	cerebral cortex
GUCY2C	ENSG00000070019	P25092	0.8489	0.6619	small intestine
GUCY2D	ENSG00000132518	Q02846	0.9883	0.9413	dendritic cells
GUCY2F	ENSG00000101890	P51841	0.9799	0.9704	fallopian tube
GYPA	ENSG00000170180	P02724	0.9768	0.9409	bone marrow
GYPB	ENSG00000250361	P06028	0.9821	0.9704	bone marrow
GYPE	ENSG00000197465	P15421	0.7884	0.4775	bone marrow
HAS1	ENSG00000105509	Q92839	0.8454	0.6662	adipose tissue
HAS2	ENSG00000170961	Q92819	0.739	0.5094	adipose tissue
HAS3	ENSG00000103044	O00219	0.7289	0.475	urinary bladder
HAVCR1	ENSG00000113249	Q96D42	0.8724	0.5896	kidney
HCAR1	ENSG00000196917	Q9BXC0	0.8615	0.5031	parathyroid gland
HCAR2	ENSG00000182782	Q8TDS4	0.7461	0.5438	granulocytes
HCAR3	ENSG00000255398	P49019	0.8063	0.6268	granulocytes
HCN1	ENSG00000164588	O60741	0.983	0.9586	cerebral cortex
HCN2	ENSG00000099822	Q9UL51	0.947	0.7854	cerebral cortex
HCN3	ENSG00000143630	Q9P1Z3	0.6334	0.4024	cerebral cortex
HCN4	ENSG00000138622	Q9Y3Q4	0.933	0.889	heart muscle
HCRTR1	ENSG00000121764	O43613	0.8759	0.7364	adrenal gland
HCRTR2	ENSG00000137252	O43614	0.9394	0.929	kidney
HEPACAM	ENSG00000165478	Q14CZ8	0.944	0.7786	cerebral cortex
HEPACAM2	ENSG00000188175	A8MVW5	0.8469	0.7401	rectum
HEPHL1	ENSG00000181333	Q6MZM0	0.976	0.9571	tonsil
HHLA2	ENSG00000114455	Q9UM44	0.8117	0.6586	small intestine
HIGD1C	ENSG00000214511	A8MV81	0.775	0.5121	parathyroid gland
HLA-DQA2	ENSG00000237541	P01906	0.9653	0.9494	tonsil
HLA-DQB2	ENSG00000232629	P05538	0.8479	0.6557	skin
HLA-G	ENSG00000204632	P17693	0.9752	0.8866	placenta
HPN	ENSG00000105707	P05981	0.7623	0.5742	liver
HRCT1	ENSG00000196196	Q6UXD1	0.6863	0.4662	adipose tissue
HRH3	ENSG00000101180	Q9Y5N1	0.9863	0.9609	cerebral cortex
HRH4	ENSG00000134489	Q9H3N8	0.962	0.6497	granulocytes
HRK	ENSG00000135116	O00198	0.9208	0.8061	cerebral cortex
HS6ST2	ENSG00000171004	Q96MM7	0.7604	0.5888	ovary
HS6ST3	ENSG00000185352	Q8IZP7	0.8866	0.723	cerebral cortex
HSD17B2	ENSG00000086696	P37059	0.7534	0.5811	placenta
HTR1A	ENSG00000178394	P08908	0.9834	0.9803	ovary
HTR1B	ENSG00000135312	P28222	0.899	0.7407	placenta
HTR1D	ENSG00000179546	P28221	0.9135	0.7041	duodenum
HTR1E	ENSG00000168830	P28566	0.923	0.8651	ovary
HTR1F	ENSG00000179097	P30939	0.843	0.5887	placenta
HTR2A	ENSG00000102468	P28223	0.9113	0.6449	cerebral cortex
HTR2B	ENSG00000135914	P41595	0.7424	0.4967	cervix, uterine
HTR3A	ENSG00000166736	P46098	0.8703	0.7821	dendritic cells
HTR3B	ENSG00000149305	O95264	0.8486	0.4438	cerebral cortex
HTR3C	ENSG00000178084	Q8WXA8	0.9841	0.9682	lung
HTR3E	ENSG00000186038	A5X5Y0	0.9455	0.9339	duodenum
HTR4	ENSG00000164270	Q13639	0.8898	0.8039	small intestine
HTR5A	ENSG00000157219	P47898	1	1	cerebral cortex
HTR6	ENSG00000158748	P50406	0.977	0.9482	cerebral cortex
HTR7	ENSG00000148680	P34969	0.9044	0.5659	parathyroid gland

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HYAL4	ENSG00000106302	Q2M3T9	0.867	0.497	placenta
ICAM4	ENSG00000105371	Q14773	0.8454	0.4759	monocytes
ICAM5	ENSG00000105376	Q9UMF0	0.9843	0.9579	cerebral cortex
ICOS	ENSG00000163600	Q9Y6W8	0.8134	0.6544	t-cells
IER3	ENSG00000137331	P46695	0.8201	0.7179	appendix
IFITM10	ENSG00000244242	A6NMD0	0.9543	0.8357	adrenal gland
IFITM5	ENSG00000206013	A6NNB3	0.9239	0.8699	bone marrow
IGDCC3	ENSG00000174498	Q8IVU1	0.917	0.8218	parathyroid gland
IGDCC4	ENSG00000103742	Q8TDY8	0.7176	0.5429	ovary
IGSF1	ENSG00000147255	Q8N6C5	0.7444	0.5376	adrenal gland
IGSF11	ENSG00000144847	Q5DX21	0.8331	0.6085	cerebral cortex
IGSF23	ENSG00000216588	A1L1A6	0.9158	0.8474	small intestine
IGSF5	ENSG00000183067	Q9NSI5	0.7132	0.4364	placenta
IGSF6	ENSG00000140749	Q95976	0.824	0.5122	granulocytes
IGSF9	ENSG00000085552	Q9P2J2	0.7633	0.5713	skin
IGSF9B	ENSG00000080854	Q9UPX0	0.7092	0.4747	cerebral cortex
IL12RB2	ENSG00000081985	Q99665	0.8055	0.4751	nk-cells
IL13RA2	ENSG00000123496	Q14627	0.7211	0.5956	prostate
IL17RD	ENSG00000144730	Q8NFM7	0.6713	0.5023	parathyroid gland
IL17RE	ENSG00000163701	Q8NFR9	0.6001	0.4393	small intestine
IL18RAP	ENSG00000115607	Q95256	0.7749	0.5374	nk-cells
IL1R2	ENSG00000115590	P27930	0.6745	0.4111	granulocytes
IL1RAPL1	ENSG00000169306	Q9NZN1	0.9518	0.7378	cerebral cortex
IL1RAPL2	ENSG00000189108	Q9NP60	0.9314	0.8204	parathyroid gland
IL1RL1	ENSG00000115602	Q01638	0.7907	0.469	placenta
IL1RL2	ENSG00000115598	Q9HB29	0.7646	0.5332	skin
IL20RA	ENSG00000016402	Q9UHF4	0.6787	0.5026	skin
IL20RB	ENSG00000174564	Q6UXL0	0.927	0.8353	skin
IL21R	ENSG00000103522	Q9HBE5	0.7339	0.5311	lymph node
IL22RA1	ENSG00000142677	Q8N6P7	0.784	0.6542	skin
IL23R	ENSG00000162594	Q5VWK5	0.9487	0.7894	t-cells
IL2RA	ENSG00000134460	P01589	0.7733	0.4982	t-cells
IL31RA	ENSG00000164509	Q8NI17	0.8857	0.625	bone marrow
IL5RA	ENSG00000091181	Q01344	0.9003	0.5793	granulocytes
IL9R	ENSG00000124334	Q01113	0.8254	0.5829	urinary bladder
ILDR1	ENSG00000145103	Q86SU0	0.6806	0.475	parathyroid gland
IMPG2	ENSG00000081148	Q9BZV3	0.9714	0.7483	fallopian tube
INSRR	ENSG00000027644	P14616	0.9281	0.8545	adrenal gland
ISLR2	ENSG00000167178	Q6UXK2	0.843	0.4714	cerebral cortex
ITGA10	ENSG00000143127	Q75578	0.668	0.407	cervix, uterine
ITGA11	ENSG00000137809	Q9UKX5	0.6997	0.4556	smooth muscle
ITGA2B	ENSG00000005961	P08514	0.8468	0.5862	granulocytes
ITGA8	ENSG00000077943	P53708	0.6175	0.4242	prostate
ITGAD	ENSG00000156886	Q13349	0.9298	0.772	spleen
ITGAE	ENSG00000083457	P38570	0.7801	0.5601	lung
ITGB3	ENSG00000259207	P05106	0.6934	0.4142	thyroid gland
ITGB6	ENSG00000115221	P18564	0.6863	0.5334	lung
IYD	ENSG00000009765	Q6PHW0	0.8931	0.6823	thyroid gland
IZUMO1	ENSG00000182264	Q8IYV9	0.8728	0.7902	lung
IZUMO2	ENSG00000161652	Q6UXV1	0.9385	0.9367	prostate
JAG2	ENSG00000184916	Q9Y219	0.7347	0.4239	skin
JPH1	ENSG00000104369	Q9HDC5	0.8392	0.5298	skeletal muscle

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JPH2	ENSG00000149596	Q9BR39	0.6739	0.5031	skeletal muscle
JPH3	ENSG00000154118	Q8WXH2	0.9738	0.8806	cerebral cortex
JPH4	ENSG00000092051	Q96JJ6	0.7876	0.5622	cerebral cortex
KCNA1	ENSG00000111262	Q09470	0.9692	0.9064	cerebral cortex
KCNA10	ENSG00000143105	Q16322	1	1	spleen
KCNA2	ENSG00000177301	P16389	0.8905	0.5561	cerebral cortex
KCNA3	ENSG00000177272	P22001	0.672	0.437	t-cells
KCNA4	ENSG00000182255	P22459	0.9417	0.8738	adrenal gland
KCNA5	ENSG00000130037	P22460	0.8081	0.5462	heart muscle
KCNA6	ENSG00000151079	P17658	0.9512	0.9512	appendix
KCNA7	ENSG00000104848	Q96RP8	0.9616	0.6927	skeletal muscle
KCNB1	ENSG00000158445	Q14721	0.8187	0.618	cerebral cortex
KCNB2	ENSG00000182674	Q92953	0.9306	0.8475	spleen
KCNC1	ENSG00000129159	P48547	0.9087	0.5839	cerebral cortex
KCNC2	ENSG00000166006	Q96PR1	0.9801	0.9638	cerebral cortex
KCNC3	ENSG00000131398	Q14003	0.723	0.4768	parathyroid gland
KCND2	ENSG00000184408	Q9NZV8	0.8556	0.6652	cerebral cortex
KCND3	ENSG00000171385	Q9UK17	0.607	0.4304	cerebral cortex
KCNE1	ENSG00000180509	P15382	0.8903	0.6834	fallopian tube
KCNE2	ENSG00000159197	Q9Y6J6	0.935	0.5809	stomach
KCNE5	ENSG00000176076	Q9UJ90	0.8582	0.7018	cerebral cortex
KCNF1	ENSG00000162975	Q9H3M0	0.9708	0.7972	cerebral cortex
KCNG1	ENSG00000026559	Q9UIX4	0.7559	0.5741	endometrium
KCNG2	ENSG00000178342	Q9UJ96	0.9655	0.9142	cerebral cortex
KCNG3	ENSG00000171126	Q8TAE7	0.9217	0.8349	cerebral cortex
KCNG4	ENSG00000168418	Q8TDN1	0.8521	0.6923	adrenal gland
KCNH1	ENSG00000143473	Q95259	0.9604	0.7711	cerebral cortex
KCNH2	ENSG00000055118	Q12809	0.7084	0.5165	bone marrow
KCNH3	ENSG00000135519	Q9ULD8	0.8975	0.6586	cerebral cortex
KCNH4	ENSG00000089558	Q9UQ05	0.9278	0.7565	cerebral cortex
KCNH5	ENSG00000140015	Q8NCM2	0.9803	0.9702	cerebral cortex
KCNH6	ENSG00000173826	Q9H252	0.8972	0.797	kidney
KCNH7	ENSG00000184611	Q9NS40	0.9699	0.8941	cerebral cortex
KCNH8	ENSG00000183960	Q96L42	0.8522	0.5871	cerebral cortex
KCNJ1	ENSG00000151704	P48048	0.9755	0.8648	kidney
KCNJ10	ENSG00000177807	P78508	0.9133	0.7408	cerebral cortex
KCNJ12	ENSG00000184185	Q14500	0.8194	0.5279	skeletal muscle
KCNJ13	ENSG00000115474	O60928	0.8975	0.7549	small intestine
KCNJ15	ENSG00000157551	Q99712	0.6824	0.4665	kidney
KCNJ16	ENSG00000153822	Q9NPI9	0.7928	0.6131	parathyroid gland
KCNJ3	ENSG00000162989	P48549	0.8023	0.6127	parathyroid gland
KCNJ4	ENSG00000168135	P48050	0.9682	0.9402	cerebral cortex
KCNJ5	ENSG00000120457	P48544	0.7996	0.4801	adrenal gland
KCNJ6	ENSG00000157542	P48051	0.9366	0.7923	cerebral cortex
KCNJ9	ENSG00000162728	Q92806	0.9974	0.9942	cerebral cortex
KCNK10	ENSG00000100433	P57789	0.873	0.7631	dendritic cells
KCNK12	ENSG00000184261	Q9HB15	0.9856	0.9436	cerebral cortex
KCNK13	ENSG00000152315	Q9HB14	0.8666	0.5491	parathyroid gland
KCNK16	ENSG00000095981	Q96T55	0.9377	0.8945	stomach
KCNK17	ENSG00000124780	Q96T54	0.8649	0.5428	dendritic cells
KCNK18	ENSG00000186795	Q7Z418	1	1	cerebral cortex
KCNK2	ENSG00000082482	O95069	0.8437	0.629	adrenal gland

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KCNK3	ENSG00000171303	O14649	0.801	0.53	adrenal gland
KCNK4	ENSG00000182450	Q9NYG8	0.988	0.9601	cerebral cortex
KCNK5	ENSG00000164626	O95279	0.6158	0.4046	small intestine
KCNK7	ENSG00000173338	Q9Y2U2	0.8857	0.5634	skin
KCNK9	ENSG00000169427	Q9NPC2	0.9595	0.9396	cerebral cortex
KCNMB2	ENSG00000197584	Q9Y691	0.8134	0.6289	epididymis
KCNMB4	ENSG00000135643	Q86W47	0.7679	0.4047	cerebral cortex
KCNN1	ENSG00000105642	Q92952	0.9589	0.7325	cerebral cortex
KCNN2	ENSG00000080709	Q9H2S1	0.7821	0.5713	adrenal gland
KCNQ2	ENSG00000075043	O43526	0.9735	0.9336	cerebral cortex
KCNQ3	ENSG00000184156	O43525	0.9184	0.5983	cerebral cortex
KCNQ4	ENSG00000117013	P56696	0.7381	0.5498	smooth muscle
KCNQ5	ENSG00000185760	Q9NR82	0.8415	0.5809	cerebral cortex
KCNS1	ENSG00000124134	Q96KK3	0.9308	0.8631	cerebral cortex
KCNS2	ENSG00000156486	Q9ULS6	0.9041	0.7179	cerebral cortex
KCNT1	ENSG00000107147	Q5JUK3	0.917	0.8021	cerebral cortex
KCNT2	ENSG00000162687	Q6UVM3	0.7776	0.5365	ovary
KCNU1	ENSG00000215262	A8MYU2	0.9618	0.9541	adipose tissue
KCNV1	ENSG00000164794	Q6PIU1	0.9429	0.5772	cerebral cortex
KCNV2	ENSG00000168263	Q8TDN2	0.9756	0.9756	b-cells
KEL	ENSG00000197993	P23276	0.9256	0.8338	bone marrow
KIAA0319	ENSG00000137261	Q5VV43	0.935	0.7682	cerebral cortex
KIAA1549	ENSG00000122778	Q9HCM3	0.6803	0.4504	seminal vesicle
KIAA1549L	ENSG00000110427	Q6ZVL6	0.9459	0.8124	parathyroid gland
KIR2DL4	ENSG00000189013	Q99706	1	1	nk-cells
KIR3DL1	ENSG00000167633	P43629	0.9892	0.9822	t-cells
KIR3DL2	ENSG00000240403	P43630	1	1	t-cells
KIRREL3	ENSG00000149571	Q8IZU9	0.9044	0.6553	cerebral cortex
KISS1R	ENSG00000116014	Q969F8	0.9664	0.9119	cerebral cortex
KL	ENSG00000133116	Q9UEF7	0.8335	0.5447	parathyroid gland
KLB	ENSG00000134962	Q86Z14	0.9039	0.6768	adipose tissue
KLHDC7A	ENSG00000179023	Q5VTJ3	0.864	0.7067	kidney
KLRB1	ENSG00000111796	Q12918	0.7677	0.4149	t-cells
KLRC1	ENSG00000134545	P26715	0.8204	0.4208	nk-cells
KLRC3	ENSG00000205810	Q07444	0.9011	0.6979	nk-cells
KLRC4	ENSG00000183542	O43908	0.7286	0.4793	spleen
KLRF1	ENSG00000150045	Q9NZS2	0.8489	0.4614	nk-cells
KLRF2	ENSG00000256797	D3W0D1	0.94	0.8161	skin
KLRG2	ENSG00000188883	A4D1S0	0.8656	0.8029	thyroid gland
KREMEN2	ENSG00000131650	Q8NCW0	0.927	0.748	skin
L1CAM	ENSG00000198910	P32004	0.7264	0.4563	cerebral cortex
LAG3	ENSG00000089692	P18627	0.7239	0.5025	spleen
LAMP5	ENSG00000125869	Q9UJQ1	0.7748	0.4879	dendritic cells
LAX1	ENSG00000122188	Q8IWV1	0.6998	0.5126	tonsil
LCT	ENSG00000115850	P09848	0.9743	0.9664	duodenum
LDLRAD1	ENSG00000203985	Q5T700	0.9372	0.752	fallopian tube
LDLRAD2	ENSG00000187942	Q5SZI1	0.741	0.4888	adipose tissue
LEMD1	ENSG00000186007	Q68G75	0.9453	0.7786	epididymis
LGR5	ENSG00000139292	O75473	0.7737	0.5888	placenta
LGR6	ENSG00000133067	Q9HBX8	0.7406	0.5152	t-cells
LHCGR	ENSG00000138039	P22888	0.9155	0.8824	ovary
LHFPL1	ENSG00000182508	Q86WI0	0.8287	0.6423	cerebral cortex

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LHFPL4	ENSG00000156959	Q7Z7J7	0.9777	0.9204	cerebral cortex
LHFPL5	ENSG00000197753	Q8TAF8	0.7749	0.4209	epididymis
LILRA1	ENSG00000104974	O75019	0.9511	0.8844	monocytes
LILRA5	ENSG00000187116	A6NI73	0.8829	0.7109	monocytes
LIM2	ENSG00000105370	P55344	0.981	0.9464	t-cells
LIME1	ENSG00000203896	Q9H400	0.814	0.612	dendritic cells
LINGO1	ENSG00000169783	Q96FE5	0.817	0.4679	cerebral cortex
LINGO2	ENSG00000174482	Q7L985	0.8559	0.748	smooth muscle
LINGO3	ENSG00000220008	P0C6S8	0.8984	0.8303	spleen
LINGO4	ENSG00000213171	Q6UY18	0.8889	0.6497	skeletal muscle
LMTK3	ENSG00000142235	Q96Q04	0.8839	0.6242	cerebral cortex
LPAR3	ENSG00000171517	Q9UBY5	0.8097	0.5882	fallopian tube
LPAR4	ENSG00000147145	Q99677	0.822	0.5977	ovary
LPCAT1	ENSG00000153395	Q8NF37	0.7879	0.4599	lung
LRFN1	ENSG00000128011	Q9P244	0.8453	0.4576	cerebral cortex
LRFN2	ENSG00000156564	Q9ULH4	0.9674	0.9055	cerebral cortex
LRFN5	ENSG00000165379	Q96NI6	0.8195	0.6066	parathyroid gland
LRIT2	ENSG00000204033	A6NDA9	0.9814	0.9602	skin
LRIT3	ENSG00000183423	Q3SXY7	0.8689	0.6618	kidney
LRP1B	ENSG00000168702	Q9NZR2	0.9029	0.7876	cerebral cortex
LRP2	ENSG00000081479	P98164	0.913	0.8631	parathyroid gland
LRP4	ENSG00000134569	O75096	0.7087	0.4445	skin
LRP8	ENSG00000157193	Q14114	0.7881	0.4515	thyroid gland
LRRC15	ENSG00000172061	Q8TF66	0.6834	0.5809	cervix, uterine
LRRC19	ENSG00000184434	Q9H756	0.863	0.8065	kidney
LRRC26	ENSG00000184709	Q2I0M4	0.9209	0.8594	dendritic cells
LRRC37A	ENSG00000176681	A6NMS7	0.7528	0.4355	skeletal muscle
LRRC38	ENSG00000162494	Q5VT99	0.9533	0.8611	adrenal gland
LRRC3B	ENSG00000179796	Q96PB8	0.9222	0.7338	cerebral cortex
LRRC3C	ENSG00000204913	A6NJW4	0.9591	0.9178	parathyroid gland
LRRC4	ENSG00000128594	Q9HBW1	0.7186	0.4284	cerebral cortex
LRRC4B	ENSG00000131409	Q9NT99	0.8376	0.568	cerebral cortex
LRRC4C	ENSG00000148948	Q9HCJ2	0.8489	0.5469	cerebral cortex
LRRC52	ENSG00000162763	Q8N7C0	0.9678	0.9506	parathyroid gland
LRRC55	ENSG00000183908	Q6ZSA7	0.8646	0.6325	cerebral cortex
LRRC66	ENSG00000188993	Q68CR7	0.8603	0.7096	duodenum
LRRN1	ENSG00000175928	Q6UXK5	0.7324	0.4796	cerebral cortex
LRRN2	ENSG00000170382	O75325	0.6768	0.4438	cerebral cortex
LRRN3	ENSG00000173114	Q9H3W5	0.6934	0.4958	thyroid gland
LRRN4	ENSG00000125872	Q8WUT4	0.9767	0.9317	lung
LRRN4CL	ENSG00000177363	Q8ND94	0.6509	0.4579	endometrium
LRRTM1	ENSG00000162951	Q86UE6	0.8861	0.6817	cerebral cortex
LRRTM2	ENSG00000146006	O43300	0.943	0.7453	cerebral cortex
LRRTM3	ENSG00000198739	Q86VH5	0.9607	0.9108	cerebral cortex
LRTM1	ENSG00000144771	Q9HBL6	0.8814	0.6793	skeletal muscle
LRTM2	ENSG00000166159	Q8N967	1	1	cerebral cortex
LTB	ENSG00000227507	Q06643	0.7932	0.6701	t-cells
LTK	ENSG00000062524	P29376	0.6759	0.5109	placenta
LVRN	ENSG00000172901	Q6Q4G3	0.9498	0.833	placenta
LY6G6F	ENSG00000204424	Q5SQ64	0.9401	0.9017	bone marrow
LY9	ENSG00000122224	Q9HBG7	0.7229	0.4772	t-cells
MADCAM1	ENSG00000099866	Q13477	0.8279	0.5918	appendix

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MAG	ENSG00000105695	P20916	0.9472	0.8486	cerebral cortex
MARCO	ENSG00000019169	Q9UEW3	0.7384	0.4998	lung
MARVELD2	ENSG00000152939	Q8N4S9	0.6804	0.4561	thyroid gland
MAS1	ENSG00000130368	P04201	0.9377	0.7909	cerebral cortex
MAS1L	ENSG00000204687	P35410	0.8744	0.7078	cervix, uterine
MC2R	ENSG00000185231	Q01718	0.9865	0.9659	adrenal gland
MC4R	ENSG00000166603	P32245	0.9571	0.8937	fallopian tube
MC5R	ENSG00000176136	P33032	0.9843	0.961	epididymis
MCEMP1	ENSG00000183019	Q8IX19	0.8506	0.7534	lung
MCHR1	ENSG00000128285	Q99705	0.9341	0.7882	cerebral cortex
MCHR2	ENSG00000152034	Q969V1	0.9979	0.9943	cerebral cortex
MCOLN2	ENSG00000153898	Q8IZK6	0.6509	0.4273	dendritic cells
MCOLN3	ENSG00000055732	Q8TDD5	0.7659	0.5313	adrenal gland
MEGF10	ENSG00000145794	Q96KG7	0.9212	0.7039	cerebral cortex
MEGF11	ENSG00000157890	A6BM72	0.9427	0.8741	cerebral cortex
MEP1A	ENSG00000112818	Q16819	0.9082	0.8432	small intestine
MEP1B	ENSG00000141434	Q16820	0.9003	0.6451	small intestine
MFAP3L	ENSG00000198948	O75121	0.6233	0.4148	epididymis
MFRP	ENSG00000235718	Q9BY79	1	1	parathyroid gland
MFSD2A	ENSG00000168389	Q8NA29	0.6258	0.4075	epididymis
MFSD2B	ENSG00000205639	A6NFX1	0.9714	0.923	bone marrow
MFSD4A	ENSG00000174514	Q8N468	0.7568	0.5524	stomach
MGAM	ENSG00000257335	O43451	0.8462	0.7228	small intestine
MGAM2	ENSG00000257743	Q2M2H8	0.915	0.8281	duodenum
MICB	ENSG00000204516	Q29980	0.7297	0.4835	lymph node
MIP	ENSG00000135517	P30301	0.8991	0.8565	cerebral cortex
MLC1	ENSG00000100427	Q15049	0.8843	0.6848	cerebral cortex
MLNR	ENSG00000102539	O43193	0.9693	0.9106	thyroid gland
MME	ENSG00000196549	P08473	0.6103	0.4207	duodenum
MMEL1	ENSG00000142606	Q495T6	0.7688	0.6414	granulocytes
MMP16	ENSG00000156103	P51512	0.8139	0.5655	cerebral cortex
MMP23B	ENSG00000189409	Q75900	0.7057	0.4499	dendritic cells
MMP24	ENSG00000125966	Q9Y5R2	0.7529	0.5117	cerebral cortex
MOG	ENSG00000204655	Q16653	1	1	cerebral cortex
MPIG6B	ENSG00000204420	Q95866	0.9075	0.7976	nk-cells
MPL	ENSG00000117400	P40238	0.7722	0.4893	ovary
MPZ	ENSG00000158887	P25189	0.6402	0.4013	seminal vesicle
MRAP	ENSG00000170262	Q8TCY5	0.911	0.7895	adrenal gland
MRAP2	ENSG00000135324	Q96G30	0.6705	0.4606	cerebral cortex
MRGPRD	ENSG00000172938	Q8TDS7	0.9468	0.883	seminal vesicle
MRGPRE	ENSG00000184350	Q86SM8	0.8762	0.7484	cervix, uterine
MRGPRF	ENSG00000172935	Q96AM1	0.5848	0.4214	smooth muscle
MRGPRX2	ENSG00000183695	Q96LB1	0.9138	0.8541	breast
MRGPRX3	ENSG00000179826	Q96LB0	0.9028	0.7178	salivary gland
MROH7	ENSG00000184313	Q68CQ1	0.74	0.55	ovary
MS4A1	ENSG00000156738	P11836	0.7323	0.5145	tonsil
MS4A10	ENSG00000172689	Q96PG2	0.9594	0.8651	small intestine
MS4A12	ENSG00000071203	Q9NXJ0	0.9481	0.9211	rectum
MS4A14	ENSG00000166928	Q96JA4	0.6946	0.4546	spleen
MS4A15	ENSG00000166961	Q8N5U1	0.8253	0.5051	lung
MS4A18	ENSG00000214782	Q3C1V0	0.966	0.9538	duodenum
MS4A2	ENSG00000149534	Q01362	0.803	0.5073	granulocytes

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MS4A5	ENSG00000166930	Q9H3V2	0.9872	0.9833	duodenum
MS4A6E	ENSG00000166926	Q96DS6	0.9437	0.876	appendix
MS4A8	ENSG00000166959	Q9BY19	0.8039	0.7146	fallopian tube
MSLNL	ENSG00000162006	Q96KJ4	0.9806	0.952	epididymis
MST1R	ENSG00000164078	Q04912	0.7262	0.5155	skin
MTNR1A	ENSG00000168412	P48039	0.9224	0.8431	kidney
MTNR1B	ENSG00000134640	P49286	0.9778	0.9525	placenta
MUC1	ENSG00000185499	P15941	0.608	0.4207	stomach
MUC12	ENSG00000205277	Q9UKN1	0.9557	0.9286	rectum
MUC13	ENSG00000173702	Q9H3R2	0.8227	0.7339	duodenum
MUC15	ENSG00000169550	Q8N387	0.8744	0.7307	epididymis
MUC16	ENSG00000181143	Q8WXI7	0.9503	0.9121	cervix, uterine
MUC17	ENSG00000169876	Q685J3	0.9551	0.9336	small intestine
MUC21	ENSG00000204544	Q5SSG8	0.9874	0.9765	esophagus
MUC22	ENSG00000261272	E2RYF6	0.9992	0.9985	esophagus
MUC4	ENSG00000145113	Q99102	0.9556	0.8949	colon
MUSK	ENSG0000030304	O15146	0.7693	0.6893	rectum
MYADML2	ENSG00000185105	A6NDP7	0.9741	0.9273	skeletal muscle
MYMK	ENSG00000187616	A6NI61	0.9329	0.9203	cerebral cortex
MYRFL	ENSG00000166268	Q96LU7	0.9248	0.7562	small intestine
NAALAD2	ENSG00000077616	Q9Y3Q0	0.6922	0.5092	adrenal gland
NAALADL2	ENSG00000177694	Q58DX5	0.7304	0.4312	parathyroid gland
NALCN	ENSG00000102452	Q8IZF0	0.7967	0.4599	cerebral cortex
NAT8L	ENSG00000185818	Q8N9F0	0.8855	0.6792	cerebral cortex
NCAM1	ENSG00000149294	P13591	0.6599	0.4035	cerebral cortex
NCAM2	ENSG00000154654	O15394	0.8649	0.5689	cerebral cortex
NCMAP	ENSG00000184454	Q5T1S8	0.7744	0.5474	gallbladder
NCR1	ENSG00000189430	O76036	0.9802	0.9454	spleen
NCR2	ENSG00000096264	O95944	0.9632	0.9079	dendritic cells
NCR3	ENSG00000204475	O14931	0.9371	0.8624	t-cells
NCR3LG1	ENSG00000188211	Q68D85	0.7446	0.4619	parathyroid gland
NETIN4	ENSG00000143217	Q96NY8	0.7706	0.5933	skin
NETO1	ENSG00000166342	Q8TDF5	0.948	0.8266	cerebral cortex
NFAM1	ENSG00000235568	Q8NET5	0.7162	0.4392	granulocytes
NIPAL1	ENSG00000163293	Q6NVV3	0.6965	0.5014	skin
NIPAL4	ENSG00000172548	Q0D2K0	0.8609	0.6806	skin
NKAIN1	ENSG00000084628	Q4KMZ8	0.8874	0.7963	adrenal gland
NKAIN2	ENSG00000188580	Q5VXU1	0.9441	0.6405	cerebral cortex
NKAIN3	ENSG00000185942	Q8N8D7	0.9264	0.8723	adrenal gland
NKAIN4	ENSG00000101198	Q8IVV8	0.951	0.8012	cerebral cortex
NKPD1	ENSG00000179846	Q17RQ9	0.9695	0.8498	skin
NLGN1	ENSG00000169760	Q8N2Q7	0.7962	0.5518	cerebral cortex
NLGN3	ENSG00000196338	Q9NZ94	0.8258	0.5652	cerebral cortex
NLGN4X	ENSG00000146938	Q8N0W4	0.7084	0.4705	cerebral cortex
NLGN4Y	ENSG00000165246	Q8NFZ3	0.8089	0.6538	seminal vesicle
NMBR	ENSG00000135577	P28336	0.9486	0.8103	fallopian tube
NMUR1	ENSG00000171596	Q9HB89	0.7528	0.44	t-cells
NMUR2	ENSG00000132911	Q9GZQ4	0.9256	0.8519	stomach
NOMO1	ENSG00000103512	Q15155	0.5756	0.4604	thyroid gland
NOTCH4	ENSG00000204301	Q99466	0.8648	0.6619	lung
NOX1	ENSG00000007952	Q9Y5S8	0.9057	0.7242	rectum
NOX3	ENSG00000074771	Q9HBY0	1	1	adrenal gland

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NOX4	ENSG00000086991	Q9NPH5	0.8662	0.5719	kidney
NOX5	ENSG00000255346	Q96PH1	0.9359	0.7661	spleen
NPBWR2	ENSG00000125522	P48146	0.9756	0.9756	adrenal gland
NPC1L1	ENSG00000015520	Q9UHC9	0.9233	0.8565	small intestine
NPFFR2	ENSG00000056291	Q9Y5X5	0.9176	0.7584	seminal vesicle
NPHS1	ENSG00000161270	O60500	0.9451	0.9045	kidney
NPR1	ENSG00000169418	P16066	0.6483	0.4094	adipose tissue
NPSR1	ENSG00000187258	Q6W5P4	0.9828	0.9597	stomach
NPY2R	ENSG00000185149	P49146	0.9279	0.8467	cerebral cortex
NPY5R	ENSG00000164129	Q15761	0.7905	0.5786	spleen
NRCAM	ENSG00000091129	Q92823	0.7837	0.5128	cerebral cortex
NRG2	ENSG00000158458	Q14511	0.7334	0.5251	parathyroid gland
NRG3	ENSG00000185737	P56975	0.9264	0.7613	cerebral cortex
NRG4	ENSG00000169752	Q8WWG1	0.8997	0.8148	fallopian tube
NRSN1	ENSG00000152954	Q8IZ57	0.9525	0.7085	cerebral cortex
NRXN1	ENSG00000179915	Q9ULB1	0.857	0.5042	cerebral cortex
NRXN2	ENSG00000110076	Q9P2S2	0.8504	0.5482	cerebral cortex
NRXN3	ENSG00000021645	Q9Y4C0	0.7146	0.4647	cerebral cortex
NSG1	ENSG00000168824	P42857	0.6397	0.4208	skin
NSG2	ENSG00000170091	Q9Y328	0.9278	0.8113	cerebral cortex
NTRK1	ENSG00000198400	P04629	0.9497	0.7575	granulocytes
NTRK2	ENSG00000148053	Q16620	0.7032	0.4316	cerebral cortex
NTRK3	ENSG00000140538	Q16288	0.7303	0.4476	cerebral cortex
NTSR1	ENSG00000101188	P30989	0.941	0.9093	cerebral cortex
NTSR2	ENSG00000169006	Q95665	0.992	0.982	cerebral cortex
NUP210L	ENSG00000143552	Q5VU65	0.9098	0.8718	seminal vesicle
NXPE2	ENSG00000204361	Q96DL1	0.9059	0.803	epididymis
OCLN	ENSG00000197822	Q16625	0.6232	0.4107	thyroid gland
OCSTAMP	ENSG00000149635	Q9BR26	0.9931	0.9892	dendritic cells
OLR1	ENSG00000173391	P78380	0.7517	0.4572	placenta
OPALIN	ENSG00000197430	Q96PE5	1	1	cerebral cortex
OPN1SW	ENSG00000128617	P03999	0.6951	0.5377	heart muscle
OPN4	ENSG00000122375	Q9UHM6	0.9364	0.8682	cerebral cortex
OPN5	ENSG00000124818	Q6U736	1	1	heart muscle
OPRD1	ENSG00000116329	P41143	0.8954	0.5128	cerebral cortex
OPRK1	ENSG00000082556	P41145	0.9538	0.8863	cerebral cortex
OPRL1	ENSG00000125510	P41146	0.802	0.504	cerebral cortex
OPRM1	ENSG00000112038	P35372	0.7979	0.5593	adrenal gland
OR10A3	ENSG00000170683	P58181	0.9742	0.9663	granulocytes
OR10A4	ENSG00000170782	Q9H209	1	1	dendritic cells
OR10G3	ENSG00000169208	Q8NGC4	0.9265	0.8037	granulocytes
OR10G4	ENSG00000254737	Q8NGN3	0.8366	0.6068	bone marrow
OR10J1	ENSG00000196184	P30954	0.9724	0.9352	granulocytes
OR10J3	ENSG00000196266	Q5JRS4	1	1	placenta
OR10P1	ENSG00000175398	Q8NGE3	0.9831	0.98	t-cells
OR10S1	ENSG00000196248	Q8NGN2	1	1	thyroid gland
OR10Z1	ENSG00000198967	Q8NGY1	0.9974	0.9953	bone marrow
OR13A1	ENSG00000256574	Q8NGR1	0.9302	0.8759	urinary bladder
OR13C8	ENSG00000186943	Q8NGS7	1	1	t-cells
OR14C36	ENSG00000177174	Q8NHC7	1	1	prostate
OR14I1	ENSG00000189181	A6ND48	0.9907	0.9843	cerebral cortex
OR14K1	ENSG00000153230	Q8NGZ2	1	1	fallopian tube

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OR1F1	ENSG00000168124	O43749	0.9402	0.914	cerebral cortex
OR1J2	ENSG00000197233	Q8NGS2	0.9872	0.9833	urinary bladder
OR1N1	ENSG00000171505	Q8NGS0	1	1	cervix, uterine
OR2A5	ENSG00000221836	Q96R48	0.9024	0.9024	appendix
OR2AG2	ENSG00000188124	A6NM03	0.878	0.878	appendix
OR2AP1	ENSG00000179615	Q8NGE2	0.9024	0.9024	cerebral cortex
OR2B11	ENSG00000177535	Q5JQS5	0.9246	0.9122	appendix
OR2B6	ENSG00000124657	P58173	0.9246	0.9008	placenta
OR2H2	ENSG00000204657	O95918	0.9697	0.8626	epididymis
OR2L13	ENSG00000196071	Q8N349	0.934	0.831	cerebral cortex
OR2L2	ENSG00000203663	Q8NH16	0.6724	0.4039	bone marrow
OR2L3	ENSG00000198128	Q8NG85	0.9448	0.8091	prostate
OR2L5	ENSG00000197454	Q8NG80	0.9756	0.9756	bone marrow
OR2T10	ENSG00000184022	Q8NGZ9	0.9929	0.9774	kidney
OR2T33	ENSG00000177212	Q8NG76	0.811	0.7268	bone marrow
OR2V2	ENSG00000182613	Q96R30	0.8548	0.6345	granulocytes
OR2W3	ENSG00000238243	Q7Z3T1	0.8785	0.6888	thyroid gland
OR3A1	ENSG00000180090	P47881	0.9182	0.8532	t-cells
OR3A2	ENSG00000221882	P47893	0.8088	0.6479	cerebral cortex
OR3A3	ENSG00000159961	P47888	0.9848	0.9026	dendritic cells
OR4A47	ENSG00000237388	Q6IF82	1	1	t-cells
OR4C6	ENSG00000181903	Q8NH72	0.9512	0.9512	b-cells
OR4D1	ENSG00000141194	Q15615	0.9219	0.819	nk-cells
OR4D9	ENSG00000172742	Q8NGE8	0.7751	0.464	granulocytes
OR4F15	ENSG00000182854	Q8NGB8	0.9599	0.8786	granulocytes
OR4P4	ENSG00000181927	Q8NGL7	0.8875	0.8604	bone marrow
OR51B4	ENSG00000183251	Q9Y5P0	0.9024	0.9024	breast
OR51E2	ENSG00000167332	Q9H255	0.9085	0.6836	prostate
OR51T1	ENSG00000176900	Q8NGJ9	1	1	prostate
OR52A1	ENSG00000182070	Q9UKL2	0.7079	0.5011	granulocytes
OR52I1	ENSG00000232268	Q8NGK6	0.739	0.481	skin
OR52I2	ENSG00000226288	Q8NH67	1	1	epididymis
OR52K1	ENSG00000196778	Q8NGK4	0.7	0.417	bone marrow
OR52K2	ENSG00000181963	Q8NGK3	0.9869	0.9803	granulocytes
OR52N1	ENSG00000181001	Q8NH53	0.9024	0.9024	adipose tissue
OR52N4	ENSG00000181074	Q8NGI2	0.728	0.5138	spleen
OR52W1	ENSG00000175485	Q6IF63	1	1	bone marrow
OR56A4	ENSG00000183389	Q8NGH8	0.9745	0.9626	granulocytes
OR5AN1	ENSG00000176495	Q8NGI8	0.9745	0.9626	bone marrow
OR5AU1	ENSG00000169327	Q8NGC0	0.7646	0.5563	bone marrow
OR5B21	ENSG00000198283	A6NL26	1	1	urinary bladder
OR5P2	ENSG00000183303	Q8WZ92	1	1	skin
OR5P3	ENSG00000182334	Q8WZ94	0.9756	0.9756	epididymis
OR5T2	ENSG00000181718	Q8NGG2	0.9872	0.9833	skin
OR6B3	ENSG00000178586	Q8NGW1	0.9978	0.996	epididymis
OR6C2	ENSG00000179695	Q9NZP2	1	1	epididymis
OR6C4	ENSG00000179626	Q8NGE1	0.7696	0.5384	granulocytes
OR6N1	ENSG00000197403	Q8NGY5	0.9935	0.9898	granulocytes
OR6N2	ENSG00000188340	Q8NGY6	0.9814	0.9789	bone marrow
OR6T1	ENSG00000181499	Q8NGN1	1	1	pancreas
OR6X1	ENSG00000221931	Q8NH79	1	1	epididymis
OR7A17	ENSG00000185385	O14581	0.7494	0.5889	granulocytes

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OR7A5	ENSG00000188269	Q15622	0.8984	0.7465	epididymis
OR7C1	ENSG00000127530	O76099	0.8511	0.5418	parathyroid gland
OR7D4	ENSG00000174667	Q8NG98	0.9112	0.6384	granulocytes
OR8A1	ENSG00000196119	Q8NGG7	0.7554	0.4787	parathyroid gland
OR8B8	ENSG00000197125	Q15620	0.7567	0.5074	skin
OR8D1	ENSG00000196341	Q8WZ84	0.9756	0.9756	epididymis
OR9A4	ENSG00000258083	Q8NGU2	0.9756	0.9756	bone marrow
OR9Q1	ENSG00000186509	Q8NGQ5	0.9756	0.9756	skeletal muscle
OTOF	ENSG00000115155	Q9HC10	0.9348	0.7627	bone marrow
OTOP1	ENSG00000163982	Q7RTM1	0.9872	0.9833	skin
OTOP2	ENSG00000183034	Q7RTS6	0.9586	0.9242	colon
OXGR1	ENSG00000165621	Q96P68	0.7366	0.5499	breast
OXTR	ENSG00000180914	P30559	0.9111	0.6361	breast
P2RX1	ENSG00000108405	P51575	0.6004	0.41	seminal vesicle
P2RX2	ENSG00000187848	Q9UBL9	0.8616	0.7141	epididymis
P2RX3	ENSG00000109991	P56373	0.9502	0.8705	heart muscle
P2RX5	ENSG00000083454	Q93086	0.7794	0.6037	lymph node
P2RX6	ENSG00000099957	O15547	0.8347	0.6838	cerebral cortex
P2RY10	ENSG00000078589	O00398	0.7558	0.5012	granulocytes
P2RY2	ENSG00000175591	P41231	0.6975	0.4126	granulocytes
P2RY4	ENSG00000186912	P51582	0.9553	0.8394	small intestine
P2RY6	ENSG00000171631	Q15077	0.778	0.4329	dendritic cells
PANX2	ENSG00000073150	Q96RD6	0.8492	0.5647	cerebral cortex
PANX3	ENSG00000154143	Q96QZ0	1	1	placenta
PAQR5	ENSG00000137819	Q9NXX6	0.729	0.4852	kidney
PAQR6	ENSG00000160781	Q6TCH4	0.8427	0.4182	cerebral cortex
PAQR9	ENSG00000188582	Q6ZVX9	0.9276	0.907	liver
PCDH10	ENSG00000138650	Q9P2E7	0.8557	0.7177	cerebral cortex
PCDH11X	ENSG00000102290	Q9BZA7	0.9198	0.8332	ovary
PCDH11Y	ENSG00000099715	Q9BZA8	0.9642	0.8435	cerebral cortex
PCDH12	ENSG00000113555	Q9NPG4	0.687	0.4012	placenta
PCDH15	ENSG00000150275	Q96QU1	0.9119	0.7677	adrenal gland
PCDH17	ENSG00000118946	O14917	0.7611	0.4945	spleen
PCDH19	ENSG00000165194	Q8TAB3	0.8636	0.6075	cerebral cortex
PCDH7	ENSG00000169851	O60245	0.5813	0.4438	cerebral cortex
PCDH8	ENSG00000136099	Q95206	0.9919	0.9751	cerebral cortex
PCDH9	ENSG00000184226	Q9HC56	0.8268	0.4676	cerebral cortex
PCDHA1	ENSG00000204970	Q9Y5I3	0.9804	0.9344	cerebral cortex
PCDHA10	ENSG00000250120	Q9Y5I2	0.8342	0.6027	cerebral cortex
PCDHA11	ENSG00000249158	Q9Y5I1	0.9056	0.7359	cerebral cortex
PCDHA12	ENSG00000251664	Q9UN75	0.8544	0.747	lung
PCDHA13	ENSG00000239389	Q9Y5I0	0.9476	0.7811	parathyroid gland
PCDHA2	ENSG00000204969	Q9Y5H9	0.901	0.7794	cerebral cortex
PCDHA3	ENSG00000255408	Q9Y5H8	0.767	0.577	endometrium
PCDHA4	ENSG00000204967	Q9UN74	0.8016	0.4153	cerebral cortex
PCDHA5	ENSG00000204965	Q9Y5H7	0.9742	0.8747	cerebral cortex
PCDHA6	ENSG00000081842	Q9UN73	0.893	0.6789	cerebral cortex
PCDHA7	ENSG00000204963	Q9UN72	0.9297	0.6986	cerebral cortex
PCDHA8	ENSG00000204962	Q9Y5H6	0.9872	0.9775	cerebral cortex
PCDHA9	ENSG00000204961	Q9Y5H5	0.9308	0.7294	cerebral cortex
PCDHAC1	ENSG00000248383	Q9H158	0.9366	0.73	parathyroid gland
PCDHAC2	ENSG00000243232	Q9Y5I4	0.8931	0.6482	parathyroid gland

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PCDHB1	ENSG00000171815	Q9Y5F3	0.7003	0.4239	fallopian tube
PCDHB10	ENSG00000120324	Q9UN67	0.7177	0.4821	cerebral cortex
PCDHB11	ENSG00000197479	Q9Y5F2	0.7826	0.403	parathyroid gland
PCDHB12	ENSG00000120328	Q9Y5F1	0.6989	0.4872	endometrium
PCDHB14	ENSG00000120327	Q9Y5E9	0.6367	0.4303	parathyroid gland
PCDHB15	ENSG00000113248	Q9Y5E8	0.6583	0.4206	cerebral cortex
PCDHB2	ENSG00000112852	Q9Y5E7	0.7427	0.4815	cerebral cortex
PCDHB3	ENSG00000113205	Q9Y5E6	0.6095	0.4663	endometrium
PCDHB4	ENSG00000081818	Q9Y5E5	0.6242	0.4281	endometrium
PCDHB7	ENSG00000113212	Q9Y5E2	0.7388	0.5031	endometrium
PCDHB8	ENSG00000120322	Q9UN66	0.7449	0.5383	endometrium
PCDHGA1	ENSG00000204956	Q9Y5H4	0.8128	0.4355	cerebral cortex
PCDHGA10	ENSG00000253846	Q9Y5H3	0.7948	0.4234	cerebral cortex
PCDHGA11	ENSG00000253873	Q9Y5H2	0.7177	0.4483	cerebral cortex
PCDHGA12	ENSG00000253159	O60330	0.6848	0.4452	cerebral cortex
PCDHGA3	ENSG00000254245	Q9Y5H0	0.7762	0.5422	cerebral cortex
PCDHGA4	ENSG00000262576	Q9Y5G9	0.7258	0.4894	cerebral cortex
PCDHGA5	ENSG00000253485	Q9Y5G8	0.6832	0.4648	cerebral cortex
PCDHGA6	ENSG00000253731	Q9Y5G7	0.5792	0.4047	endometrium
PCDHGA7	ENSG00000253537	Q9Y5G6	0.8012	0.5292	cerebral cortex
PCDHGA8	ENSG00000253767	Q9Y5G5	0.7213	0.4271	granulocytes
PCDHGB2	ENSG00000253910	Q9Y5G2	0.6751	0.4516	cerebral cortex
PCDHGB4	ENSG00000253953	Q9UN71	0.6459	0.4344	placenta
PCDHGC5	ENSG00000240764	Q9Y5F6	0.9689	0.8024	cerebral cortex
PCSK4	ENSG00000115257	Q6UW60	0.7894	0.4729	fallopian tube
PDCD1	ENSG00000188389	Q15116	0.8737	0.7137	lymph node
PHEX	ENSG00000102174	P78562	0.7949	0.6459	dendritic cells
PIANP	ENSG00000139200	Q8IYJ0	0.85	0.6013	cerebral cortex
PIEZO2	ENSG00000154864	Q9H5I5	0.6755	0.4761	lung
PIGR	ENSG00000162896	P01833	0.6844	0.5599	duodenum
PIRT	ENSG00000233670	P0C851	0.8546	0.821	adrenal gland
PKD1L1	ENSG00000158683	Q8TDX9	0.8081	0.5315	adipose tissue
PKD2L1	ENSG00000107593	Q9P0L9	0.8892	0.7104	spleen
PKDREJ	ENSG00000130943	Q9NTG1	0.8672	0.565	skin
PKHD1	ENSG00000170927	P08F94	0.9385	0.8592	kidney
PKHD1L1	ENSG00000205038	Q86WI1	0.8606	0.6404	thyroid gland
PLA2R1	ENSG00000153246	Q13018	0.6517	0.4002	thyroid gland
PLB1	ENSG00000163803	Q6P1J6	0.7647	0.4021	small intestine
PLD5	ENSG00000180287	Q8N7P1	0.7947	0.6287	seminal vesicle
PLN	ENSG00000198523	P26678	0.6573	0.4228	heart muscle
PLP1	ENSG00000123560	P60201	0.8036	0.4933	cerebral cortex
PLPP2	ENSG00000141934	O43688	0.5639	0.4073	fallopian tube
PLPP4	ENSG00000203805	Q5VZY2	0.8344	0.6443	cerebral cortex
PLPP7	ENSG00000160539	Q8NBV4	0.7813	0.4492	skeletal muscle
PLPPR1	ENSG00000148123	Q8TBJ4	0.9424	0.8988	cerebral cortex
PLPPR3	ENSG00000129951	Q6T4P5	0.9264	0.882	cerebral cortex
PLPPR4	ENSG00000117600	Q7Z2D5	0.8553	0.532	cerebral cortex
PLPPR5	ENSG00000117598	Q32ZL2	0.9873	0.9602	cerebral cortex
PLSCR2	ENSG00000163746	Q9NRY7	0.7914	0.4692	epididymis
PLXNA4	ENSG00000221866	Q9HCM2	0.7313	0.4975	adipose tissue
PLXNB3	ENSG00000198753	Q9ULL4	0.733	0.4715	cerebral cortex
PMEL	ENSG00000185664	P40967	0.82	0.4213	skin

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PNPLA3	ENSG00000100344	Q9NST1	0.8733	0.6059	liver
POPDC2	ENSG00000121577	Q9HBU9	0.76	0.4634	heart muscle
POPDC3	ENSG00000132429	Q9HBV1	0.8935	0.7327	skeletal muscle
PPP1R3A	ENSG00000154415	Q16821	0.9667	0.956	skeletal muscle
PRIMA1	ENSG00000175785	Q86XR5	0.6391	0.478	smooth muscle
PRLHR	ENSG00000119973	P49683	0.927	0.9092	adrenal gland
PRLR	ENSG00000113494	P16471	0.7021	0.5318	placenta
PROKR1	ENSG00000169618	Q8TCW9	0.9658	0.9425	epididymis
PROKR2	ENSG00000101292	Q8NFI6	0.964	0.9251	cerebral cortex
PROM1	ENSG00000007062	Q43490	0.624	0.4688	cervix, uterine
PROM2	ENSG00000155066	Q8N271	0.6316	0.4945	skin
PRR7	ENSG00000131188	Q8TB68	0.7546	0.5063	cerebral cortex
PRRG3	ENSG00000130032	Q9BZD7	0.7336	0.4765	cerebral cortex
PRRT1	ENSG00000204314	Q99946	0.9829	0.9506	cerebral cortex
PRRT4	ENSG00000224940	C9JH25	0.8911	0.6251	bone marrow
PRSS8	ENSG00000052344	Q16651	0.5284	0.439	small intestine
PRTG	ENSG00000166450	Q2VWP7	0.8416	0.6137	thyroid gland
PSD2	ENSG00000146005	Q9BQI7	0.9699	0.8254	cerebral cortex
PTCHD1	ENSG00000165186	Q96NR3	0.8119	0.665	seminal vesicle
PTCHD4	ENSG00000244694	Q6ZW05	0.7537	0.556	seminal vesicle
PTCRA	ENSG00000171611	Q6ISU1	0.9503	0.8011	dendritic cells
PTGDR	ENSG00000168229	Q13258	0.8153	0.4775	nk-cells
PTGDR2	ENSG00000183134	Q9Y5Y4	0.8665	0.6091	granulocytes
PTGER1	ENSG00000160951	P34995	0.9001	0.7788	kidney
PTGER3	ENSG00000050628	P43115	0.6911	0.4703	endometrium
PTGFR	ENSG00000122420	P43088	0.68	0.4826	endometrium
PTH1R	ENSG00000160801	Q03431	0.7502	0.4656	kidney
PTH2R	ENSG00000144407	P49190	0.8088	0.7026	bone marrow
PTPRCAP	ENSG00000213402	Q14761	0.7318	0.4997	t-cells
PTPRD	ENSG00000153707	P23468	0.7603	0.5186	parathyroid gland
PTPRH	ENSG00000080031	Q9HD43	0.7928	0.6938	small intestine
PTPRN	ENSG00000054356	Q16849	0.9033	0.7277	cerebral cortex
PTPRO	ENSG00000151490	Q16827	0.6578	0.4226	rectum
PTPRR	ENSG00000153233	Q15256	0.8522	0.7643	cerebral cortex
PTPRT	ENSG00000196090	Q14522	0.8989	0.7632	cerebral cortex
PTPRZ1	ENSG00000106278	P23471	0.888	0.629	cerebral cortex
PVRIG	ENSG00000213413	Q6DKI7	0.8516	0.6584	nk-cells
QRFRP	ENSG00000186867	Q96P65	0.8795	0.8335	heart muscle
RAET1E	ENSG00000164520	Q8TD07	0.8824	0.6399	esophagus
RAET1G	ENSG00000203722	Q6H3X3	0.8283	0.5924	esophagus
RARRES1	ENSG00000118849	P49788	0.543	0.4023	appendix
RDH8	ENSG00000080511	Q9NYR8	0.9971	0.9947	kidney
REEP1	ENSG00000068615	Q9H902	0.6543	0.4109	cerebral cortex
REEP2	ENSG00000132563	Q9BRK0	0.7712	0.4602	cerebral cortex
RET	ENSG00000165731	P07949	0.8487	0.451	parathyroid gland
RGR	ENSG00000148604	P47804	0.9543	0.6467	cerebral cortex
RGS9BP	ENSG00000186326	Q6ZS82	0.9538	0.8087	skeletal muscle
RGL1	ENSG00000121446	A5PLK6	0.9816	0.9336	epididymis
RHAG	ENSG00000112077	Q02094	0.9792	0.9235	bone marrow
RHBDL1	ENSG00000103269	Q75783	0.7795	0.4256	cerebral cortex
RHBDL2	ENSG00000158315	Q9NX52	0.6567	0.4468	skin
RHBDL3	ENSG00000141314	P58872	0.881	0.6614	cerebral cortex

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RHCG	ENSG00000140519	Q9UBD6	0.928	0.8177	esophagus
RHD	ENSG00000187010	Q02161	0.8331	0.4732	bone marrow
RHO	ENSG00000163914	P08100	1	1	cerebral cortex
RNF112	ENSG00000128482	Q9ULX5	0.7934	0.5037	cerebral cortex
RNF148	ENSG00000235631	Q8N7C7	0.8243	0.6246	lung
RNF175	ENSG00000145428	Q8N4F7	0.7948	0.5438	cerebral cortex
RNF182	ENSG00000180537	Q8N6D2	0.8605	0.6404	cerebral cortex
RNF222	ENSG00000189051	A6NCQ9	0.952	0.8976	esophagus
RNF223	ENSG00000237330	E7ERA6	0.8817	0.6938	esophagus
RNF225	ENSG00000269855	M0QZC1	0.946	0.9147	esophagus
ROBO2	ENSG00000185008	Q9HCK4	0.7569	0.5148	cerebral cortex
ROBO3	ENSG00000154134	Q96MS0	0.8747	0.7313	smooth muscle
ROR2	ENSG00000169071	Q01974	0.6343	0.4484	parathyroid gland
ROS1	ENSG00000047936	P08922	0.9529	0.9008	epididymis
RPRM	ENSG00000177519	Q9NS64	0.7764	0.687	endometrium
RPRML	ENSG00000179673	Q8N4K4	0.9866	0.9637	cerebral cortex
RRH	ENSG00000180245	O14718	0.7327	0.566	breast
RTL1	ENSG00000254656	A6NKG5	0.9774	0.9698	placenta
RTP1	ENSG00000175077	P59025	0.9867	0.972	cerebral cortex
RTP2	ENSG00000198471	Q5QGT7	1	1	skeletal muscle
RTP3	ENSG00000163825	Q9BQQ7	0.9941	0.9836	liver
RTP5	ENSG00000188011	Q14D33	0.9897	0.9732	cerebral cortex
RXFP1	ENSG00000171509	Q9HBX9	0.8424	0.669	cerebral cortex
RXFP2	ENSG00000133105	Q8WXD0	0.9493	0.9222	monocytes
RXFP3	ENSG00000182631	Q9NSD7	1	1	adrenal gland
RXFP4	ENSG00000173080	Q8TDU9	0.9129	0.8636	rectum
RYR2	ENSG00000198626	Q92736	0.8859	0.6388	heart muscle
RYR3	ENSG00000198838	Q15413	0.8296	0.567	parathyroid gland
S1PR4	ENSG00000125910	O95977	0.7406	0.5629	granulocytes
S1PR5	ENSG00000180739	Q9H228	0.8568	0.5896	t-cells
SCN11A	ENSG00000168356	Q9UI33	0.8821	0.6541	spleen
SCN1A	ENSG00000144285	P35498	0.974	0.9633	cerebral cortex
SCN2A	ENSG00000136531	Q99250	0.9473	0.7604	cerebral cortex
SCN2B	ENSG00000149575	O60939	0.8563	0.5637	cerebral cortex
SCN3A	ENSG00000153253	Q9NY46	0.8293	0.4866	cerebral cortex
SCN3B	ENSG00000166257	Q9NY72	0.8692	0.4782	cerebral cortex
SCN4A	ENSG00000007314	P35499	0.9349	0.793	skeletal muscle
SCN4B	ENSG00000177098	Q8IWT1	0.6202	0.4058	adipose tissue
SCN5A	ENSG00000183873	Q14524	0.9437	0.7035	heart muscle
SCN7A	ENSG00000136546	Q01118	0.6636	0.4402	ovary
SCN8A	ENSG00000196876	Q9UQD0	0.9037	0.5596	cerebral cortex
SCN9A	ENSG00000169432	Q15858	0.7881	0.4445	dendritic cells
SCNN1A	ENSG00000111319	P37088	0.5277	0.4318	cervix, uterine
SCNN1B	ENSG00000168447	P51168	0.707	0.5506	cervix, uterine
SCNN1G	ENSG00000166828	P51170	0.8182	0.6521	kidney
SCTR	ENSG00000080293	P47872	0.878	0.7221	duodenum
SDK2	ENSG00000069188	Q58EX2	0.7795	0.5188	cervix, uterine
SEL1L2	ENSG00000101251	Q5TEA6	0.9617	0.9404	endometrium
SELE	ENSG00000007908	P16581	0.6892	0.5071	prostate
SEMA5B	ENSG00000082684	Q9P283	0.7593	0.4843	cerebral cortex
SEMA6B	ENSG00000167680	Q9H3T3	0.7045	0.4161	cerebral cortex
SERP2	ENSG00000151778	Q8N6R1	0.7751	0.4271	cerebral cortex

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SERTM1	ENSG00000180440	A2A2V5	0.8446	0.7758	cerebral cortex
SEZ6	ENSG00000063015	Q53EL9	0.958	0.7217	cerebral cortex
SEZ6L2	ENSG00000174938	Q6UXD5	0.6797	0.4507	cerebral cortex
SFT2D3	ENSG00000173349	Q587I9	0.6691	0.5922	parathyroid gland
SGCA	ENSG00000108823	Q16586	0.7014	0.4472	skeletal muscle
SGCD	ENSG00000170624	Q92629	0.5904	0.4037	thyroid gland
SGCG	ENSG00000102683	Q13326	0.8438	0.6823	heart muscle
SGCZ	ENSG00000185053	Q96LD1	0.9608	0.9027	ovary
SHISA6	ENSG00000188803	Q6ZSJ9	0.8349	0.6684	cervix, uterine
SHISA7	ENSG00000187902	A6NL88	0.9922	0.9823	cerebral cortex
SHISA8	ENSG00000234965	B8ZZ34	0.9321	0.853	adrenal gland
SHISAL1	ENSG00000138944	Q3SXP7	0.7804	0.6151	smooth muscle
SHISAL2A	ENSG00000182183	Q6UWV7	0.7595	0.6059	b-cells
SHISAL2B	ENSG00000145642	A6NkW6	0.981	0.9632	stomach
SI	ENSG00000090402	P14410	0.9324	0.8998	duodenum
SIGLEC11	ENSG00000161640	Q96RL6	0.8723	0.5709	ovary
SIGLEC12	ENSG00000254521	Q96PQ1	0.8527	0.6937	spleen
SIGLEC14	ENSG00000254415	Q08ET2	0.7217	0.4751	granulocytes
SIGLEC15	ENSG00000197046	Q6ZMC9	0.9505	0.891	monocytes
SIGLEC5	ENSG00000105501	Q15389	0.8471	0.6196	granulocytes
SIGLEC6	ENSG00000105492	Q43699	0.8527	0.5153	placenta
SIGLEC7	ENSG00000168995	Q9Y286	0.7482	0.4953	granulocytes
SIGLEC8	ENSG00000105366	Q9NYZ4	0.8619	0.4837	granulocytes
SIGLEC9	ENSG00000129450	Q9Y336	0.702	0.4291	monocytes
SIGLECL1	ENSG00000179213	Q8N7X8	0.9411	0.9048	cervix, uterine
SIRPB1	ENSG00000101307	Q00241	0.7715	0.4569	granulocytes
SIRPB2	ENSG00000196209	Q5JXA9	0.7054	0.4564	granulocytes
SIRPG	ENSG00000089012	Q9P1W8	0.816	0.5225	t-cells
SIT1	ENSG00000137078	Q9Y3P8	0.7848	0.533	t-cells
SLAMF1	ENSG00000117090	Q13291	0.7622	0.5084	t-cells
SLAMF9	ENSG00000162723	Q96A28	0.9497	0.8349	dendritic cells
SLC10A1	ENSG00000100652	Q14973	0.9905	0.9167	liver
SLC10A2	ENSG00000125255	Q12908	0.9535	0.9283	small intestine
SLC10A4	ENSG00000145248	Q96EP9	0.9021	0.7547	adrenal gland
SLC10A5	ENSG00000253598	Q5PT55	0.7628	0.5802	liver
SLC10A6	ENSG00000145283	Q3KNW5	0.8449	0.6271	skin
SLC11A1	ENSG00000018280	P49279	0.7876	0.5626	lung
SLC12A1	ENSG00000074803	Q13621	0.9907	0.9446	kidney
SLC12A3	ENSG00000070915	P55017	0.9631	0.8474	kidney
SLC12A5	ENSG00000124140	Q9H2X9	0.8701	0.4743	cerebral cortex
SLC12A8	ENSG00000221955	A0AV02	0.721	0.4524	thyroid gland
SLC13A1	ENSG00000081800	Q9BZW2	0.9694	0.956	kidney
SLC13A2	ENSG00000007216	Q13183	0.8838	0.8296	duodenum
SLC13A3	ENSG00000158296	Q8WWT9	0.8376	0.4803	kidney
SLC13A4	ENSG00000164707	Q9UKG4	0.9799	0.9409	placenta
SLC13A5	ENSG00000141485	Q86YT5	0.9527	0.8733	liver
SLC14A1	ENSG00000141469	Q13336	0.7642	0.4272	prostate
SLC14A2	ENSG00000132874	Q15849	0.8762	0.6362	kidney
SLC15A1	ENSG00000088386	P46059	0.8252	0.6239	small intestine
SLC15A5	ENSG00000188991	A6NIM6	0.9629	0.9604	adipose tissue
SLC16A11	ENSG00000174326	Q8NCK7	0.775	0.5095	parathyroid gland
SLC16A12	ENSG00000152779	Q6ZSM3	0.8255	0.6336	kidney

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SLC16A8	ENSG00000100156	Q95907	0.7056	0.558	prostate
SLC16A9	ENSG00000165449	Q7RTY1	0.6897	0.494	kidney
SLC17A1	ENSG00000124568	Q14916	0.9798	0.9596	kidney
SLC17A2	ENSG00000112337	O00624	0.9978	0.996	liver
SLC17A3	ENSG00000124564	O00476	0.9792	0.9549	kidney
SLC17A4	ENSG00000146039	Q9Y2C5	0.8613	0.8429	small intestine
SLC17A6	ENSG00000091664	Q9P2U8	1	1	cerebral cortex
SLC17A7	ENSG00000104888	Q9P2U7	0.9353	0.6051	cerebral cortex
SLC17A8	ENSG00000179520	Q8NDX2	0.9553	0.8749	small intestine
SLC17A9	ENSG00000101194	Q9BYT1	0.591	0.4005	stomach
SLC18A1	ENSG00000036565	P54219	0.9507	0.8657	adrenal gland
SLC18A3	ENSG00000187714	Q16572	0.9587	0.9372	placenta
SLC19A3	ENSG00000135917	Q9BZV2	0.7471	0.4282	adipose tissue
SLC1A1	ENSG00000106688	P43005	0.6164	0.4487	small intestine
SLC1A2	ENSG00000110436	P43004	0.9075	0.5781	cerebral cortex
SLC1A6	ENSG00000105143	P48664	0.8808	0.5326	cerebral cortex
SLC1A7	ENSG00000162383	O00341	0.8381	0.6539	gallbladder
SLC22A1	ENSG00000175003	O15245	0.9661	0.6918	liver
SLC22A10	ENSG00000184999	Q63ZE4	0.997	0.9925	liver
SLC22A11	ENSG00000168065	Q9NSA0	0.9595	0.9449	placenta
SLC22A12	ENSG00000197891	Q96S37	0.9964	0.9904	kidney
SLC22A13	ENSG00000172940	Q9Y226	0.9965	0.9922	kidney
SLC22A14	ENSG00000144671	Q9Y267	0.9226	0.7935	kidney
SLC22A16	ENSG00000004809	Q86VW1	0.8944	0.8282	parathyroid gland
SLC22A2	ENSG00000112499	O15244	0.9806	0.897	kidney
SLC22A24	ENSG00000197658	Q8N4F4	1	1	kidney
SLC22A25	ENSG00000196600	Q6T423	1	1	liver
SLC22A3	ENSG00000146477	O75751	0.5788	0.4105	seminal vesicle
SLC22A6	ENSG00000197901	Q4U2R8	0.9926	0.9867	kidney
SLC22A7	ENSG00000137204	Q9Y694	0.9738	0.9529	liver
SLC22A8	ENSG00000149452	Q8TCC7	0.9964	0.991	kidney
SLC22A9	ENSG00000149742	Q8IVM8	0.969	0.7552	liver
SLC23A3	ENSG00000213901	Q6PIS1	0.8547	0.5553	kidney
SLC24A2	ENSG00000155886	Q9UI40	0.9694	0.8602	cerebral cortex
SLC24A4	ENSG00000140090	Q8NFF2	0.8397	0.5774	monocytes
SLC26A1	ENSG00000145217	Q9H2B4	0.6166	0.4052	adrenal gland
SLC26A10	ENSG00000135502	Q8NG04	0.7903	0.598	endometrium
SLC26A3	ENSG00000091138	P40879	0.8347	0.7579	colon
SLC26A4	ENSG00000091137	O43511	0.9293	0.6932	thyroid gland
SLC26A5	ENSG00000170615	P58743	0.7588	0.637	breast
SLC26A8	ENSG00000112053	Q96RN1	0.944	0.8715	bone marrow
SLC26A9	ENSG00000174502	Q7LBE3	0.9203	0.8883	salivary gland
SLC27A2	ENSG00000140284	O14975	0.6902	0.4576	kidney
SLC27A6	ENSG00000113396	Q9Y2P4	0.7566	0.5881	fallopian tube
SLC28A1	ENSG00000156222	O00337	0.8985	0.8388	small intestine
SLC28A2	ENSG00000137860	O43868	0.8688	0.7571	small intestine
SLC28A3	ENSG00000197506	Q9HAS3	0.7837	0.6299	gallbladder
SLC2A12	ENSG00000146411	Q8TD20	0.699	0.4579	prostate
SLC2A14	ENSG00000173262	Q8TDB8	0.7432	0.4994	bone marrow
SLC2A2	ENSG00000163581	P11168	0.9418	0.9175	liver
SLC2A4	ENSG00000181856	P14672	0.7253	0.4887	skeletal muscle
SLC30A10	ENSG00000196660	Q6XR72	0.9328	0.9103	liver

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SLC30A3	ENSG00000115194	Q99726	0.9512	0.9046	epididymis
SLC30A8	ENSG00000164756	Q8IWU4	0.8977	0.7099	pancreas
SLC34A1	ENSG00000131183	Q06495	0.9914	0.9633	kidney
SLC34A2	ENSG00000157765	Q95436	0.8382	0.6518	lung
SLC34A3	ENSG00000198569	Q8N130	0.9429	0.8274	kidney
SLC35D3	ENSG00000182747	Q5M8T2	0.9532	0.9034	adrenal gland
SLC35F1	ENSG00000196376	Q5T1Q4	0.8889	0.5963	cerebral cortex
SLC35F3	ENSG00000183780	Q8IY50	0.8666	0.6339	cerebral cortex
SLC35F4	ENSG00000151812	A4IF30	0.9534	0.9027	seminal vesicle
SLC35G1	ENSG00000176273	Q2M3R5	0.8073	0.4033	duodenum
SLC35G5	ENSG00000177710	Q96KT7	0.8088	0.6445	dendritic cells
SLC36A2	ENSG00000186335	Q495M3	0.9483	0.8046	kidney
SLC38A11	ENSG00000169507	Q08AI6	0.7182	0.4802	epididymis
SLC38A4	ENSG00000139209	Q969I6	0.8838	0.5506	liver
SLC38A8	ENSG00000166558	A6NNN8	0.9681	0.9534	cerebral cortex
SLC39A12	ENSG00000148482	Q504Y0	0.9914	0.9706	cerebral cortex
SLC39A2	ENSG00000165794	Q9NP94	0.8727	0.7699	seminal vesicle
SLC39A4	ENSG00000147804	Q6P5W5	0.8882	0.7091	duodenum
SLC39A5	ENSG00000139540	Q6ZMH5	0.8324	0.7644	small intestine
SLC3A1	ENSG00000138079	Q07837	0.8372	0.6064	kidney
SLC44A4	ENSG00000204385	Q53GD3	0.7177	0.6109	duodenum
SLC44A5	ENSG00000137968	Q8NCS7	0.7016	0.4532	skin
SLC45A3	ENSG00000158715	Q96JT2	0.8204	0.4595	prostate
SLC46A2	ENSG00000119457	Q9BY10	0.8515	0.7783	cervix, uterine
SLC47A1	ENSG00000142494	Q96FL8	0.6863	0.4253	adrenal gland
SLC47A2	ENSG00000180638	Q86VL8	0.9503	0.892	kidney
SLC4A1	ENSG00000004939	P02730	0.8985	0.5254	bone marrow
SLC4A10	ENSG00000144290	Q6U841	0.915	0.7725	t-cells
SLC4A11	ENSG00000088836	Q8NBS3	0.7342	0.5459	thyroid gland
SLC4A3	ENSG00000114923	P48751	0.771	0.4927	heart muscle
SLC4A4	ENSG00000080493	Q9Y6R1	0.6589	0.5026	kidney
SLC4A8	ENSG00000050438	Q2Y0W8	0.7924	0.4355	cerebral cortex
SLC4A9	ENSG00000113073	Q96Q91	0.992	0.9786	kidney
SLC51A	ENSG00000163959	Q86UW1	0.8253	0.5723	small intestine
SLC51B	ENSG00000186198	Q86UW2	0.7683	0.5757	small intestine
SLC52A1	ENSG00000132517	Q9NWF4	0.8553	0.6142	duodenum
SLC52A3	ENSG00000101276	Q9NQ40	0.6844	0.4693	small intestine
SLC5A1	ENSG00000100170	P13866	0.8145	0.6105	duodenum
SLC5A10	ENSG00000154025	A0PJK1	0.9509	0.8327	kidney
SLC5A11	ENSG00000158865	Q8WWX8	0.9184	0.8684	small intestine
SLC5A12	ENSG00000148942	Q1EHB4	0.9238	0.7677	kidney
SLC5A2	ENSG00000140675	P31639	0.9861	0.9364	kidney
SLC5A4	ENSG00000100191	Q9NY91	0.8808	0.6648	small intestine
SLC5A5	ENSG00000105641	Q92911	0.9136	0.7865	stomach
SLC5A7	ENSG00000115665	Q9GZV3	0.7973	0.6496	thyroid gland
SLC5A8	ENSG00000256870	Q8N695	0.936	0.908	cervix, uterine
SLC5A9	ENSG00000117834	Q2M3M2	0.8998	0.7956	small intestine
SLC6A1	ENSG00000157103	P30531	0.8446	0.5297	cerebral cortex
SLC6A11	ENSG00000132164	P48066	0.9295	0.8563	cerebral cortex
SLC6A12	ENSG00000111181	P48065	0.7957	0.577	liver
SLC6A13	ENSG00000010379	Q9NSD5	0.9324	0.8286	kidney
SLC6A15	ENSG00000072041	Q9H2J7	0.9083	0.7324	cerebral cortex

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SLC6A17	ENSG00000197106	Q9H1V8	0.9417	0.8011	cerebral cortex
SLC6A18	ENSG00000164363	Q96N87	1	1	kidney
SLC6A19	ENSG00000174358	Q695T7	0.9183	0.8875	small intestine
SLC6A2	ENSG00000103546	P23975	0.8853	0.769	adrenal gland
SLC6A20	ENSG00000163817	Q9NP91	0.8472	0.6098	duodenum
SLC6A3	ENSG00000142319	Q01959	0.9734	0.9491	thyroid gland
SLC6A4	ENSG00000108576	P31645	0.8909	0.7967	small intestine
SLC6A5	ENSG00000165970	Q9Y345	0.9973	0.9952	lung
SLC6A7	ENSG00000011083	Q99884	0.9483	0.9017	cerebral cortex
SLC7A10	ENSG00000130876	Q9NS82	0.9694	0.9141	adipose tissue
SLC7A11	ENSG00000151012	Q9UPY5	0.8173	0.5644	cerebral cortex
SLC7A13	ENSG00000164893	Q8TCU3	0.997	0.9881	kidney
SLC7A3	ENSG00000165349	Q8WY07	0.8603	0.7607	prostate
SLC7A4	ENSG00000099960	O43246	0.705	0.529	esophagus
SLC7A9	ENSG00000021488	P82251	0.9203	0.8334	small intestine
SLC8A2	ENSG00000118160	Q9UPR5	0.9233	0.7824	cerebral cortex
SLC8A3	ENSG00000100678	P57103	0.9136	0.666	cerebral cortex
SLC9A2	ENSG00000115616	Q9UBY0	0.7636	0.6095	stomach
SLC9A4	ENSG00000180251	Q6AI14	0.9138	0.6322	stomach
SLC9A5	ENSG00000135740	Q14940	0.8546	0.5252	spleen
SLC9C1	ENSG00000172139	Q4G0N8	0.9843	0.9563	skin
SLC9C2	ENSG00000162753	Q5TAH2	0.9657	0.9192	fallopian tube
SLCO1A2	ENSG00000084453	P46721	0.8637	0.5882	cerebral cortex
SLCO1B1	ENSG00000134538	Q9Y6L6	0.993	0.9794	liver
SLCO1B3	ENSG00000111700	Q9NPD5	0.9723	0.9195	liver
SLCO1C1	ENSG00000139155	Q9NYB5	0.9569	0.7548	cerebral cortex
SLCO4C1	ENSG00000173930	Q6ZQN7	0.826	0.5574	kidney
SLCO5A1	ENSG00000137571	Q9H2Y9	0.8387	0.6516	prostate
SLCO6A1	ENSG00000205359	Q86UG4	1	1	placenta
SLITRK1	ENSG00000178235	Q96PX8	0.9945	0.9774	cerebral cortex
SLITRK2	ENSG00000185985	Q9H156	0.9077	0.7097	cerebral cortex
SLITRK3	ENSG00000121871	Q94933	0.8165	0.6982	cerebral cortex
SLITRK4	ENSG00000179542	Q8IW52	0.7253	0.5213	adrenal gland
SLITRK5	ENSG00000165300	Q94991	0.8948	0.7924	cerebral cortex
SLITRK6	ENSG00000184564	Q9H5Y7	0.7513	0.5855	urinary bladder
SMCO2	ENSG00000165935	A6NFE2	0.8786	0.8161	skin
SMCO3	ENSG00000179256	A2RU48	0.8201	0.6598	cervix, uterine
SMIM18	ENSG00000253457	P0DKX4	0.9462	0.8582	cerebral cortex
SMIM2	ENSG00000139656	Q9BVW6	0.783	0.526	epididymis
SMIM22	ENSG00000267795	K7EJ46	0.5943	0.4667	colon
SMIM23	ENSG00000185662	A6NLE4	1	1	spleen
SMIM24	ENSG00000095932	O75264	0.7921	0.6177	epididymis
SMIM28	ENSG00000262543	A0A1B0GU29	0.9147	0.8985	appendix
SMIM5	ENSG00000204323	Q71RC9	0.7747	0.4264	dendritic cells
SMIM6	ENSG00000259120	P0DI80	0.7505	0.5941	fallopian tube
SMLR1	ENSG00000256162	H3BR10	0.9504	0.9357	liver
SNORC	ENSG00000182600	Q6UX34	0.8447	0.5738	breast
SOGA3	ENSG00000214338	Q5TF21	0.8808	0.6291	cerebral cortex
SORCS1	ENSG00000108018	Q8WY21	0.767	0.4845	thyroid gland
SORCS2	ENSG00000184985	Q96PQ0	0.6845	0.4427	cerebral cortex
SORCS3	ENSG00000156395	Q9UPU3	0.9562	0.8303	cerebral cortex

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SPACA3	ENSG00000141316	Q8IXA5	0.9161	0.5714	pancreas
SPATA9	ENSG00000145757	Q9BWV2	0.8682	0.6293	adipose tissue
SPNS3	ENSG00000182557	Q6ZMD2	0.9197	0.7735	granulocytes
SSMEM1	ENSG00000165120	Q8WWF3	0.9756	0.9756	lung
SSTR1	ENSG00000139874	P30872	0.7857	0.5928	stomach
SSTR4	ENSG00000132671	P31391	0.9921	0.9821	cerebral cortex
SSTR5	ENSG00000162009	P35346	0.9403	0.8624	adrenal gland
STAB2	ENSG00000136011	Q8WWQ8	0.8967	0.6423	spleen
STEAP1B	ENSG00000105889	Q6NZ63	0.7731	0.5256	b-cells
STOML3	ENSG00000133115	Q8TAV4	0.9811	0.9529	fallopian tube
STRA6	ENSG00000137868	Q9BX79	0.8446	0.7104	cervix, uterine
STUM	ENSG00000203685	Q69YW2	0.7731	0.4636	cerebral cortex
STX1A	ENSG00000106089	Q16623	0.7997	0.407	cerebral cortex
STX1B	ENSG00000099365	P61266	0.8793	0.4947	cerebral cortex
STYK1	ENSG00000060140	Q6J9G0	0.6552	0.4952	rectum
SUCNR1	ENSG00000198829	Q9BXA5	0.8119	0.5613	kidney
SUN3	ENSG00000164744	Q8TAQ9	0.9045	0.7731	placenta
SUSD2	ENSG00000099994	Q9UGT4	0.7536	0.4576	lung
SUSD4	ENSG00000143502	Q5VX71	0.6452	0.46	esophagus
SUSD5	ENSG00000173705	Q60279	0.6387	0.4572	cerebral cortex
SV2A	ENSG00000159164	Q7LQJ3	0.7621	0.4298	cerebral cortex
SV2B	ENSG00000185518	Q7L1I2	0.9342	0.5981	cerebral cortex
SV2C	ENSG00000122012	Q496J9	0.9086	0.7211	cerebral cortex
SVOP	ENSG00000166111	Q8N4V2	0.9738	0.8783	cerebral cortex
SVOPL	ENSG00000157703	Q8N434	0.8985	0.6747	parathyroid gland
SYNDIG1	ENSG00000101463	Q9H7V2	0.7711	0.5726	cerebral cortex
SYNDIG1L	ENSG00000183379	A6NDD5	0.9543	0.7651	epididymis
SYNGR3	ENSG00000127561	Q43761	0.8556	0.5475	cerebral cortex
SYNGR4	ENSG00000105467	Q95473	0.9564	0.8782	parathyroid gland
SYNPR	ENSG00000163630	Q8TBG9	0.9824	0.9232	cerebral cortex
SYN	ENSG00000102003	P08247	0.8395	0.4297	cerebral cortex
SYPL2	ENSG00000143028	Q5VXT5	0.8005	0.5181	skeletal muscle
SYT1	ENSG00000067715	P21579	0.8511	0.5748	cerebral cortex
SYT12	ENSG00000173227	Q8IV01	0.905	0.7293	parathyroid gland
SYT13	ENSG0000019505	Q7L8C5	0.8262	0.7027	cerebral cortex
SYT14	ENSG00000143469	Q8NB59	0.9598	0.8916	thyroid gland
SYT2	ENSG00000143858	Q8N9I0	0.8725	0.6758	cerebral cortex
SYT3	ENSG00000213023	Q9BQG1	0.9652	0.7863	cerebral cortex
SYT5	ENSG00000129990	Q00445	0.9264	0.6625	cerebral cortex
SYT6	ENSG00000134207	Q5T7P8	0.9314	0.8261	cerebral cortex
SYT7	ENSG00000011347	Q43581	0.7122	0.4306	cerebral cortex
SYT8	ENSG00000149043	Q8NBV8	0.8668	0.7587	skin
SYT9	ENSG00000170743	Q86SS6	0.856	0.7636	cerebral cortex
TAAR1	ENSG00000146399	Q96RJ0	0.9745	0.9279	stomach
TAAR6	ENSG00000146383	Q96RI8	1	1	kidney
TACR1	ENSG00000115353	P25103	0.7228	0.5325	cervix, uterine
TACR2	ENSG00000075073	P21452	0.7753	0.5562	smooth muscle
TACR3	ENSG00000169836	P29371	0.9573	0.9401	cerebral cortex
TACSTD2	ENSG00000184292	P09758	0.6326	0.4719	esophagus
TAS1R1	ENSG00000173662	Q7RTX1	0.7229	0.5737	gallbladder
TAS1R3	ENSG00000169962	Q7RTX0	0.8835	0.6039	epididymis
TAS2R1	ENSG00000169777	Q9NYW7	0.9734	0.9491	fallopian tube

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TAS2R10	ENSG00000121318	Q9NYW0	0.8991	0.8565	breast
TAS2R14	ENSG00000212127	Q9NYV8	0.8207	0.457	epididymis
TAS2R19	ENSG00000212124	P59542	0.9617	0.9404	ovary
TAS2R20	ENSG00000255837	P59543	0.8718	0.6638	skin
TAS2R3	ENSG00000127362	Q9NYW6	0.8488	0.7448	ovary
TAS2R30	ENSG00000256188	P59541	0.7738	0.6885	endometrium
TAS2R31	ENSG00000256436	P59538	0.862	0.7756	endometrium
TAS2R38	ENSG00000257138	P59533	0.9498	0.9445	rectum
TAS2R4	ENSG00000127364	Q9NYW5	0.7348	0.4364	skin
TAS2R5	ENSG00000127366	Q9NYW4	0.7351	0.4339	skin
TCP11	ENSG00000124678	Q8WWU5	0.869	0.6076	fallopian tube
TECRL	ENSG00000205678	Q5HYJ1	0.9462	0.7504	heart muscle
TEDDM1	ENSG00000203730	Q5T9Z0	0.9895	0.9292	epididymis
TENM1	ENSG00000009694	Q9UKZ4	0.7365	0.5526	prostate
TENM2	ENSG00000145934	Q9NT68	0.8751	0.6913	heart muscle
TENM3	ENSG00000218336	Q9P273	0.6999	0.4995	placenta
TENM4	ENSG00000149256	Q6N022	0.8458	0.617	parathyroid gland
TEX29	ENSG00000153495	Q8N6K0	0.9195	0.591	cerebral cortex
TEX38	ENSG00000186118	Q6PEX7	0.8944	0.6462	parathyroid gland
TEX51	ENSG00000237524	A0A1B0GU A7	1	1	kidney
TFR2	ENSG00000106327	Q9UP52	0.9662	0.9341	liver
TGFBR3L	ENSG00000260001	H3BV60	0.8695	0.7942	small intestine
THSD7A	ENSG00000005108	Q9UPZ6	0.6632	0.4927	kidney
THSD7B	ENSG00000144229	Q9C0I4	0.886	0.7052	epididymis
TIGIT	ENSG00000181847	Q495A1	0.7953	0.4813	t-cells
TIMD4	ENSG00000145850	Q96H15	0.8194	0.6305	lymph node
TLR10	ENSG00000174123	Q9BXR5	0.7734	0.5508	lymph node
TM4SF19	ENSG00000145107	Q96DZ7	0.8432	0.4504	t-cells
TM4SF20	ENSG00000168955	Q53R12	0.9418	0.8281	duodenum
TM4SF4	ENSG00000169903	P48230	0.8854	0.7801	gallbladder
TM4SF5	ENSG00000142484	Q14894	0.8803	0.8327	duodenum
TMC1	ENSG00000165091	Q8TDI8	0.9215	0.8429	cervix, uterine
TMC2	ENSG00000149488	Q8TDI7	0.937	0.8576	lung
TMC3	ENSG00000188869	Q7Z5M5	0.9456	0.6093	parathyroid gland
TMC5	ENSG00000103534	Q6UXY8	0.6831	0.5594	small intestine
TMC7	ENSG00000170537	Q7Z402	0.6989	0.4468	cerebral cortex
TMCO2	ENSG00000188800	Q7Z6W1	1	1	urinary bladder
TMCO5A	ENSG00000166069	Q8N6Q1	0.9646	0.9553	fallopian tube
TMEFF1	ENSG00000241697	Q8IYR6	0.9649	0.8661	cerebral cortex
TMEFF2	ENSG00000144339	Q9UIK5	0.8949	0.7835	prostate
TMEM100	ENSG00000166292	Q9NV29	0.6522	0.4322	lung
TMEM108	ENSG00000144868	Q6UXF1	0.6842	0.4661	cerebral cortex
TMEM114	ENSG00000232258	B3SHH9	0.9969	0.9933	seminal vesicle
TMEM121	ENSG00000184986	Q9BTD3	0.8174	0.4963	cerebral cortex
TMEM125	ENSG00000179178	Q96AQ2	0.6355	0.4566	lung
TMEM132B	ENSG00000139364	Q14DG7	0.9324	0.7198	cerebral cortex
TMEM132C	ENSG00000181234	Q8N3T6	0.7671	0.5363	adipose tissue
TMEM132D	ENSG00000151952	Q14C87	0.9839	0.9112	cerebral cortex
TMEM132E	ENSG00000181291	Q6IEE7	0.9061	0.7371	cerebral cortex
TMEM139	ENSG00000178826	Q8IV31	0.6635	0.4612	kidney
TMEM150B	ENSG00000180061	A6NC51	0.7577	0.5222	duodenum

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TMEM151A	ENSG00000179292	Q8N4L1	0.978	0.9391	cerebral cortex
TMEM151B	ENSG00000178233	Q8IW70	0.9642	0.8543	cerebral cortex
TMEM156	ENSG00000121895	Q8N614	0.7119	0.4753	b-cells
TMEM158	ENSG00000249992	Q8WZ71	0.7111	0.5516	endometrium
TMEM163	ENSG00000152128	Q8TC26	0.6972	0.5342	lung
TMEM169	ENSG00000163449	Q96HH4	0.7746	0.402	cerebral cortex
TMEM171	ENSG00000157111	Q8WVE6	0.7486	0.6289	thyroid gland
TMEM178B	ENSG00000261115	H3BS89	0.8316	0.6226	parathyroid gland
TMEM179	ENSG00000258986	Q6ZVK1	0.9425	0.8058	cerebral cortex
TMEM184A	ENSG00000164855	Q6ZMB5	0.6607	0.4951	skin
TMEM190	ENSG00000160472	Q8WZ59	0.9519	0.8179	fallopian tube
TMEM196	ENSG00000173452	Q5HYL7	0.9489	0.8654	cerebral cortex
TMEM200A	ENSG00000164484	Q86VY9	0.6372	0.4026	endometrium
TMEM200B	ENSG00000253304	Q69YZ2	0.6313	0.435	endometrium
TMEM200C	ENSG00000206432	A6NKL6	0.8334	0.6523	cerebral cortex
TMEM207	ENSG00000198398	Q6UWW9	1	1	kidney
TMEM210	ENSG00000185863	A6NLX4	0.8708	0.7003	dendritic cells
TMEM211	ENSG00000206069	Q6ICI0	0.9168	0.8483	cervix, uterine
TMEM213	ENSG00000214128	A2RRL7	0.8895	0.5834	kidney
TMEM215	ENSG00000188133	Q68D42	0.9679	0.9477	endometrium
TMEM217	ENSG00000172738	Q8N7C4	0.8097	0.6135	adrenal gland
TMEM229A	ENSG00000234224	B2RXF0	0.8993	0.8089	duodenum
TMEM232	ENSG00000186952	C9JQI7	0.8214	0.5365	fallopian tube
TMEM233	ENSG00000224982	B4DJY2	0.8755	0.6497	thyroid gland
TMEM235	ENSG00000204278	A6NFC5	0.9992	0.9984	cerebral cortex
TMEM236	ENSG00000148483	Q5W0B7	0.8488	0.5784	small intestine
TMEM239	ENSG00000198326	Q8WW34	0.9512	0.9512	endometrium
TMEM240	ENSG00000205090	Q5SV17	0.7488	0.4689	cerebral cortex
TMEM244	ENSG00000203756	Q5VVB8	0.9039	0.7619	cerebral cortex
TMEM252	ENSG00000181778	Q8N6L7	0.8339	0.632	kidney
TMEM253	ENSG00000232070	P0C7T8	0.8508	0.6319	duodenum
TMEM255A	ENSG00000125355	Q5JRV8	0.7117	0.42	ovary
TMEM26	ENSG00000196932	Q6ZUK4	0.7492	0.5397	spleen
TMEM262	ENSG00000187066	E9PQX1	0.9745	0.9626	cervix, uterine
TMEM266	ENSG00000169758	Q2M3C6	0.9063	0.8506	cerebral cortex
TMEM270	ENSG00000175877	Q6UE05	1	1	duodenum
TMEM31	ENSG00000179363	Q5JXX7	0.745	0.5571	ovary
TMEM40	ENSG00000088726	Q8WWA1	0.8467	0.6879	esophagus
TMEM45B	ENSG00000151715	Q96B21	0.6284	0.4348	small intestine
TMEM52	ENSG00000178821	Q8NDY8	0.8125	0.5194	skeletal muscle
TMEM52B	ENSG00000165685	Q4KMG9	0.9367	0.6494	kidney
TMEM61	ENSG00000143001	Q8N0U2	0.7421	0.5896	parathyroid gland
TMEM63C	ENSG00000165548	Q9P1W3	0.7858	0.5453	cerebral cortex
TMEM72	ENSG00000187783	A0PK05	0.9511	0.8824	kidney
TMEM74B	ENSG00000125895	Q9NUR3	0.6474	0.4362	small intestine
TMEM82	ENSG00000162460	A0PJX8	0.9196	0.8958	duodenum
TMEM88B	ENSG00000205116	A6NKF7	0.9928	0.9593	cerebral cortex
TMEM92	ENSG00000167105	Q6UXU6	0.8017	0.6433	small intestine
TMIE	ENSG00000181585	Q8NEW7	0.7843	0.455	adrenal gland
TMIGD1	ENSG00000182271	Q6UXZ0	0.9385	0.9193	small intestine
TMIGD2	ENSG00000167664	Q96BF3	0.8416	0.64	t-cells
TMIGD3	ENSG00000121933	P0DMS9	0.862	0.5243	granulocytes

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
TMPRSS11B	ENSG00000185873	Q86T26	0.9709	0.9227	esophagus
TMPRSS11D	ENSG00000153802	Q60235	0.9714	0.9602	esophagus
TMPRSS11E	ENSG00000087128	Q9UL52	0.9229	0.8539	esophagus
TMPRSS11F	ENSG00000198092	Q6ZWK6	0.9533	0.9353	esophagus
TMPRSS12	ENSG00000186452	Q86WS5	0.9713	0.9209	epididymis
TMPRSS13	ENSG00000137747	Q9BYE2	0.806	0.5436	skin
TMPRSS15	ENSG00000154646	P98073	0.9787	0.9274	duodenum
TMPRSS2	ENSG00000184012	Q15393	0.6939	0.5219	prostate
TMPRSS4	ENSG00000137648	Q9NRS4	0.7007	0.6161	urinary bladder
TMPRSS5	ENSG00000166682	Q9H3S3	0.8756	0.5459	cerebral cortex
TMPRSS6	ENSG00000187045	Q8IU80	0.9215	0.72	liver
TMPRSS7	ENSG00000176040	Q7RTY8	0.9234	0.8185	fallopian tube
TMPRSS9	ENSG00000178297	Q7Z410	0.903	0.6829	spleen
TNF	ENSG00000232810	P01375	0.8625	0.6544	monocytes
TNFRSF11A	ENSG00000141655	Q9Y6Q6	0.6834	0.4509	duodenum
TNFRSF13B	ENSG00000240505	Q14836	0.8115	0.6221	b-cells
TNFRSF13C	ENSG00000159958	Q96RJ3	0.7895	0.569	tonsil
TNFRSF17	ENSG00000048462	Q02223	0.7029	0.5256	dendritic cells
TNFRSF18	ENSG00000186891	Q9Y5U5	0.7812	0.5109	nk-cells
TNFRSF19	ENSG00000127863	Q9NS68	0.6707	0.4033	skin
TNFRSF4	ENSG00000186827	P43489	0.7814	0.5591	t-cells
TNFRSF8	ENSG00000120949	P28908	0.8899	0.6601	monocytes
TNFRSF9	ENSG00000049249	Q07011	0.7643	0.5105	t-cells
TNFSF11	ENSG00000120659	Q14788	0.8312	0.6901	lymph node
TNFSF14	ENSG00000125735	Q43557	0.7948	0.4852	granulocytes
TNFSF15	ENSG00000181634	Q95150	0.6607	0.4575	duodenum
TNFSF18	ENSG00000120337	Q9UNG2	0.8426	0.6081	gallbladder
TNFSF9	ENSG00000125657	P41273	0.7236	0.5092	cerebral cortex
TNMD	ENSG00000000005	Q9H2S6	0.9008	0.7151	seminal vesicle
TPBGL	ENSG00000261594	P0DKB5	0.8978	0.7203	cerebral cortex
TPO	ENSG00000115705	P07202	0.9389	0.7179	thyroid gland
TRABD2A	ENSG00000186854	Q86V40	0.7433	0.5337	t-cells
TRABD2B	ENSG00000269113	A6NFA1	0.7693	0.4913	kidney
TRAT1	ENSG00000163519	Q6PIZ9	0.8336	0.5594	granulocytes
TRDN	ENSG00000186439	Q13061	0.8852	0.744	skeletal muscle
TREM1	ENSG00000124731	Q9NP99	0.7737	0.5353	granulocytes
TREM2	ENSG00000095970	Q9NZC2	0.6811	0.4447	lung
TREML1	ENSG00000161911	Q86YW5	0.8783	0.6138	granulocytes
TREML2	ENSG00000112195	Q5T2D2	0.794	0.6796	granulocytes
TRHDE	ENSG00000072657	Q9UKU6	0.7191	0.5526	cerebral cortex
TRHR	ENSG00000174417	P34981	0.9872	0.9833	thyroid gland
TRPA1	ENSG00000104321	Q75762	0.834	0.6815	urinary bladder
TRPC3	ENSG00000138741	Q13507	0.8522	0.6691	smooth muscle
TRPC4	ENSG00000133107	Q9UBN4	0.8046	0.6247	endometrium
TRPC5	ENSG00000072315	Q9UL62	0.9918	0.9845	cerebral cortex
TRPC6	ENSG00000137672	Q9Y210	0.7054	0.4515	placenta
TRPC7	ENSG00000069018	Q9HCX4	0.9667	0.949	adrenal gland
TRPM1	ENSG00000134160	Q7Z4N2	0.9987	0.9975	skin

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
TRPM3	ENSG00000083067	Q9HCF6	0.8849	0.6614	kidney
TRPM5	ENSG00000070985	Q9NZQ8	0.8895	0.8472	duodenum
TRPM6	ENSG00000119121	Q9BX84	0.7984	0.5741	rectum
TRPM8	ENSG00000144481	Q7Z2W7	0.9746	0.9062	prostate
TRPV3	ENSG00000167723	Q8NET8	0.8549	0.6042	skin
TRPV4	ENSG00000111199	Q9HBA0	0.6971	0.5086	kidney
TSHR	ENSG00000165409	P16473	0.9193	0.478	thyroid gland
TSPAN11	ENSG00000110900	A1L157	0.5707	0.4003	cerebral cortex
TSPAN16	ENSG00000130167	Q9UKR8	0.9657	0.8961	granulocytes
TSPAN19	ENSG00000231738	P0C672	0.7643	0.4476	lung
TSPAN32	ENSG00000064201	Q96QS1	0.772	0.5576	nk-cells
TSPAN8	ENSG00000127324	P19075	0.6163	0.4484	rectum
TSPO2	ENSG00000112212	Q5TGU0	0.9632	0.8681	bone marrow
TTYH1	ENSG00000167614	Q9H313	0.9773	0.9012	cerebral cortex
TVP23A	ENSG00000166676	A6NH52	0.7612	0.4407	cerebral cortex
UGT2A3	ENSG00000135220	Q6UWM9	0.849	0.8059	small intestine
UGT3A1	ENSG00000145626	Q6NUS8	0.9396	0.9042	kidney
UGT3A2	ENSG00000168671	Q3SY77	0.9323	0.8459	skin
UGT8	ENSG00000174607	Q16880	0.7181	0.4897	cerebral cortex
UMODL1	ENSG00000177398	Q5DID0	0.9862	0.9525	fallopian tube
UNC5A	ENSG00000113763	Q6ZN44	0.9416	0.7625	cerebral cortex
UNC5C	ENSG00000182168	Q95185	0.6989	0.4543	thyroid gland
UNC5CL	ENSG00000124602	Q8IV45	0.7915	0.5306	duodenum
UNC5D	ENSG00000156687	Q6UXZ4	0.8519	0.7835	cerebral cortex
UNC79	ENSG00000133958	Q9P2D8	0.9738	0.9173	cerebral cortex
UNC80	ENSG00000144406	Q8N2C7	0.9325	0.8017	cerebral cortex
UNC93A	ENSG00000112494	Q86WB7	0.8877	0.81	skin
UPK1A	ENSG00000105668	O00322	0.926	0.7878	urinary bladder
UPK1B	ENSG00000114638	O75841	0.8245	0.7324	urinary bladder
UPK2	ENSG00000110375	O00526	0.974	0.8701	urinary bladder
UPK3B	ENSG00000243566	Q9BT76	0.9267	0.8361	lung
USH2A	ENSG00000042781	Q75445	0.9843	0.9665	liver
UTS2R	ENSG00000181408	Q9UKP6	0.9568	0.8471	thyroid gland
VIPR2	ENSG00000106018	P41587	0.6874	0.4614	seminal vesicle
VN1R1	ENSG00000178201	Q9GZP7	0.6791	0.4448	epididymis
VSIG1	ENSG00000101842	Q86XK7	0.9155	0.7056	stomach
VSIG10L	ENSG00000186806	Q86VR7	0.9317	0.8632	esophagus
VSIG2	ENSG00000019102	Q96IQ7	0.7055	0.4608	stomach
VSIG8	ENSG00000243284	P0DPA2	0.9382	0.8247	skin
VSTM1	ENSG00000189068	Q6UX27	0.9617	0.9334	granulocytes
VSTM2B	ENSG00000187135	A6NLU5	0.9854	0.96	cerebral cortex
VSTM5	ENSG00000214376	A8MXK1	0.8483	0.6388	placenta
VTCN1	ENSG00000134258	Q7Z7D3	0.8472	0.7231	breast
WSCD1	ENSG00000179314	Q658N2	0.7597	0.4749	cerebral cortex
WSCD2	ENSG00000075035	Q2TBF2	0.8152	0.656	thyroid gland
XCR1	ENSG00000173578	P46094	0.6896	0.4338	lymph node
XG	ENSG00000124343	P55808	0.8478	0.663	skin
XK	ENSG00000047597	P51811	0.6198	0.4369	rectum
XKR3	ENSG00000172967	Q5GH77	0.9933	0.9842	granulocytes
XKR4	ENSG00000206579	Q5GH76	0.9082	0.6061	cerebral cortex
XKR6	ENSG00000171044	Q5GH73	0.6236	0.4395	cerebral cortex
XKR7	ENSG00000260903	Q5GH72	0.9929	0.9845	cerebral cortex

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
XKR9	ENSG00000221947	Q5GH70	0.7604	0.4506	small intestine
XKRX	ENSG00000182489	Q6PP77	0.835	0.5806	skin
ZDHHC11B	ENSG00000206077	P0C7U3	0.6605	0.4713	cerebral cortex
ZDHHC15	ENSG00000102383	Q96MV8	0.6646	0.4601	cerebral cortex
ZP1	ENSG00000149506	P60852	0.9899	0.9687	dendritic cells
ZP2	ENSG00000103310	Q05996	0.9395	0.9097	placenta
ZP4	ENSG00000116996	Q12836	0.9745	0.9626	tonsil
ZPLD1	ENSG00000170044	Q8TCW7	0.958	0.8929	gallbladder

Table 2B contains address targets based on a Gtex database analysis:

Table 2B: Exemplary Address Targets (Gtex database analysis)

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Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
AADACL4	ENSG00000204518	Q5VUY2	0.8989	0.835	vagina
ABCA12	ENSG00000144452	Q86UK0	0.9572	0.9191	skin
ABCA13	ENSG00000179869	Q86UQ4	0.8778	0.7422	thyroid gland
ABCA4	ENSG00000198691	P78363	0.8822	0.6752	kidney
ABCB11	ENSG00000073734	O95342	0.9699	0.9393	liver
ABCB4	ENSG00000005471	P21439	0.8807	0.5882	liver
ABCB5	ENSG00000004846	Q2M3G0	0.8633	0.8033	cervix, uterine
ABCC11	ENSG00000121270	Q96J66	0.9143	0.8074	breast
ABCC12	ENSG00000140798	Q96J65	0.9753	0.9471	cerebral cortex
ABCC2	ENSG00000023839	Q92887	0.8753	0.5552	liver
ABCC3	ENSG00000108846	O15438	0.6722	0.4456	adrenal gland
ABCC6	ENSG00000091262	O95255	0.7202	0.4101	liver
ABCC8	ENSG00000006071	Q09428	0.7232	0.4722	cerebellum
ABCG4	ENSG00000172350	Q9H172	0.8477	0.6202	cerebellum
ABCG5	ENSG00000138075	Q9H222	0.9915	0.9853	liver
ABCG8	ENSG00000143921	Q9H221	0.9782	0.9514	liver
ACKR2	ENSG00000144648	O00590	0.7425	0.5222	adipose tissue
ACKR4	ENSG00000129048	Q9NPB9	0.6548	0.4434	adipose tissue
ACP4	ENSG00000142513	Q9BZG2	1	1	skin
ACVR1C	ENSG00000123612	Q8NER5	0.7767	0.5035	adipose tissue
ADAM11	ENSG00000073670	O75078	0.7977	0.5251	cerebellum
ADAM12	ENSG00000148848	O43184	0.735	0.4805	ovary
ADAM20	ENSG00000134007	O43506	0.8511	0.6232	cerebellum
ADAM21	ENSG00000139985	Q9UKJ8	0.7415	0.6204	adrenal gland
ADAM29	ENSG00000168594	Q9UKF5	0.9339	0.9072	cervix, uterine
ADCY1	ENSG00000164742	Q08828	0.6979	0.4014	cerebellum
ADCY2	ENSG00000078295	Q08462	0.6206	0.4319	cerebral cortex
ADCY8	ENSG00000155897	P40145	0.7714	0.7388	cerebellum
ADGRA1	ENSG00000197177	Q86SQ6	0.8153	0.7342	cerebral cortex
ADGRB1	ENSG00000181790	O14514	0.69	0.4802	cerebral cortex
ADGRB2	ENSG00000121753	O60241	0.718	0.5019	cerebral cortex
ADGRB3	ENSG00000135298	O60242	0.6602	0.4405	cerebellum
ADGRE1	ENSG00000174837	Q14246	0.9433	0.728	spleen

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
ADGRE2	ENSG00000127507	Q9UHX3	0.8197	0.4098	spleen
ADGRE3	ENSG00000131355	Q9BY15	0.9253	0.9025	spleen
ADGRF1	ENSG00000153292	Q5T601	0.7994	0.7451	esophagus
ADGRF3	ENSG00000173567	Q8IZF5	0.7853	0.5041	cerebellum
ADGRF4	ENSG00000153294	Q8IZF3	0.8768	0.7624	skin
ADGRG2	ENSG00000173698	Q8IZP9	0.7417	0.4908	fallopian tube
ADGRG3	ENSG00000182885	Q86Y34	0.822	0.5524	spleen
ADGRG5	ENSG00000159618	Q8IZF4	0.8999	0.6892	spleen
ADGRG7	ENSG00000144820	Q96K78	0.9151	0.7474	small intestine
ADGRV1	ENSG00000164199	Q8WXG9	0.8204	0.6182	adrenal gland
ADIG	ENSG00000182035	Q0VDE8	0.9763	0.9274	thyroid gland
ADORA1	ENSG00000163485	P30542	0.6015	0.4359	spinal cord
ADORA2B	ENSG00000170425	P29275	0.6191	0.4465	skin
ADRA1A	ENSG00000120907	P35348	0.7609	0.4698	liver
ADRA1D	ENSG00000171873	P25100	0.6935	0.4701	cervix, uterine
ADRB3	ENSG00000188778	P13945	0.8966	0.8098	ovary
ADTRP	ENSG00000111863	Q96IZ2	0.8265	0.7087	colon
AGTR2	ENSG00000180772	P50052	0.9248	0.849	lung
AJAP1	ENSG00000196581	Q9UKB5	0.6332	0.4242	cerebral cortex
ALK	ENSG00000171094	Q9UM73	0.8644	0.7105	pituitary gland
ALPP	ENSG00000163283	P05187	0.9749	0.9592	lung
AMHR2	ENSG00000135409	Q16671	0.9163	0.8041	adrenal gland
AMN	ENSG00000166126	Q9BXJ7	0.8347	0.6656	small intestine
ANO3	ENSG00000134343	Q9BYT9	0.922	0.742	basal ganglia
ANO4	ENSG00000151572	Q32M45	0.6904	0.6144	cervix, uterine
ANO7	ENSG00000146205	Q6IWH7	0.882	0.6368	prostate
ANO9	ENSG00000185101	A1A5B4	0.7384	0.56	small intestine
APCDD1L	ENSG00000198768	Q8NCL9	0.8561	0.7015	salivary gland
APLNR	ENSG00000134817	P35414	0.7974	0.5614	spinal cord
APLP1	ENSG00000105290	P51693	0.6626	0.4667	spinal cord
AQP10	ENSG00000143595	Q96PS8	0.9596	0.9353	fallopian tube
AQP12A	ENSG00000184945	Q8IXF9	0.9975	0.9938	pancreas
AQP12B	ENSG00000185176	A6NM10	0.9949	0.983	pancreas
AQP2	ENSG00000167580	P41181	0.9798	0.9418	kidney
AQP4	ENSG00000171885	P55087	0.72	0.6407	basal ganglia
AQP5	ENSG00000161798	P55064	0.7966	0.5051	salivary gland
AQP7	ENSG00000165269	O14520	0.7466	0.473	adipose tissue
AQP9	ENSG00000103569	O43315	0.8013	0.5358	liver
AREG	ENSG00000109321	P15514	0.6191	0.4843	esophagus
ARSH	ENSG00000205667	Q5FYA8	0.9688	0.9688	esophagus
ASGR2	ENSG00000161944	P07307	0.9297	0.5961	liver
ASIC1	ENSG00000110881	P78348	0.6609	0.4246	cerebellum
ASIC2	ENSG00000108684	Q16515	0.7764	0.7059	cerebellum
ASIC4	ENSG00000072182	Q96FT7	0.8687	0.7419	pituitary gland
ASPHD1	ENSG00000174939	Q5U4P2	0.6268	0.5052	cerebellum
ASTN1	ENSG00000152092	O14525	0.7137	0.6117	cerebral cortex
ATP12A	ENSG00000075673	P54707	0.9503	0.919	skin
ATP13A4	ENSG00000127249	Q4VNC1	0.6941	0.4676	thyroid gland
ATP13A5	ENSG00000187527	Q4VNC0	0.8887	0.7293	skin
ATP1A3	ENSG00000105409	P13637	0.7338	0.6684	cerebral cortex
ATP1A4	ENSG00000132681	Q13733	0.9581	0.8285	urinary bladder
ATP2B2	ENSG00000157087	Q01814	0.8001	0.6662	cerebellum

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
ATP2B3	ENSG00000067842	Q16720	0.8402	0.7707	cerebellum
ATP2C2	ENSG00000064270	O75185	0.6722	0.5135	colon
ATP4A	ENSG00000105675	P20648	0.9779	0.9161	stomach
ATP4B	ENSG00000186009	P51164	0.9749	0.8349	stomach
ATP6V0A4	ENSG00000105929	Q9HBG4	0.9177	0.8026	kidney
ATP8A2	ENSG00000132932	Q9NTI2	0.8268	0.7218	cerebellum
ATP8B4	ENSG00000104043	Q8TF62	0.8819	0.6168	fallopian tube
ATRN1	ENSG00000107518	Q5VV63	0.7608	0.493	cerebral cortex
AVPR1A	ENSG00000166148	P37288	0.7667	0.5661	adrenal gland
AVPR1B	ENSG00000198049	P47901	0.9935	0.9849	pituitary gland
AVPR2	ENSG00000126895	P30518	0.6887	0.4753	adipose tissue
B3GAT1	ENSG00000109956	Q9P2W7	0.7055	0.5761	spinal cord
BDKRB1	ENSG00000100739	P46663	0.6817	0.5196	esophagus
BDKRB2	ENSG00000168398	P30411	0.6259	0.4487	cervix, uterine
BEST2	ENSG00000039987	Q8NFU1	0.94	0.9193	colon
BEST3	ENSG00000127325	Q8N1M1	0.8897	0.7282	skeletal muscle
BEST4	ENSG00000142959	Q8NFU0	0.789	0.5119	colon
BMPR1B	ENSG00000138696	O00238	0.6286	0.4094	prostate
BRS3	ENSG00000102239	P32247	0.8802	0.8064	fallopian tube
BSND	ENSG00000162399	Q8WZ55	0.9678	0.9248	kidney
BTBD11	ENSG00000151136	A6QL63	0.6655	0.4431	esophagus
BTC	ENSG00000174808	P35070	0.7263	0.4532	colon
BTLA	ENSG00000186265	Q7Z6A9	0.9309	0.7922	spleen
BTN1A1	ENSG00000124557	Q13410	0.9504	0.9049	breast
BTNL2	ENSG00000204290	Q9UIR0	0.8395	0.7937	hypothalamus
BTNL3	ENSG00000168903	Q6UXE8	0.9575	0.9205	small intestine
BTNL8	ENSG00000113303	Q6UX41	0.9053	0.7554	small intestine
C10orf105	ENSG00000214688	Q8TEF2	0.7844	0.6569	hypothalamus
C11orf87	ENSG00000185742	Q6NUJ2	0.8892	0.809	cerebral cortex
C16orf54	ENSG00000185905	Q6UWD8	0.8507	0.5709	spleen
C1orf210	ENSG00000253313	Q8IVY1	0.601	0.5385	colon
C20orf141	ENSG00000258713	Q9NUB4	0.9334	0.8893	endometrium
C3orf80	ENSG00000180044	F5H4A9	0.8005	0.5354	cerebral cortex
C8A	ENSG00000157131	P07357	0.9978	0.9948	liver
C9	ENSG00000113600	P02748	0.9938	0.982	liver
C9orf135	ENSG00000204711	Q5VTT2	0.8841	0.8073	pituitary gland
CA14	ENSG00000118298	Q9ULX7	0.7572	0.5196	spinal cord
CA9	ENSG00000107159	Q16790	0.9013	0.6825	stomach
CABP7	ENSG00000100314	Q86V35	0.8373	0.6335	hippocampal formation
CACNA1A	ENSG00000141837	O00555	0.814	0.5316	cerebellum
CACNA1B	ENSG00000148408	Q00975	0.8321	0.7204	cerebellum
CACNA1E	ENSG00000198216	Q15878	0.8597	0.7723	basal ganglia
CACNA1F	ENSG00000102001	O60840	0.7955	0.4964	cerebellum
CACNA1G	ENSG00000006283	O43497	0.7611	0.5529	cerebellum
CACNA1I	ENSG00000100346	Q9P0X4	0.7978	0.6741	cerebellum
CACNA1S	ENSG00000081248	Q13698	0.9861	0.9524	skeletal muscle
CACNA2D4	ENSG00000151062	Q7Z3S7	0.7702	0.6706	cervix, uterine
CACNG1	ENSG00000108878	Q06432	0.9585	0.832	skeletal muscle
CACNG2	ENSG00000166862	Q9Y698	0.905	0.8191	cerebellum
CACNG3	ENSG00000006116	O60359	0.8861	0.8491	cerebral cortex
CACNG4	ENSG00000075461	Q9UBN1	0.7424	0.5817	basal ganglia

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CACNG5	ENSG00000075429	Q9UF02	0.8959	0.8298	cerebral cortex
CACNG6	ENSG00000130433	Q9BXT2	0.9262	0.8218	skeletal muscle
CACNG7	ENSG00000105605	P62955	0.7979	0.7687	cerebellum
CADM2	ENSG00000175161	Q8N3J6	0.7098	0.5567	cerebral cortex
CALCR	ENSG00000004948	P30988	0.9673	0.9007	hypothalamus
CALHM1	ENSG00000185933	Q8IU99	0.9243	0.8662	cerebral cortex
CALHM3	ENSG00000183128	Q86XJ0	0.7812	0.7813	basal ganglia
CALHM4	ENSG00000164451	Q5JW98	0.9929	0.9796	skin
CALN1	ENSG00000183166	Q9BXU9	0.8276	0.6864	cerebellum
CALY	ENSG00000130643	Q9NYX4	0.7262	0.6046	hypothalamus
CASR	ENSG00000036828	P41180	0.9491	0.9043	kidney
CATSPER1	ENSG00000175294	Q8NEC5	0.9659	0.9348	lung
CATSPERB	ENSG00000133962	Q9H7T0	0.8538	0.6277	pancreas
CATSPERG	ENSG00000099338	Q6ZRH7	0.8309	0.4479	cerebellum
CBARP	ENSG00000099625	Q8N350	0.734	0.4897	pituitary gland
CKAR	ENSG00000163394	P32238	0.9791	0.9379	stomach
CCKBR	ENSG00000110148	P32239	0.8408	0.7516	stomach
CCR2	ENSG00000121807	P41597	0.8123	0.5303	spleen
CCR3	ENSG00000183625	P51677	0.9223	0.8592	skin
CCR4	ENSG00000183813	P51679	0.8585	0.6996	spleen
CCR5	ENSG00000160791	P51681	0.7574	0.4025	spleen
CCR6	ENSG00000112486	P51684	0.929	0.7695	spleen
CCR7	ENSG00000126353	P32248	0.7273	0.4091	spleen
CCR8	ENSG00000179934	P51685	1	1	spleen
CCR9	ENSG00000173585	P51686	0.9832	0.9654	small intestine
CD101	ENSG00000134256	Q93033	0.7331	0.4345	lung
CD163L1	ENSG00000177675	Q9NR16	0.8456	0.488	spleen
CD164L2	ENSG00000174950	Q6UWJ8	0.79	0.6586	fallopian tube
CD180	ENSG00000134061	Q99467	0.8481	0.4806	spleen
CD19	ENSG00000177455	P15391	0.9325	0.8014	spleen
CD1A	ENSG00000158477	P06126	0.9497	0.8817	skin
CD1B	ENSG00000158485	P29016	0.9144	0.8504	skin
CD1C	ENSG00000158481	P29017	0.8465	0.6094	spleen
CD1D	ENSG00000158473	P15813	0.7386	0.44	spleen
CD2	ENSG00000116824	P06729	0.7241	0.445	spleen
CD207	ENSG00000116031	Q9UJ71	0.9176	0.7564	skin
CD209	ENSG00000090659	Q9NNX6	0.7338	0.4689	adipose tissue
CD22	ENSG00000012124	P20273	0.6676	0.4227	spleen
CD244	ENSG00000122223	Q9BZW8	0.8937	0.5888	spleen
CD27	ENSG00000139193	P26842	0.8136	0.5699	spleen
CD28	ENSG00000178562	P10747	0.7989	0.5927	spleen
CD300C	ENSG00000167850	Q08708	0.7726	0.4033	spleen
CD300E	ENSG00000186407	Q496F6	0.9673	0.9521	lung
CD300LB	ENSG00000178789	A8K4G0	0.8427	0.6226	spleen
CD300LD	ENSG00000204345	Q6UXZ3	1	1	spleen
CD300LF	ENSG00000186074	Q8TDQ1	0.8462	0.4747	spleen
CD300LG	ENSG00000161649	Q6UXG3	0.7617	0.501	adipose tissue
CD3D	ENSG00000167286	P04234	0.7248	0.4255	spleen
CD3E	ENSG00000198851	P07766	0.6996	0.4103	spleen
CD3G	ENSG00000160654	P09693	0.8741	0.6646	spleen
CD40LG	ENSG00000102245	P29965	0.83	0.6454	small intestine
CD5	ENSG00000110448	P06127	0.7783	0.4795	spleen

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CD6	ENSG00000013725	P30203	0.795	0.4477	spleen
CD70	ENSG00000125726	P32970	0.8157	0.67	spleen
CD79A	ENSG00000105369	P11912	0.8114	0.5571	spleen
CD79B	ENSG00000007312	P40259	0.7786	0.4463	spleen
CD80	ENSG00000121594	P33681	0.9101	0.7655	lung
CD8B	ENSG00000172116	P10966	0.6817	0.4102	cervix, uterine
CD96	ENSG00000153283	P40200	0.6722	0.4813	spleen
CDCP1	ENSG00000163814	Q9H5V8	0.6613	0.4714	esophagus
CDH1	ENSG000000039068	P12830	0.5228	0.4193	esophagus
CDH10	ENSG00000040731	Q9Y6N8	0.8758	0.7872	cerebellum
CDH12	ENSG00000154162	P55289	0.7807	0.7068	pituitary gland
CDH15	ENSG00000129910	P55291	0.9365	0.8157	cerebellum
CDH16	ENSG00000166589	Q75309	0.9707	0.9466	kidney
CDH17	ENSG00000079112	Q12864	0.9548	0.9	colon
CDH18	ENSG00000145526	Q13634	0.9024	0.8297	cerebellum
CDH20	ENSG00000101542	Q9HBT6	0.7348	0.6582	spinal cord
CDH22	ENSG00000149654	Q9UJ99	0.84	0.6067	cerebellum
CDH3	ENSG00000062038	P22223	0.618	0.4292	ovary
CDH4	ENSG00000179242	P55283	0.7382	0.5687	basal ganglia
CDH7	ENSG00000081138	Q9ULB5	0.9614	0.8965	cerebellum
CDH8	ENSG00000150394	P55286	0.8131	0.7176	cerebral cortex
CDH9	ENSG00000113100	Q9ULB4	0.9137	0.8766	cerebral cortex
CDHR1	ENSG00000148600	Q96JP9	0.8274	0.562	skin
CDHR2	ENSG00000074276	Q9BYE9	0.9281	0.8493	small intestine
CDHR3	ENSG00000128536	Q6ZTQ4	0.7865	0.4509	fallopian tube
CDHR4	ENSG00000187492	A6H8M9	0.9178	0.7427	fallopian tube
CDHR5	ENSG00000099834	Q9HBB8	0.9075	0.8039	small intestine
CEACAM1	ENSG00000079385	P13688	0.6625	0.45	colon
CEACAM3	ENSG00000170956	P40198	0.9395	0.8117	spleen
CEACAM4	ENSG00000105352	Q75871	0.8741	0.5218	spleen
CELSR1	ENSG00000075275	Q9NYQ6	0.6442	0.4918	skin
CELSR3	ENSG00000008300	Q9NYQ7	0.8998	0.4722	pituitary gland
CEND1	ENSG00000184524	Q8N111	0.7386	0.6293	cerebellum
CFAP65	ENSG00000181378	Q6ZU64	0.8943	0.7567	fallopian tube
CFTR	ENSG00000001626	P13569	0.8847	0.7268	pancreas
CHODL	ENSG00000154645	Q9H9P2	0.6737	0.4448	hypothalamus
CHRM1	ENSG00000168539	P11229	0.8158	0.7203	cerebral cortex
CHRM2	ENSG00000181072	P08172	0.9428	0.9143	colon
CHRM3	ENSG00000133019	P20309	0.7198	0.4937	urinary bladder
CHRM4	ENSG00000180720	P08173	0.8309	0.6842	basal ganglia
CHRM5	ENSG00000184984	P08912	0.9148	0.7366	spinal cord
CHRNA1	ENSG00000138435	P02708	0.9387	0.8197	skeletal muscle
CHRNA2	ENSG00000120903	Q15822	0.9315	0.8106	prostate
CHRNA3	ENSG00000080644	P32297	0.8346	0.6794	adrenal gland
CHRNA4	ENSG00000101204	P43681	0.8178	0.703	liver
CHRNA6	ENSG00000147434	Q15825	0.948	0.8738	cerebellum
CHRNA9	ENSG00000174343	Q9UGM1	0.9579	0.9415	skin
CHRN2	ENSG00000160716	P17787	0.8098	0.7622	cerebral cortex
CHRN3	ENSG00000147432	Q05901	0.9521	0.9339	midbrain
CHRN4	ENSG00000117971	P30926	0.8743	0.766	colon
CHRNA	ENSG00000135902	Q07001	0.9977	0.9957	skeletal muscle
CHRNA	ENSG00000108556	Q04844	0.8408	0.4426	heart muscle

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CHRNA	ENSG00000196811	P07510	0.9969	0.9924	skeletal muscle
CHST9	ENSG00000154080	Q7L1S5	0.7739	0.4625	salivary gland
CLCA2	ENSG00000137975	Q9UQC9	0.861	0.7963	esophagus
CLCA4	ENSG0000016602	Q14CN2	0.7943	0.6561	esophagus
CLCN1	ENSG00000188037	P35523	0.9742	0.8952	skeletal muscle
CLCNKA	ENSG00000186510	P51800	0.8866	0.7024	kidney
CLCNKB	ENSG00000184908	P51801	0.8865	0.6748	kidney
CLDN1	ENSG00000163347	O95832	0.6447	0.4024	skin
CLDN10	ENSG00000134873	P78369	0.6156	0.4714	pancreas
CLDN14	ENSG00000159261	O95500	0.961	0.908	liver
CLDN17	ENSG00000156282	P56750	0.9271	0.9133	vagina
CLDN18	ENSG00000066405	P56856	0.9418	0.7883	stomach
CLDN19	ENSG00000164007	Q8N6F1	0.9432	0.8148	kidney
CLDN2	ENSG00000165376	P57739	0.8898	0.8058	kidney
CLDN22	ENSG00000177300	Q8N7P3	0.9068	0.5104	salivary gland
CLDN23	ENSG00000253958	Q96B33	0.6008	0.4221	colon
CLDN24	ENSG00000185758	A6NM45	0.9659	0.9348	salivary gland
CLDN25	ENSG00000228607	C9JDP6	1	1	pituitary gland
CLDN3	ENSG00000165215	O15551	0.6637	0.5255	colon
CLDN4	ENSG00000189143	O14493	0.5427	0.4551	esophagus
CLDN6	ENSG00000184697	P56747	0.907	0.8192	cerebellum
CLDN7	ENSG00000181885	O95471	0.5513	0.4036	colon
CLDN9	ENSG00000213937	O95484	0.8093	0.5125	cerebellum
CLEC12A	ENSG00000172322	Q5QGZ9	0.8172	0.4773	spleen
CLEC12B	ENSG00000256660	Q2HXU8	0.9356	0.8836	spleen
CLEC17A	ENSG00000187912	Q6ZS10	0.9475	0.8684	spleen
CLEC1B	ENSG00000165682	Q9P126	0.9576	0.9305	liver
CLEC2A	ENSG00000188393	Q6UVW9	0.993	0.9734	skin
CLEC2L	ENSG00000236279	P0C7M8	0.8031	0.7071	cerebral cortex
CLEC4C	ENSG00000198178	Q8WTT0	1	1	spleen
CLEC4D	ENSG00000166527	Q8WXI8	0.9288	0.7879	spleen
CLEC4F	ENSG00000152672	Q8N1N0	0.7414	0.5147	spleen
CLEC4G	ENSG00000182566	Q6UXB4	0.7468	0.4562	cerebellum
CLEC4M	ENSG00000104938	Q9H2X3	0.9138	0.749	liver
CLEC6A	ENSG00000205846	Q6EIG7	1	1	lung
CLEC9A	ENSG00000197992	Q6UXN8	0.8512	0.6867	spinal cord
CLECL1	ENSG00000184293	Q8IZS7	0.8401	0.4617	spleen
CLIC3	ENSG00000169583	O95833	0.7265	0.5223	esophagus
CLIC5	ENSG00000112782	Q9NZA1	0.7142	0.4696	skeletal muscle
CLRN1	ENSG00000163646	P58418	0.9937	0.986	adrenal gland
CLRN3	ENSG00000180745	Q8NCR9	0.9148	0.8504	small intestine
CLTRN	ENSG00000147003	Q9HBJ8	0.8752	0.445	kidney
CMTM5	ENSG00000166091	Q96DZ9	0.7382	0.4918	spinal cord
CNGA1	ENSG00000198515	P29973	0.6656	0.4626	urinary bladder
CNGA3	ENSG00000144191	Q16281	0.8959	0.7568	pituitary gland
CNGA4	ENSG00000132259	Q8IV77	0.8702	0.5214	fallopian tube
CNGB1	ENSG00000070729	Q14028	0.9262	0.8284	hypothalamus
CNGB3	ENSG00000170289	Q9NQW8	0.9752	0.9511	fallopian tube
CNIH2	ENSG00000174871	Q6PI25	0.7562	0.5911	hippocampal formation
CNIH3	ENSG00000143786	Q8TBE1	0.7254	0.4483	cerebral cortex
CNMD	ENSG00000136110	O75829	0.8366	0.7254	basal ganglia

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CNNM1	ENSG00000119946	Q9NRU3	0.8366	0.6526	cerebellum
CNR2	ENSG00000188822	P34972	0.9766	0.9672	spleen
CNTNAP2	ENSG00000174469	Q9UHC6	0.8745	0.8133	spinal cord
CNTNAP3B	ENSG00000154529	Q96NU0	0.7863	0.4851	breast
CNTNAP4	ENSG00000152910	Q9C0A0	0.9269	0.8729	cerebellum
CNTNAP5	ENSG00000155052	Q8WYK1	0.9008	0.8446	cerebral cortex
COL13A1	ENSG00000197467	Q5TAT6	0.7396	0.41	cerebellum
COL17A1	ENSG00000065618	Q9UMD9	0.7538	0.5497	skin
COL25A1	ENSG00000188517	Q9BXS0	0.8455	0.5864	pituitary gland
CORIN	ENSG00000145244	Q9Y5Q5	0.8373	0.6117	heart muscle
CR2	ENSG00000117322	P20023	0.9618	0.9157	spleen
CRB1	ENSG00000134376	P82279	0.8149	0.7518	cerebellum
CRB2	ENSG00000148204	Q5IJ48	0.7767	0.706	basal ganglia
CRB3	ENSG00000130545	Q9BUF7	0.5596	0.4382	esophagus
CRHR1	ENSG00000120088	P34998	0.8456	0.6816	cerebellum
CRHR2	ENSG00000106113	Q13324	0.836	0.5029	pituitary gland
CRLF2	ENSG00000205755	Q9HC73	0.843	0.6956	lung
CRTAM	ENSG00000109943	O95727	0.9618	0.7549	cerebellum
CSMD1	ENSG00000183117	Q96PZ7	0.8515	0.7587	cerebral cortex
CSMD2	ENSG00000121904	Q7Z408	0.774	0.6539	cerebellum
CSMD3	ENSG00000164796	Q7Z407	0.8467	0.8064	basal ganglia
CSPG5	ENSG00000114646	O95196	0.7452	0.6423	cerebral cortex
CT83	ENSG00000204019	Q5H943	0.9972	0.9949	salivary gland
CTLA4	ENSG00000163599	P16410	0.7908	0.5171	small intestine
CTXN2	ENSG00000233932	P0C2S0	0.8038	0.7611	hypothalamus
CTXN3	ENSG00000205279	Q4LDR2	0.8686	0.8178	cerebral cortex
CWH43	ENSG00000109182	Q9H720	0.7916	0.7203	skin
CX3CR1	ENSG00000168329	P49238	0.7028	0.4454	spinal cord
CXCR1	ENSG00000163464	P25024	0.8905	0.5619	spleen
CXCR2	ENSG00000180871	P25025	0.7982	0.576	spleen
CXCR3	ENSG00000186810	P49682	0.8596	0.6327	spleen
CXCR5	ENSG00000160683	P32302	0.8137	0.5221	spleen
CXCR6	ENSG00000172215	O00574	0.7626	0.4668	spleen
CYP46A1	ENSG00000036530	Q9Y6A2	0.7299	0.4964	basal ganglia
CYSLTR1	ENSG00000173198	Q9Y271	0.7058	0.4018	spleen
CYSLTR2	ENSG00000152207	Q9NS75	0.7776	0.4897	adrenal gland
DBH	ENSG00000123454	P09172	0.9069	0.6122	adrenal gland
DCC	ENSG00000187323	P43146	0.8342	0.7006	basal ganglia
DCHS2	ENSG00000197410	Q6V1P9	0.6957	0.5475	colon
DCST1	ENSG00000163357	Q5T197	0.9499	0.8397	skin
DCST2	ENSG00000163354	Q5T1A1	0.754	0.5165	skin
DCSTAMP	ENSG00000164935	Q9H295	0.9519	0.9188	lung
DIO2	ENSG00000211448	Q92813	0.6367	0.4297	thyroid gland
DIO3	ENSG00000197406	P55073	0.7628	0.5173	cervix, uterine
DISP2	ENSG00000140323	A7MBM2	0.8262	0.5491	cerebellum
DLK1	ENSG00000185559	P80370	0.8191	0.5867	adrenal gland
DLK2	ENSG00000171462	Q6UY11	0.6504	0.4945	prostate
DLL3	ENSG00000090932	Q9NYJ7	0.8117	0.7735	basal ganglia
DNAJC22	ENSG00000178401	Q8N4W6	0.8014	0.5869	liver
DNER	ENSG00000187957	Q8NFT8	0.6092	0.4844	hypothalamus
DPP10	ENSG00000175497	Q8N608	0.7894	0.6696	cerebral cortex
DPP4	ENSG00000197635	P27487	0.6865	0.4677	small intestine

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DPP6	ENSG00000130226	P42658	0.6277	0.4764	endometrium
DRD1	ENSG00000184845	P21728	0.9102	0.6467	basal ganglia
DRD2	ENSG00000149295	P14416	0.8203	0.5983	pituitary gland
DRD5	ENSG00000169676	P21918	0.8907	0.8184	cerebral cortex
DSC1	ENSG00000134765	Q08554	0.9803	0.9427	skin
DSC2	ENSG00000134755	Q02487	0.7146	0.4509	esophagus
DSC3	ENSG00000134762	Q14574	0.8544	0.7665	skin
DSCAM	ENSG00000171587	O60469	0.7965	0.7756	hypothalamus
DSG1	ENSG00000134760	Q02413	0.9193	0.8369	skin
DSG2	ENSG00000046604	Q14126	0.5691	0.4327	colon
DSG3	ENSG00000134757	P32926	0.8883	0.8524	esophagus
DSG4	ENSG00000175065	Q86SJ6	0.9799	0.9545	skin
DUOX1	ENSG00000137857	Q9NRD9	0.6518	0.5116	lung
DUOX2	ENSG00000140279	Q9NRD8	0.7868	0.6292	thyroid gland
DUOXA1	ENSG00000140254	Q1HG43	0.6971	0.5608	esophagus
DYNAP	ENSG00000178690	Q8N1N2	0.9761	0.9483	esophagus
ECEL1	ENSG00000171551	Q95672	0.7888	0.5018	ovary
EDAR	ENSG00000135960	Q9UNE0	0.8857	0.8186	esophagus
EFNB3	ENSG00000108947	Q15768	0.6495	0.4066	basal ganglia
EGF	ENSG00000138798	P01133	0.8386	0.6819	skeletal muscle
ELFN2	ENSG00000166897	Q5R3F8	0.8285	0.769	cerebral cortex
ENPEP	ENSG00000138792	Q07075	0.7491	0.4497	small intestine
ENPP1	ENSG00000197594	P22413	0.6634	0.4243	endometrium
ENPP3	ENSG00000154269	O14638	0.7105	0.5263	salivary gland
ENTPD8	ENSG00000188833	Q5MY95	0.8489	0.731	small intestine
EPGN	ENSG00000182585	Q6UW88	0.8985	0.8211	esophagus
EPHA1	ENSG00000146904	P21709	0.7307	0.5445	esophagus
EPHA10	ENSG00000183317	Q5JZY3	0.7465	0.5994	colon
EPHA5	ENSG00000145242	P54756	0.8268	0.6816	cerebral cortex
EPHA6	ENSG00000080224	Q9UF33	0.7922	0.5514	colon
EPHA7	ENSG00000135333	Q15375	0.7399	0.496	colon
EPHA8	ENSG00000070886	P29322	0.9028	0.7866	spleen
EPHB1	ENSG00000154928	P54762	0.7367	0.4094	cerebellum
EPHX4	ENSG00000172031	Q8IUS5	0.8213	0.5259	cerebral cortex
ERBB4	ENSG00000178568	Q15303	0.6627	0.5179	fallopian tube
EREG	ENSG00000124882	O14944	0.8382	0.7341	skin
ERVFRD-1	ENSG00000244476	P60508	0.6812	0.6136	adrenal gland
ERVMER34-1	ENSG00000226887	Q9H9K5	0.7591	0.5227	ovary
ERVW-1	ENSG00000242950	Q9UQF0	0.9183	0.8644	cerebellum
ESR1	ENSG000000091831	P03372	0.7228	0.495	cervix, uterine
ESYT3	ENSG00000158220	A0FGR9	0.6935	0.4867	skin
EVC	ENSG00000072840	P57679	0.7282	0.5347	endometrium
F2RL2	ENSG00000164220	O00254	0.7389	0.5252	colon
F2RL3	ENSG00000127533	Q96RI0	0.7305	0.4611	lung
FAM151A	ENSG00000162391	Q8WW52	0.9455	0.9038	small intestine
FAM155A	ENSG00000204442	B1AL88	0.7277	0.5824	cerebral cortex
FAM155B	ENSG00000130054	O75949	0.8259	0.569	heart muscle
FAM163A	ENSG00000143340	Q96GL9	0.9253	0.7271	pituitary gland
FAM163B	ENSG00000196990	P0C2L3	0.8371	0.684	cerebral cortex
FAM171A2	ENSG00000161682	A8MVW0	0.681	0.4745	cerebellum
FAM171B	ENSG00000144369	Q6P995	0.6049	0.4019	cerebral cortex

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FAM187B	ENSG00000177558	Q17R55	0.902	0.8341	spleen
FAM189A1	ENSG00000104059	O60320	0.7129	0.5345	hippocampal formation
FAM209A	ENSG00000124103	Q5JX71	0.7554	0.4299	spleen
FAP	ENSG00000078098	Q12884	0.7726	0.513	endometrium
FASLG	ENSG00000117560	P48023	0.9253	0.6958	spleen
FAT2	ENSG00000086570	Q9NYQ8	0.8516	0.6952	cerebellum
FAT3	ENSG00000165323	Q8TDW7	0.7727	0.5779	basal ganglia
FCAR	ENSG00000186431	P24071	0.8301	0.5151	spleen
FCER1A	ENSG00000179639	P12319	0.7176	0.4535	skin
FCER2	ENSG00000104921	P06734	0.9142	0.7048	spleen
FCMR	ENSG00000162894	O60667	0.8118	0.4981	spleen
FCRL1	ENSG00000163534	Q96LA6	0.9534	0.9081	spleen
FCRL2	ENSG00000132704	Q96LA5	0.936	0.8364	spleen
FCRL3	ENSG00000160856	Q96P31	0.9569	0.8905	spleen
FCRL4	ENSG00000163518	Q96PJ5	0.9848	0.9795	small intestine
FCRL5	ENSG00000143297	Q96RD9	0.895	0.7421	spleen
FCRL6	ENSG00000181036	Q6DN72	0.8649	0.4642	spleen
FER1L6	ENSG00000214814	Q2WQJ9	0.9325	0.8828	stomach
FFAR1	ENSG00000126266	O14842	0.8687	0.738	ovary
FFAR2	ENSG00000126262	O15552	0.8748	0.6402	spleen
FFAR3	ENSG00000185897	O14843	0.8504	0.6178	adipose tissue
FFAR4	ENSG00000186188	Q5NUL3	0.8933	0.7082	pituitary gland
FIBCD1	ENSG00000130720	Q8N539	0.8896	0.729	hippocampal formation
FLT3	ENSG00000122025	P36888	0.8835	0.6222	cerebellum
FNDC5	ENSG00000160097	Q8NAU1	0.7087	0.4366	cerebellum
FNDC9	ENSG00000172568	Q8TBE3	0.8491	0.7807	hypothalamus
FOLH1	ENSG00000086205	Q04609	0.7199	0.5144	spinal cord
FPR2	ENSG00000171049	P25090	0.8596	0.5311	spleen
FRAS1	ENSG00000138759	Q86XX4	0.8232	0.4932	thyroid gland
FRMD5	ENSG00000171877	Q7Z6J6	0.7123	0.596	spinal cord
FRRS1	ENSG00000156869	Q6ZNA5	0.6353	0.4465	esophagus
FUT6	ENSG00000156413	P51993	0.8254	0.7699	esophagus
FXYD2	ENSG00000137731	P54710	0.8746	0.5585	kidney
FXYD3	ENSG00000089356	Q14802	0.5752	0.4063	colon
FXYD4	ENSG00000150201	P59646	0.9483	0.8097	kidney
FXYD7	ENSG00000221946	P58549	0.7272	0.5279	cerebral cortex
FZD10	ENSG00000111432	Q9ULW2	0.7497	0.5184	esophagus
FZD9	ENSG00000188763	O00144	0.6263	0.4699	pituitary gland
GABBR2	ENSG00000136928	Q75899	0.8414	0.774	cerebral cortex
GABRA1	ENSG00000022355	P14867	0.8723	0.8224	cerebellum
GABRA2	ENSG00000151834	P47869	0.7724	0.6364	cerebral cortex
GABRA3	ENSG00000011677	P34903	0.8469	0.7788	cerebral cortex
GABRA4	ENSG00000109158	P48169	0.8951	0.8263	basal ganglia
GABRA5	ENSG00000186297	P31644	0.8825	0.8281	basal ganglia
GABRA6	ENSG00000145863	Q16445	0.9874	0.9614	cerebellum
GABRB1	ENSG00000163288	P18505	0.8566	0.7934	basal ganglia
GABRB2	ENSG00000145864	P47870	0.8578	0.7178	cerebellum
GABRB3	ENSG00000166206	P28472	0.6826	0.4658	cerebral cortex
GABRD	ENSG00000187730	O14764	0.8541	0.6607	cerebellum
GABRE	ENSG00000102287	P78334	0.8923	0.746	hypothalamus

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GABRG1	ENSG00000163285	Q8N1C3	0.8063	0.7803	basal ganglia
GABRG2	ENSG00000113327	P18507	0.828	0.7812	cerebral cortex
GABRG3	ENSG00000182256	Q99928	0.8362	0.7058	pituitary gland
GABRP	ENSG00000094755	O00591	0.7572	0.6659	breast
GABRR1	ENSG00000146276	P24046	0.9375	0.9375	esophagus
GALR1	ENSG00000166573	P47211	0.9152	0.7022	pituitary gland
GALR2	ENSG00000182687	O43603	0.931	0.8083	colon
GALR3	ENSG00000128310	O60755	0.9646	0.917	cerebellum
GAPT	ENSG00000175857	Q8N292	0.8353	0.4694	spleen
GCGR	ENSG00000215644	P47871	0.932	0.7647	liver
GDPD2	ENSG00000130055	Q9HCC8	0.8428	0.6784	spleen
GDPD4	ENSG00000178795	Q6W3E5	0.9361	0.9258	adrenal gland
GGT6	ENSG00000167741	Q6P531	0.6893	0.6128	skin
GHRHR	ENSG00000106128	Q02643	0.9953	0.9814	pituitary gland
GHSR	ENSG00000121853	Q92847	0.9874	0.9735	pituitary gland
GJA3	ENSG00000121743	Q9Y6H8	0.9627	0.8685	heart muscle
GJB1	ENSG00000169562	P08034	0.673	0.507	liver
GJB2	ENSG00000165474	P29033	0.776	0.5476	esophagus
GJB3	ENSG00000188910	O75712	0.8432	0.6709	skin
GJB4	ENSG00000189433	Q9NTQ9	0.9564	0.8901	skin
GJB5	ENSG00000189280	Q95377	0.8284	0.6748	skin
GJB6	ENSG00000121742	O95452	0.7078	0.6111	esophagus
GJB7	ENSG00000164411	Q6PEY0	0.9692	0.9486	pituitary gland
GJC3	ENSG00000176402	Q8NFK1	0.7789	0.4855	salivary gland
GJD2	ENSG00000159248	Q9UKL4	0.912	0.8031	pituitary gland
GJD3	ENSG00000183153	Q8N144	0.7456	0.5963	urinary bladder
GJD4	ENSG00000177291	Q96KN9	0.9886	0.9833	cerebral cortex
GLDN	ENSG00000186417	Q6ZMI3	0.6649	0.4243	spinal cord
GLP1R	ENSG00000112164	P43220	0.934	0.8555	pancreas
GLP2R	ENSG00000065325	O95838	0.7814	0.6252	colon
GLRA1	ENSG00000145888	P23415	0.9452	0.9279	hypothalamus
GLRA2	ENSG00000101958	P23416	0.893	0.8292	cerebellum
GLRA3	ENSG00000145451	O75311	0.8658	0.8234	cerebral cortex
GNRHR	ENSG00000109163	P30968	0.972	0.8217	pituitary gland
GP5	ENSG00000178732	P40197	0.8871	0.8448	fallopian tube
GP6	ENSG00000088053	Q9HCN6	0.7625	0.4339	cerebellum
GP9	ENSG00000169704	P14770	0.9667	0.9286	spleen
GPA33	ENSG00000143167	Q99795	0.9605	0.9499	colon
GPBAR1	ENSG00000179921	Q8TDU6	0.7547	0.4867	adipose tissue
GPM6A	ENSG00000150625	P51674	0.6609	0.4441	cerebellum
GPR1	ENSG00000183671	P46091	0.7682	0.5848	vagina
GPR101	ENSG00000165370	Q96P66	0.9832	0.976	basal ganglia
GPR119	ENSG00000147262	Q8TDV5	1	1	pancreas
GPR12	ENSG00000132975	P47775	0.8467	0.7404	cerebellum
GPR139	ENSG00000180269	Q6DWJ6	0.9831	0.978	basal ganglia
GPR141	ENSG00000187037	Q7Z602	0.8654	0.5665	spleen
GPR142	ENSG00000257008	Q7Z601	1	1	cerebellum
GPR148	ENSG00000173302	Q8TDV2	0.9604	0.9483	cerebellum
GPR149	ENSG00000174948	Q86SP6	0.9592	0.9361	basal ganglia
GPR15	ENSG00000154165	P49685	0.8276	0.7181	colon
GPR150	ENSG00000178015	Q8NGU9	0.7823	0.4746	pancreas
GPR152	ENSG00000175514	Q8TDT2	0.9688	0.9688	small intestine

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GPR156	ENSG00000175697	Q8NFN8	0.8632	0.7378	urinary bladder
GPR158	ENSG00000151025	Q5T848	0.9258	0.8411	cerebellum
GPR171	ENSG00000174946	O14626	0.724	0.519	spleen
GPR174	ENSG00000147138	Q9BXC1	0.8314	0.6287	spleen
GPR18	ENSG00000125245	Q14330	0.9105	0.644	spleen
GPR182	ENSG00000166856	O15218	0.9168	0.7009	spleen
GPR19	ENSG00000183150	Q15760	0.7766	0.6709	cerebellum
GPR20	ENSG00000204882	Q99678	0.7043	0.5179	cervix, uterine
GPR21	ENSG00000188394	Q99679	0.7192	0.5098	adipose tissue
GPR22	ENSG00000172209	Q99680	0.8477	0.7564	cerebral cortex
GPR25	ENSG00000170128	O00155	0.8161	0.7352	small intestine
GPR26	ENSG00000154478	Q8NDV2	0.9161	0.8789	cerebral cortex
GPR37	ENSG00000170775	O15354	0.7701	0.5764	spinal cord
GPR37L1	ENSG00000170075	O60883	0.7768	0.7402	cerebral cortex
GPR39	ENSG00000183840	O43194	0.7468	0.5772	urinary bladder
GPR42	ENSG00000126251	O15529	0.9233	0.874	adipose tissue
GPR45	ENSG00000135973	Q9Y5Y3	0.892	0.8426	hypothalamus
GPR50	ENSG00000102195	Q13585	0.9923	0.9828	pituitary gland
GPR52	ENSG00000203737	Q9Y2T5	0.9607	0.8847	basal ganglia
GPR55	ENSG00000135898	Q9Y2T6	0.8655	0.6735	basal ganglia
GPR6	ENSG00000146360	P46095	0.9506	0.9037	basal ganglia
GPR61	ENSG00000156097	Q9BZJ8	0.887	0.8248	cerebellum
GPR62	ENSG00000180929	Q9BZJ7	0.8459	0.704	spinal cord
GPR78	ENSG00000155269	Q96P69	0.9937	0.9895	esophagus
GPR82	ENSG00000171657	Q96P67	0.8607	0.6348	small intestine
GPR83	ENSG00000123901	Q9NYM4	0.9016	0.7456	cerebellum
GPR85	ENSG00000164604	P60893	0.6896	0.5482	cerebellum
GPR87	ENSG00000138271	Q9BY21	0.84	0.8133	esophagus
GPR88	ENSG00000181656	Q9GZN0	0.9049	0.6565	basal ganglia
GPRC5A	ENSG00000013588	Q8NFI5	0.6311	0.4064	lung
GPRC5D	ENSG00000111291	Q9NZD1	0.8638	0.5143	skin
GPRC6A	ENSG00000173612	Q5T6X5	0.9927	0.9881	salivary gland
GRAMD1B	ENSG00000023171	Q3KR37	0.7086	0.4335	cerebellum
GRAMD2A	ENSG00000175318	Q8IUY3	0.7208	0.5538	fallopian tube
GREB1	ENSG00000196208	Q4ZG55	0.7032	0.4087	ovary
GREB1L	ENSG00000141449	Q9C091	0.6365	0.4494	fallopian tube
GRIA1	ENSG00000155511	P42261	0.7876	0.689	cerebellum
GRIA2	ENSG00000120251	P42262	0.7131	0.6071	cerebral cortex
GRIA3	ENSG00000125675	P42263	0.7195	0.5116	cerebral cortex
GRIA4	ENSG00000152578	P48058	0.8019	0.6615	cerebellum
GRID1	ENSG00000182771	Q9ULK0	0.7582	0.6447	basal ganglia
GRID2	ENSG00000152208	O43424	0.9194	0.8062	cerebellum
GRIK1	ENSG00000171189	P39086	0.7749	0.6756	hypothalamus
GRIK2	ENSG00000164418	Q13002	0.8032	0.5469	cerebellum
GRIK3	ENSG00000163873	Q13003	0.7189	0.5128	pituitary gland
GRIK4	ENSG00000149403	Q16099	0.679	0.608	cerebral cortex
GRIN1	ENSG00000176884	Q05586	0.8079	0.7595	cerebral cortex
GRIN2A	ENSG00000183454	Q12879	0.8674	0.7212	cerebral cortex
GRIN2B	ENSG00000273079	Q13224	0.896	0.8651	cerebral cortex
GRIN2C	ENSG00000161509	Q14957	0.832	0.6319	cerebellum
GRIN2D	ENSG00000105464	O15399	0.773	0.5131	hypothalamus
GRIN3A	ENSG00000198785	Q8TCU5	0.8259	0.5847	cerebral cortex

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GRIN3B	ENSG00000116032	O60391	0.9012	0.6475	fallopian tube
GRM1	ENSG00000152822	Q13255	0.9279	0.8348	cerebellum
GRM2	ENSG00000164082	Q14416	0.8949	0.6648	cerebral cortex
GRM3	ENSG00000198822	Q14832	0.8189	0.7909	basal ganglia
GRM4	ENSG00000124493	Q14833	0.9429	0.8382	cerebellum
GRM5	ENSG00000168959	P41594	0.8985	0.8237	cerebral cortex
GRM6	ENSG00000113262	O15303	0.8504	0.6234	pituitary gland
GRM7	ENSG00000196277	Q14831	0.8487	0.7194	cerebral cortex
GRM8	ENSG00000179603	O00222	0.8196	0.6639	cerebral cortex
GRPR	ENSG00000126010	P30550	0.9489	0.8745	pancreas
GSDMA	ENSG00000167914	Q96QA5	0.9435	0.7313	skin
GSDMC	ENSG00000147697	Q9BYG8	0.8746	0.8415	esophagus
GSG1L	ENSG00000169181	Q6UXU4	0.7886	0.7249	basal ganglia
GSG1L2	ENSG00000214978	A8MUP6	1	1	cerebral cortex
GUCY2C	ENSG00000070019	P25092	0.9576	0.9313	small intestine
GUCY2D	ENSG00000132518	Q02846	0.9688	0.9688	esophagus
GUCY2F	ENSG00000101890	P51841	1	1	fallopian tube
GYPA	ENSG00000170180	P02724	0.9617	0.8728	spleen
GYPB	ENSG00000250361	P06028	0.977	0.9135	spleen
GYPE	ENSG00000197465	P15421	0.8154	0.5311	spleen
HAS1	ENSG00000105509	Q92839	0.7883	0.5166	adipose tissue
HAS2	ENSG00000170961	Q92819	0.725	0.4638	adipose tissue
HAS3	ENSG00000103044	O00219	0.6919	0.4244	esophagus
HAVCR1	ENSG00000113249	Q96D42	0.9701	0.8838	kidney
HCAR1	ENSG00000196917	Q9BXC0	0.9886	0.9833	breast
HCAR2	ENSG00000182782	Q8TDS4	0.7293	0.5939	esophagus
HCAR3	ENSG00000255398	P49019	0.7871	0.6554	spleen
HCN1	ENSG00000164588	O60741	0.8665	0.7716	cerebral cortex
HCN2	ENSG00000099822	Q9UL51	0.7282	0.65	spinal cord
HCN4	ENSG00000138622	Q9Y3Q4	0.9412	0.8441	heart muscle
HCRTR1	ENSG00000121764	O43613	0.8759	0.7665	hypothalamus
HCRTR2	ENSG00000137252	O43614	0.9406	0.8672	hypothalamus
HEPACAM	ENSG00000165478	Q14CZ8	0.7574	0.7147	cerebral cortex
HEPACAM2	ENSG00000188175	A8MVW5	0.8845	0.8389	colon
HEPHL1	ENSG00000181333	Q6MZM0	0.9171	0.904	esophagus
HHLA2	ENSG00000114455	Q9UM44	0.9206	0.8343	colon
HIGD1C	ENSG00000214511	A8MV81	0.853	0.7423	cervix, uterine
HLA-DQB2	ENSG00000232629	P05538	0.7445	0.4372	skin
HLA-G	ENSG00000204632	P17693	0.8905	0.5237	pituitary gland
HPN	ENSG00000105707	P05981	0.7194	0.4136	liver
HRH2	ENSG00000113749	P25021	0.6272	0.4281	heart muscle
HRH3	ENSG00000101180	Q9Y5N1	0.8476	0.8071	cerebellum
HRH4	ENSG00000134489	Q9H3N8	0.9062	0.9063	adipose tissue
HRK	ENSG00000135116	O00198	0.8603	0.7482	hippocampal formation
HS6ST2	ENSG00000171004	Q96MM7	0.6839	0.4445	basal ganglia
HS6ST3	ENSG00000185352	Q8IZP7	0.8278	0.5859	cerebral cortex
HSD17B2	ENSG00000086696	P37059	0.7606	0.6499	urinary bladder
HTR1A	ENSG00000178394	P08908	0.9345	0.8929	cerebral cortex
HTR1B	ENSG00000135312	P28222	0.8025	0.5465	basal ganglia
HTR1D	ENSG00000179546	P28221	0.9696	0.957	small intestine
HTR1E	ENSG00000168830	P28566	0.8614	0.7582	cerebral cortex

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HTR1F	ENSG00000179097	P30939	0.8265	0.6591	adipose tissue
HTR2A	ENSG00000102468	P28223	0.8761	0.6431	cerebral cortex
HTR2B	ENSG00000135914	P41595	0.765	0.5872	endometrium
HTR3A	ENSG00000166736	P46098	0.8713	0.7292	salivary gland
HTR3B	ENSG00000149305	Q95264	0.9797	0.9102	cerebral cortex
HTR3C	ENSG00000178084	Q8WXA8	0.9933	0.978	lung
HTR3E	ENSG00000186038	A5X5Y0	0.9688	0.9687	colon
HTR4	ENSG00000164270	Q13639	0.895	0.8241	small intestine
HTR5A	ENSG00000157219	P47898	0.8999	0.8409	cerebellum
HTR6	ENSG00000158748	P50406	0.9656	0.915	basal ganglia
HTR7	ENSG00000148680	P34969	0.7577	0.4721	hypothalamus
HYAL4	ENSG00000106302	Q2M3T9	0.9624	0.9222	skeletal muscle
ICAM4	ENSG00000105371	Q14773	0.8794	0.6411	lung
ICAM5	ENSG00000105376	Q9UMF0	0.8386	0.7234	basal ganglia
ICOS	ENSG00000163600	Q9Y6W8	0.8638	0.7395	small intestine
IFITM10	ENSG00000244242	A6NMD0	0.8211	0.4075	adrenal gland
IFITM5	ENSG00000206013	A6NNB3	0.9589	0.8481	pancreas
IGDCC3	ENSG00000174498	Q8IVU1	0.8506	0.6279	cerebellum
IGDCC4	ENSG00000103742	Q8TDY8	0.6707	0.4077	ovary
IGSF1	ENSG00000147255	Q8N6C5	0.8291	0.4977	pituitary gland
IGSF11	ENSG00000144847	Q5DX21	0.6815	0.4547	spinal cord
IGSF23	ENSG00000216588	A1L1A6	0.9636	0.9463	liver
IGSF5	ENSG00000183067	Q9NSI5	0.7891	0.576	heart muscle
IGSF9	ENSG00000085552	Q9P2J2	0.6721	0.5287	skin
IL12RB1	ENSG00000096996	P42701	0.8087	0.4037	spleen
IL12RB2	ENSG00000081985	Q99665	0.779	0.5077	skeletal muscle
IL13RA2	ENSG00000123496	Q14627	0.7938	0.5348	pituitary gland
IL17RE	ENSG00000163701	Q8NFR9	0.7329	0.482	skin
IL18RAP	ENSG00000115607	Q95256	0.8142	0.4937	spleen
IL1R2	ENSG00000115590	P27930	0.6544	0.4119	spleen
IL1RAPL1	ENSG00000169306	Q9NZN1	0.8728	0.7725	spinal cord
IL1RAPL2	ENSG00000189108	Q9NP60	0.9197	0.9001	cerebral cortex
IL1RL2	ENSG00000115598	Q9HB29	0.7549	0.4599	skin
IL20RB	ENSG00000174564	Q6UXL0	0.8489	0.706	skin
IL21R	ENSG00000103522	Q9HBE5	0.8724	0.6412	spleen
IL22RA1	ENSG00000142677	Q8N6P7	0.8178	0.6222	pancreas
IL23R	ENSG00000162594	Q5VWK5	1	1	adrenal gland
IL2RA	ENSG00000134460	P01589	0.8174	0.6083	spleen
IL2RB	ENSG00000100385	P14784	0.8081	0.4812	spleen
IL31RA	ENSG00000164509	Q8NI17	0.9443	0.9138	skin
IL5RA	ENSG00000091181	Q01344	0.8179	0.6165	fallopian tube
IL7R	ENSG00000168685	P16871	0.6827	0.4251	lung
IL9R	ENSG00000124334	Q01113	0.9354	0.9094	spleen
ILDR1	ENSG00000145103	Q86SU0	0.6575	0.5789	salivary gland
IMPG2	ENSG00000081148	Q9BZV3	0.9391	0.645	fallopian tube
INSRR	ENSG00000027644	P14616	0.803	0.6557	kidney
ISLR2	ENSG00000167178	Q6UXK2	0.738	0.4434	basal ganglia
ITGA11	ENSG00000137809	Q9UKX5	0.7224	0.4267	endometrium
ITGA2B	ENSG00000005961	P08514	0.6981	0.4019	spleen
ITGA4	ENSG00000115232	P13612	0.7513	0.4335	spleen
ITGAD	ENSG00000156886	Q13349	0.9882	0.9413	spleen
ITGAE	ENSG00000083457	P38570	0.8396	0.6669	lung

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ITGB3	ENSG00000259207	P05106	0.6552	0.4053	thyroid gland
ITGB6	ENSG00000115221	P18564	0.7393	0.6172	urinary bladder
ITPR1PL1	ENSG00000198885	Q6GPH6	0.6527	0.407	cerebellum
IYD	ENSG00000009765	Q6PHW0	0.9648	0.9057	thyroid gland
IZUMO1	ENSG00000182264	Q8IYV9	0.8913	0.8269	lung
IZUMO2	ENSG00000161652	Q6UXV1	0.9062	0.9063	midbrain
JPH1	ENSG00000104369	Q9HDC5	0.7908	0.4363	skeletal muscle
JPH2	ENSG00000149596	Q9BR39	0.5991	0.4408	colon
JPH3	ENSG00000154118	Q8WXH2	0.7716	0.6968	cerebral cortex
JPH4	ENSG00000092051	Q96JJ6	0.6412	0.4812	cerebellum
KCNA1	ENSG00000111262	Q09470	0.9089	0.766	cerebellum
KCNA10	ENSG00000143105	Q16322	1	1	lung
KCNA2	ENSG00000177301	P16389	0.8284	0.6763	cerebellum
KCNA3	ENSG00000177272	P22001	0.7563	0.4651	lung
KCNA4	ENSG00000182255	P22459	0.8744	0.7585	basal ganglia
KCNA7	ENSG00000104848	Q96RP8	0.9897	0.9748	skeletal muscle
KCNB2	ENSG00000182674	Q92953	0.9062	0.8329	cerebral cortex
KCNC1	ENSG00000129159	P48547	0.9012	0.7854	cerebellum
KCNC2	ENSG00000166006	Q96PR1	0.888	0.8173	cerebral cortex
KCND2	ENSG00000184408	Q9NZV8	0.8448	0.605	cerebellum
KCNE1	ENSG00000180509	P15382	0.7597	0.5913	lung
KCNE2	ENSG00000159197	Q9Y6J6	0.9248	0.4234	stomach
KCNE4	ENSG00000152049	Q8WWG9	0.9104	0.7256	endometrium
KCNE5	ENSG00000176076	Q9UJ90	0.7705	0.5849	midbrain
KCNF1	ENSG00000162975	Q9H3M0	0.8289	0.7134	cerebral cortex
KCNG1	ENSG00000026559	Q9UIX4	0.7613	0.4602	endometrium
KCNG2	ENSG00000178342	Q9UJ96	0.8873	0.7214	hippocampal formation
KCNG3	ENSG00000171126	Q8TAE7	0.8506	0.7951	basal ganglia
KCNG4	ENSG00000168418	Q8TDN1	0.8584	0.8073	midbrain
KCNH1	ENSG00000143473	Q95259	0.9122	0.7757	cerebellum
KCNH3	ENSG00000135519	Q9ULD8	0.7507	0.5695	cerebral cortex
KCNH4	ENSG00000089558	Q9UQ05	0.9035	0.7533	basal ganglia
KCNH5	ENSG00000140015	Q8NCM2	0.9479	0.8973	cerebral cortex
KCNH6	ENSG00000173826	Q9H252	0.8628	0.783	pituitary gland
KCNH7	ENSG00000184611	Q9NS40	0.9514	0.9078	cerebellum
KCNH8	ENSG00000183960	Q96L42	0.7513	0.5737	pituitary gland
KCNJ1	ENSG00000151704	P48048	0.9594	0.778	kidney
KCNJ10	ENSG00000177807	P78508	0.7868	0.7152	spinal cord
KCNJ12	ENSG00000184185	Q14500	0.8054	0.4361	cerebellum
KCNJ13	ENSG00000115474	O60928	0.9437	0.6433	small intestine
KCNJ15	ENSG00000157551	Q99712	0.6926	0.5362	kidney
KCNJ16	ENSG00000153822	Q9NPI9	0.7824	0.5959	thyroid gland
KCNJ3	ENSG00000162989	P48549	0.8308	0.63	cerebellum
KCNJ4	ENSG00000168135	P48050	0.8502	0.7665	cerebral cortex
KCNJ5	ENSG00000120457	P48544	0.8368	0.5615	adrenal gland
KCNJ6	ENSG00000157542	P48051	0.97	0.9177	pituitary gland
KCNJ9	ENSG00000162728	Q92806	0.8281	0.7842	cerebellum
KCNK10	ENSG00000100433	P57789	0.7914	0.6725	cerebellum
KCNK12	ENSG00000184261	Q9HB15	0.8822	0.796	cerebellum
KCNK13	ENSG00000152315	Q9HB14	0.7547	0.5196	thyroid gland
KCNK16	ENSG00000095981	Q96T55	0.9896	0.978	pancreas

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KCNK17	ENSG00000124780	Q96T54	0.8081	0.5573	lung
KCNK18	ENSG00000186795	Q7Z418	1	1	basal ganglia
KCNK2	ENSG00000082482	O95069	0.7791	0.4459	adrenal gland
KCNK4	ENSG00000182450	Q9NYG8	0.8665	0.8379	basal ganglia
KCNK5	ENSG00000164626	Q95279	0.6005	0.4486	small intestine
KCNK9	ENSG00000169427	Q9NPC2	0.9534	0.8363	cerebellum
KCNMB1	ENSG00000145936	Q16558	0.6618	0.4612	colon
KCNMB2	ENSG00000197584	Q9Y691	0.6791	0.4511	ovary
KCNN1	ENSG00000105642	Q92952	0.8156	0.7028	hippocampal formation
KCNN2	ENSG00000080709	Q9H2S1	0.6898	0.412	adrenal gland
KCNN4	ENSG00000104783	O15554	0.6544	0.4194	salivary gland
KCNQ1	ENSG00000053918	P51787	0.6744	0.4019	adrenal gland
KCNQ2	ENSG00000075043	O43526	0.7884	0.7263	cerebellum
KCNQ3	ENSG00000184156	O43525	0.7617	0.5624	cerebral cortex
KCNQ4	ENSG00000117013	P56696	0.7056	0.4525	colon
KCNQ5	ENSG00000185760	Q9NR82	0.8074	0.5949	cerebral cortex
KCNS1	ENSG00000124134	Q96KK3	0.9432	0.719	cerebral cortex
KCNS2	ENSG00000156486	Q9ULS6	0.8596	0.5625	cerebral cortex
KCNT1	ENSG00000107147	Q5JUK3	0.8171	0.653	cerebellum
KCNT2	ENSG00000162687	Q6UVM3	0.8046	0.4677	ovary
KCNU1	ENSG00000215262	A8MYU2	1	1	prostate
KCNV1	ENSG00000164794	Q6PIU1	0.9393	0.8616	cerebral cortex
KCNV2	ENSG00000168263	Q8TDN2	0.9034	0.758	cerebellum
KEL	ENSG00000197993	P23276	0.7848	0.4941	spleen
KIAA0319	ENSG00000137261	Q5VV43	0.788	0.6989	cerebellum
KIAA1549	ENSG00000122778	Q9HCM3	0.6062	0.4282	lung
KIAA1549L	ENSG00000110427	Q6ZVL6	0.9258	0.8636	cerebral cortex
KIR2DL3	ENSG00000243772	P43628	0.9791	0.9614	spleen
KIR2DL4	ENSG00000189013	Q99706	0.963	0.8841	spleen
KIR3DL1	ENSG00000167633	P43629	0.9859	0.9806	spleen
KIR3DL2	ENSG00000240403	P43630	0.9665	0.9409	spleen
KIRREL3	ENSG00000149571	Q8IZU9	0.7495	0.6258	basal ganglia
KISS1R	ENSG00000116014	Q969F8	0.8586	0.6747	hypothalamus
KITLG	ENSG00000049130	P21583	0.6473	0.4232	urinary bladder
KL	ENSG00000133116	Q9UEF7	0.7532	0.4399	kidney
KLB	ENSG00000134962	Q86Z14	0.8862	0.7648	adipose tissue
KLHDC7A	ENSG00000179023	Q5VTJ3	0.8447	0.6983	kidney
KLRB1	ENSG00000111796	Q12918	0.8018	0.5329	spleen
KLRC1	ENSG00000134545	P26715	0.7857	0.4381	spleen
KLRC3	ENSG00000205810	Q07444	0.7624	0.6769	amygdala
KLRC4	ENSG00000183542	O43908	0.7215	0.4204	spleen
KLRD1	ENSG00000134539	Q13241	0.848	0.4559	spleen
KLRF1	ENSG00000150045	Q9NZS2	0.969	0.952	spleen
KLRF2	ENSG00000256797	D3W0D1	1	1	skin
KLRG2	ENSG00000188883	A4D1S0	0.8622	0.7762	thyroid gland
KREMEN2	ENSG00000131650	Q8NCW0	0.8559	0.6241	skin
LAG3	ENSG00000089692	P18627	0.7344	0.5106	ovary
LAMP5	ENSG00000125869	Q9UJQ1	0.7729	0.5246	basal ganglia
LAX1	ENSG00000122188	Q8IWW1	0.8727	0.69	spleen
LCT	ENSG00000115850	P09848	0.9832	0.9782	small intestine
LDLRAD1	ENSG00000203985	Q5T700	0.9468	0.8963	fallopian tube

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LEMD1	ENSG00000186007	Q68G75	0.8832	0.8108	cerebellum
LGR5	ENSG00000139292	O75473	0.7277	0.4632	skeletal muscle
LHCGR	ENSG00000138039	P22888	0.9324	0.827	ovary
LHFPL1	ENSG00000182508	Q86WI0	0.8639	0.7983	basal ganglia
LHFPL4	ENSG00000156959	Q7Z7J7	0.8374	0.7801	cerebellum
LHFPL5	ENSG00000197753	Q8TAF8	0.9173	0.8589	pancreas
LILRA1	ENSG00000104974	O75019	0.9039	0.5353	spleen
LILRA5	ENSG00000187116	A6NI73	0.8194	0.4406	spleen
LIM2	ENSG00000105370	P55344	1	1	spleen
LINGO2	ENSG00000174482	Q7L985	0.8828	0.687	endometrium
LINGO3	ENSG00000220008	P0C6S8	0.9056	0.8335	basal ganglia
LINGO4	ENSG00000213171	Q6UY18	0.9037	0.7406	skeletal muscle
LMTK3	ENSG00000142235	Q96Q04	0.6345	0.4375	cerebral cortex
LPAR3	ENSG00000171517	Q9UBY5	0.6669	0.5385	fallopian tube
LPAR4	ENSG00000147145	Q99677	0.8283	0.5001	ovary
LRFN2	ENSG00000156564	Q9ULH4	0.8782	0.7794	cerebral cortex
LRFN5	ENSG00000165379	Q96NI6	0.664	0.4403	cervix, uterine
LRIT2	ENSG00000204033	A6NDA9	0.9226	0.8081	skin
LRP1B	ENSG00000168702	Q9NZR2	0.647	0.5573	cerebral cortex
LRP2	ENSG00000081479	P98164	0.8131	0.7274	thyroid gland
LRRC15	ENSG00000172061	Q8TF66	0.9614	0.8791	skin
LRRC19	ENSG00000184434	Q9H756	0.946	0.9411	colon
LRRC26	ENSG00000184709	Q2I0M4	0.8847	0.7514	salivary gland
LRRC38	ENSG00000162494	Q5VT99	0.8952	0.7459	skeletal muscle
LRRC3B	ENSG00000179796	Q96PB8	0.7744	0.6552	cerebellum
LRRC3C	ENSG00000204913	A6NJW4	0.9688	0.9688	cervix, uterine
LRRC4C	ENSG00000148948	Q9HCJ2	0.6932	0.4728	cerebral cortex
LRRC52	ENSG00000162763	Q8N7C0	0.9566	0.9022	skeletal muscle
LRRC55	ENSG00000183908	Q6ZSA7	0.8304	0.7392	hypothalamus
LRRC8E	ENSG00000171017	Q6NSJ5	0.7422	0.5782	skin
LRRN3	ENSG00000173114	Q9H3W5	0.6609	0.4542	adrenal gland
LRRN4	ENSG00000125872	Q8WUT4	0.9221	0.8602	lung
LRRN4CL	ENSG00000177363	Q8ND94	0.5905	0.4325	endometrium
LRRTM1	ENSG00000162951	Q86UE6	0.7547	0.5412	basal ganglia
LRRTM2	ENSG00000146006	O43300	0.7881	0.6567	cerebral cortex
LRRTM3	ENSG00000198739	Q86VH5	0.8111	0.7531	cerebral cortex
LRRTM4	ENSG00000176204	Q86VH4	0.8543	0.698	cerebral cortex
LRTM1	ENSG00000144771	Q9HBL6	0.9824	0.968	spleen
LRTM2	ENSG00000166159	Q8N967	0.9029	0.8621	cerebral cortex
LTB	ENSG00000227507	Q06643	0.8217	0.4923	spleen
LTB4R2	ENSG00000213906	Q9NPC1	0.7607	0.5077	skin
LTK	ENSG00000062524	P29376	0.7801	0.457	lung
LVRN	ENSG00000172901	Q6Q4G3	0.9315	0.8118	adipose tissue
LY6G6F	ENSG00000204424	Q5SQ64	0.9668	0.9641	spleen
LY9	ENSG00000122224	Q9HBG7	0.8426	0.6146	spleen
MAG	ENSG00000105695	P20916	0.8025	0.6883	spinal cord
MARCO	ENSG0000019169	Q9UEW3	0.6975	0.4354	lung
MARVELD2	ENSG00000152939	Q8N4S9	0.637	0.4159	thyroid gland
MARVELD3	ENSG00000140832	Q96A59	0.7301	0.5439	small intestine
MAS1	ENSG00000130368	P04201	0.9253	0.9175	cerebral cortex
MAS1L	ENSG00000204687	P35410	0.8488	0.7765	adipose tissue
MBOAT1	ENSG00000172197	Q6ZNC8	0.6228	0.431	fallopian tube

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MC2R	ENSG00000185231	Q01718	0.9938	0.9897	adrenal gland
MC3R	ENSG00000124089	P41968	1	1	hypothalamus
MC4R	ENSG00000166603	P32245	0.9136	0.8421	hypothalamus
MC5R	ENSG00000176136	P33032	0.9422	0.9222	esophagus
MCEMP1	ENSG00000183019	Q8IX19	0.882	0.5879	lung
MCHR1	ENSG00000128285	Q99705	0.7825	0.6211	cerebral cortex
MCHR2	ENSG00000152034	Q969V1	0.9836	0.9584	cerebral cortex
MCOLN2	ENSG00000153898	Q8IZK6	0.7471	0.558	adrenal gland
MCOLN3	ENSG000000055732	Q8TDD5	0.7898	0.509	adrenal gland
MCTP2	ENSG00000140563	Q6DN12	0.6535	0.4107	spleen
MEGF10	ENSG00000145794	Q96KG7	0.7753	0.6594	spinal cord
MEGF11	ENSG00000157890	A6BM72	0.8685	0.7207	cerebellum
MEP1A	ENSG00000112818	Q16819	0.9728	0.9544	small intestine
MEP1B	ENSG00000141434	Q16820	0.9909	0.9817	small intestine
MFSD2B	ENSG00000205639	A6NFX1	0.946	0.9354	lung
MFSD4A	ENSG00000174514	Q8N468	0.7339	0.5104	stomach
MGAM	ENSG00000257335	O43451	0.9255	0.7566	small intestine
MGAM2	ENSG00000257743	Q2M2H8	0.9174	0.8786	small intestine
MIP	ENSG00000135517	P30301	0.902	0.8341	liver
MLC1	ENSG00000100427	Q15049	0.7313	0.6646	basal ganglia
MLNR	ENSG00000102539	O43193	0.9773	0.9605	stomach
MME	ENSG00000196549	P08473	0.654	0.4729	small intestine
MMP16	ENSG00000156103	P51512	0.6457	0.4364	cerebral cortex
MMP23B	ENSG00000189409	O75900	0.6536	0.4411	cervix, uterine
MMP24	ENSG00000125966	Q9Y5R2	0.816	0.485	cerebellum
MOG	ENSG00000204655	Q16653	0.8399	0.7949	spinal cord
MPIG6B	ENSG00000204420	O95866	0.8347	0.5921	skin
MPL	ENSG00000117400	P40238	0.8317	0.6667	lung
MRAP	ENSG00000170262	Q8TCY5	0.876	0.6914	adrenal gland
MRGPRD	ENSG00000172938	Q8TDS7	0.8727	0.798	colon
MRGPRE	ENSG00000184350	Q86SM8	0.8976	0.8023	cervix, uterine
MRGPRX2	ENSG00000183695	Q96LB1	0.9237	0.8639	skin
MRGPRX3	ENSG00000179826	Q96LB0	0.9564	0.9276	salivary gland
MS4A1	ENSG00000156738	P11836	0.8504	0.6232	spleen
MS4A10	ENSG00000172689	Q96PG2	0.9954	0.9891	small intestine
MS4A12	ENSG00000071203	Q9NXJ0	0.9965	0.9892	colon
MS4A15	ENSG00000166961	Q8N5U1	0.9965	0.991	lung
MS4A18	ENSG00000214782	Q3C1V0	1	1	small intestine
MS4A2	ENSG00000149534	Q01362	0.7345	0.622	lung
MS4A4E	ENSG00000214787	Q96PG1	0.7206	0.5617	adipose tissue
MS4A6E	ENSG00000166926	Q96DS6	0.92	0.8902	spleen
MS4A8	ENSG00000166959	Q9BY19	0.856	0.7624	small intestine
MSLN	ENSG00000162006	Q96KJ4	0.9565	0.9192	cerebral cortex
MST1R	ENSG00000164078	Q04912	0.6714	0.4971	skin
MTNR1A	ENSG00000168412	P48039	0.9691	0.9367	cerebellum
MTNR1B	ENSG00000134640	P49286	1	1	basal ganglia
MUC12	ENSG00000205277	Q9UKN1	0.971	0.959	colon
MUC13	ENSG00000173702	Q9H3R2	0.9732	0.9711	small intestine
MUC15	ENSG00000169550	Q8N387	0.8097	0.7161	thyroid gland
MUC16	ENSG00000181143	Q8WXI7	0.9092	0.8469	cervix, uterine
MUC17	ENSG00000169876	Q685J3	0.9923	0.9863	small intestine
MUC21	ENSG00000204544	Q5SSG8	0.9009	0.8207	esophagus

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MUC22	ENSG00000261272	E2RYF6	0.9665	0.962	esophagus
MUC4	ENSG00000145113	Q99102	0.8067	0.7488	colon
MUSK	ENSG00000030304	O15146	0.85	0.7775	skeletal muscle
MYADML2	ENSG00000185105	A6NDP7	0.9032	0.7632	skeletal muscle
MYMK	ENSG00000187616	A6NI61	0.9442	0.911	skeletal muscle
MYRFL	ENSG00000166268	Q96LU7	0.9084	0.6059	small intestine
NALCN	ENSG00000102452	Q8IZF0	0.6951	0.539	cerebellum
NAT8L	ENSG00000185818	Q8N9F0	0.6882	0.5521	cerebral cortex
NCAM2	ENSG00000154654	O15394	0.6635	0.4905	cerebral cortex
NCMAP	ENSG00000184454	Q5T1S8	0.7822	0.6116	salivary gland
NCR1	ENSG00000189430	O76036	0.9745	0.9226	spleen
NCR2	ENSG00000096264	O95944	1	1	small intestine
NCR3	ENSG00000204475	O14931	0.9293	0.7449	spleen
NECTIN4	ENSG00000143217	Q96NY8	0.7844	0.6951	skin
NETO1	ENSG00000166342	Q8TDF5	0.8387	0.7363	cerebral cortex
NIPAL1	ENSG00000163293	Q6NVV3	0.7922	0.626	skin
NIPAL4	ENSG00000172548	Q0D2K0	0.7756	0.5606	skin
NKAIN1	ENSG00000084628	Q4KMZ8	0.8836	0.7673	cerebellum
NKAIN2	ENSG00000188580	Q5VXU1	0.8243	0.7041	spinal cord
NKAIN3	ENSG00000185942	Q8N8D7	0.8113	0.7247	amygdala
NKAIN4	ENSG00000101198	Q8IVV8	0.7368	0.6749	basal ganglia
NKPD1	ENSG00000179846	Q17RQ9	0.9225	0.7191	skin
NLGN1	ENSG00000169760	Q8N2Q7	0.6491	0.4314	cerebellum
NLGN3	ENSG00000196338	Q9NZ94	0.6402	0.4813	cerebellum
NLGN4Y	ENSG00000165246	Q8NFFZ3	0.6204	0.438	cerebellum
NMBR	ENSG00000135577	P28336	0.9314	0.874	basal ganglia
NMUR1	ENSG00000171596	Q9HB89	0.6753	0.4881	spleen
NMUR2	ENSG00000132911	Q9GZQ4	0.8741	0.8221	spinal cord
NOX1	ENSG00000007952	Q9Y5S8	0.9707	0.8891	colon
NOX4	ENSG00000086991	Q9NPH5	0.7777	0.5032	kidney
NOX5	ENSG00000255346	Q96PH1	0.9474	0.6781	spleen
NPBWR2	ENSG00000125522	P48146	0.9783	0.9744	cerebral cortex
NPC1L1	ENSG00000015520	Q9UHC9	0.9191	0.612	liver
NPFFR1	ENSG00000148734	Q9GZQ6	0.9187	0.7889	cerebellum
NPFFR2	ENSG00000056291	Q9Y5X5	0.8887	0.8009	urinary bladder
NPHS1	ENSG00000161270	O60500	0.9659	0.9336	kidney
NPR3	ENSG00000113389	P17342	0.6036	0.4537	kidney
NPSR1	ENSG00000187258	Q6W5P4	1	1	hypothalamus
NPY2R	ENSG00000185149	P49146	0.8241	0.7534	hypothalamus
NPY5R	ENSG00000164129	Q15761	0.7209	0.4803	spleen
NRCAM	ENSG00000091129	Q92823	0.6811	0.4793	cerebral cortex
NRG3	ENSG00000185737	P56975	0.826	0.6709	cerebral cortex
NRG4	ENSG00000169752	Q8WWG1	0.9832	0.9614	cerebellum
NRSN1	ENSG00000152954	Q8IZ57	0.8056	0.7533	cerebral cortex
NRXN1	ENSG00000179915	Q9ULB1	0.7261	0.5362	cerebellum
NSG2	ENSG00000170091	Q9Y328	0.7634	0.675	basal ganglia
NTRK1	ENSG00000198400	P04629	0.6964	0.5304	basal ganglia
NTSR1	ENSG00000101188	P30989	0.9628	0.8823	colon
NTSR2	ENSG00000169006	O95665	0.8173	0.7803	basal ganglia
NUP210L	ENSG00000143552	Q5VU65	0.896	0.7679	pituitary gland
NXPE2	ENSG00000204361	Q96DL1	0.9528	0.9412	colon
ODF4	ENSG00000184650	Q2M2E3	0.9673	0.9521	esophagus

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OLR1	ENSG00000173391	P78380	0.7508	0.4809	lung
OPALIN	ENSG00000197430	Q96PE5	0.817	0.8016	hippocampal formation
OPN1SW	ENSG00000128617	P03999	0.7796	0.4889	endometrium
OPN4	ENSG00000122375	Q9UHM6	0.8161	0.6622	basal ganglia
OPN5	ENSG00000124818	Q6U736	1	1	heart muscle
OPRD1	ENSG00000116329	P41143	0.9706	0.9243	cerebral cortex
OPRK1	ENSG00000082556	P41145	0.8806	0.8114	basal ganglia
OPRM1	ENSG00000112038	P35372	0.9782	0.9532	cerebellum
OR10A3	ENSG00000170683	P58181	0.9688	0.9688	skin
OR10G3	ENSG00000169208	Q8NGC4	1	1	pituitary gland
OR10G4	ENSG00000254737	Q8NGN3	1	1	pancreas
OR10P1	ENSG00000175398	Q8NGE3	1	1	heart muscle
OR13A1	ENSG00000256574	Q8NGR1	0.8983	0.773	urinary bladder
OR14I1	ENSG00000189181	A6ND48	0.9778	0.9532	cerebral cortex
OR1F1	ENSG00000168124	O43749	0.9627	0.8976	cerebellum
OR1G1	ENSG00000183024	P47890	1	1	urinary bladder
OR2B11	ENSG00000177535	Q5JQS5	1	1	adipose tissue
OR2B6	ENSG00000124657	P58173	0.9556	0.9352	prostate
OR2H2	ENSG00000204657	O95918	0.8174	0.6287	cerebellum
OR2K2	ENSG00000171133	Q8NGT1	0.9578	0.9268	spinal cord
OR2L13	ENSG00000196071	Q8N349	0.8512	0.7924	spinal cord
OR2L2	ENSG00000203663	Q8NH16	0.9456	0.8467	spinal cord
OR2L3	ENSG00000198128	Q8NG85	0.9347	0.8943	cerebellum
OR2T10	ENSG00000184022	Q8NGZ9	1	1	kidney
OR2T33	ENSG00000177212	Q8NG76	0.9646	0.917	thyroid gland
OR2V2	ENSG00000182613	Q96R30	1	1	fallopian tube
OR2W3	ENSG00000238243	Q7Z3T1	0.8955	0.7434	thyroid gland
OR3A2	ENSG00000221882	P47893	0.8667	0.7823	pituitary gland
OR3A3	ENSG00000159961	P47888	0.9688	0.9688	cerebellum
OR4F17	ENSG00000176695	Q8NGA8	0.9688	0.9688	cervix, uterine
OR51B4	ENSG00000183251	Q9Y5P0	0.9688	0.9688	cervix, uterine
OR51E2	ENSG00000167332	Q9H255	0.9305	0.8026	prostate
OR52I1	ENSG00000232268	Q8NGK6	1	1	cerebellum
OR52N1	ENSG00000181001	Q8NH53	1	1	adipose tissue
OR52N4	ENSG00000181074	Q8NGI2	0.7646	0.5145	spleen
OR52N5	ENSG00000181009	Q8NH56	1	1	adipose tissue
OR5M11	ENSG00000255223	Q96RB7	1	1	urinary bladder
OR5P2	ENSG00000183303	Q8WZ92	0.9688	0.9688	skin
OR5P3	ENSG00000182334	Q8WZ94	0.9837	0.9785	skin
OR6B3	ENSG00000178586	Q8NGW1	0.951	0.9237	spinal cord
OR6T1	ENSG00000181499	Q8NGN1	1	1	pancreas
OR7A5	ENSG00000188269	Q15622	0.8354	0.7609	midbrain
OR7C1	ENSG00000127530	O76099	0.9114	0.7981	pituitary gland
OR9A2	ENSG00000179468	Q8NGT5	1	1	spinal cord
OR9G4	ENSG00000172457	Q8NGQ1	1	1	spleen
OTOF	ENSG00000115155	Q9HC10	0.9148	0.6449	basal ganglia
OTOP1	ENSG00000163982	Q7RTM1	0.9688	0.9688	esophagus
OTOP2	ENSG00000183034	Q7RTS6	0.977	0.9507	colon
OXGR1	ENSG00000165621	Q96P68	0.691	0.4619	salivary gland
OXTR	ENSG00000180914	P30559	0.8064	0.5619	breast
P2RX1	ENSG00000108405	P51575	0.7186	0.4753	urinary bladder

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P2RX2	ENSG00000187848	Q9UBL9	0.7587	0.5725	prostate
P2RX3	ENSG00000109991	P56373	0.973	0.9366	heart muscle
P2RX5	ENSG00000083454	Q93086	0.8053	0.5566	spleen
P2RX6	ENSG00000099957	O15547	0.8771	0.6345	skeletal muscle
P2RY10	ENSG00000078589	O00398	0.8813	0.6755	spleen
P2RY12	ENSG00000169313	Q9H244	0.742	0.5473	spinal cord
P2RY13	ENSG00000181631	Q9BPV8	0.8286	0.4452	spleen
P2RY2	ENSG00000175591	P41231	0.6519	0.4201	esophagus
P2RY4	ENSG00000186912	P51582	0.9151	0.7566	small intestine
P2RY8	ENSG00000182162	Q86VZ1	0.7504	0.4916	spleen
PANX3	ENSG00000154143	Q96QZ0	0.9688	0.9688	basal ganglia
PAQR5	ENSG00000137819	Q9NXX6	0.6807	0.4044	kidney
PAQR6	ENSG00000160781	Q6TCH4	0.6795	0.4179	spinal cord
PAQR9	ENSG00000188582	Q6ZVX9	0.9029	0.8086	liver
PCDH10	ENSG00000138650	Q9P2E7	0.7298	0.58	basal ganglia
PCDH11X	ENSG00000102290	Q9BZA7	0.8861	0.7904	basal ganglia
PCDH11Y	ENSG00000099715	Q9BZA8	0.8923	0.8333	hypothalamus
PCDH15	ENSG00000150275	Q96QU1	0.7674	0.726	hypothalamus
PCDH19	ENSG00000165194	Q8TAB3	0.7349	0.5018	hypothalamus
PCDH8	ENSG00000136099	O95206	0.8504	0.7786	cerebral cortex
PCDH9	ENSG00000184226	Q9HC56	0.6771	0.48	cerebral cortex
PCDHA1	ENSG00000204970	Q9Y5I3	0.7796	0.714	cerebral cortex
PCDHA10	ENSG00000250120	Q9Y5I2	0.7553	0.5153	cerebellum
PCDHA11	ENSG00000249158	Q9Y5I1	0.8909	0.6662	cerebellum
PCDHA12	ENSG00000251664	Q9UN75	0.9013	0.7021	cerebellum
PCDHA13	ENSG00000239389	Q9Y5I0	0.896	0.691	cerebellum
PCDHA2	ENSG00000204969	Q9Y5H9	0.8499	0.5857	cerebellum
PCDHA3	ENSG00000255408	Q9Y5H8	0.6995	0.4266	cerebellum
PCDHA4	ENSG00000204967	Q9UN74	0.8115	0.5177	cerebellum
PCDHA5	ENSG00000204965	Q9Y5H7	0.9149	0.7574	cerebellum
PCDHA6	ENSG00000081842	Q9UN73	0.8321	0.6082	cerebellum
PCDHA7	ENSG00000204963	Q9UN72	0.8732	0.5785	cerebellum
PCDHA8	ENSG00000204962	Q9Y5H6	0.9577	0.8634	cerebellum
PCDHA9	ENSG00000204961	Q9Y5H5	0.9608	0.9203	cerebellum
PCDHAC1	ENSG00000248383	Q9H158	0.8091	0.6529	cerebral cortex
PCDHAC2	ENSG00000243232	Q9Y5I4	0.8384	0.6097	cerebellum
PCDHB1	ENSG00000171815	Q9Y5F3	0.9688	0.9688	fallopian tube
PCDHGC5	ENSG00000240764	Q9Y5F6	0.7226	0.4376	cerebral cortex
PDCD1	ENSG00000188389	Q15116	0.7717	0.513	spleen
PDCD1LG2	ENSG00000197646	Q9BQ51	0.6972	0.4692	spleen
PDZK1IP1	ENSG00000162366	Q13113	0.6818	0.4854	kidney
PHEX	ENSG00000102174	P78562	0.803	0.5587	lung
PIANP	ENSG00000139200	Q8IYJ0	0.6193	0.469	basal ganglia
PIGR	ENSG00000162896	P01833	0.7579	0.6337	salivary gland
PIRT	ENSG00000233670	P0C851	0.7994	0.7286	hypothalamus
PKD2L1	ENSG00000107593	Q9P0L9	0.9205	0.7534	spleen
PKDREJ	ENSG00000130943	Q9NTG1	0.7059	0.4633	ovary
PKHD1	ENSG00000170927	P08F94	0.9624	0.9358	kidney
PKHD1L1	ENSG00000205038	Q86WI1	0.7997	0.5803	thyroid gland
PLD5	ENSG00000180287	Q8N7P1	0.8055	0.5177	cerebellum
PLP1	ENSG00000123560	P60201	0.6674	0.4246	spinal cord
PLPP4	ENSG00000203805	Q5VZY2	0.7349	0.615	hypothalamus

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PLPPR1	ENSG00000148123	Q8TBJ4	0.8028	0.7395	basal ganglia
PLPPR3	ENSG00000129951	Q6T4P5	0.793	0.7298	basal ganglia
PLPPR4	ENSG00000117600	Q7Z2D5	0.6792	0.5234	basal ganglia
PLPPR5	ENSG00000117598	Q32ZL2	0.8585	0.8181	cerebral cortex
PLSCR2	ENSG00000163746	Q9NRY7	0.9375	0.9375	fallopian tube
PMEL	ENSG00000185664	P40967	0.8657	0.6452	cervix, uterine
PNPLA3	ENSG00000100344	Q9NST1	0.8702	0.6163	liver
PODXL	ENSG00000128567	O00592	0.6626	0.4243	lung
POPDC2	ENSG00000121577	Q9HBU9	0.7461	0.4752	heart muscle
POPDC3	ENSG00000132429	Q9HBV1	0.8135	0.5652	skeletal muscle
PPP1R3A	ENSG00000154415	Q16821	0.9679	0.9599	skeletal muscle
PRLHR	ENSG00000119973	P49683	0.875	0.7717	pituitary gland
PRLR	ENSG00000113494	P16471	0.7547	0.5185	cervix, uterine
PROKR1	ENSG00000169618	Q8TCW9	0.9661	0.9512	adipose tissue
PROM1	ENSG00000007062	O43490	0.7574	0.4694	salivary gland
PROM2	ENSG00000155066	Q8N271	0.634	0.4492	esophagus
PRRG2	ENSG00000126460	O14669	0.5839	0.4027	pituitary gland
PRRG3	ENSG00000130032	Q9BZD7	0.642	0.4095	cerebral cortex
PRSS8	ENSG00000052344	Q16651	0.5791	0.491	salivary gland
PRTG	ENSG00000166450	Q2VWP7	0.8224	0.4546	thyroid gland
PSD2	ENSG00000146005	Q9BQI7	0.7797	0.7091	basal ganglia
PTCHD1	ENSG00000165186	Q96NR3	0.7997	0.5375	cerebellum
PTCHD4	ENSG00000244694	Q6ZW05	0.7552	0.5261	cervix, uterine
PTCRA	ENSG00000171611	Q6ISU1	0.9588	0.9093	spleen
PTGDR	ENSG00000168229	Q13258	0.713	0.4487	spleen
PTGDR2	ENSG00000183134	Q9Y5Y4	0.7024	0.4766	colon
PTGER1	ENSG00000160951	P34995	0.7926	0.5093	kidney
PTGER2	ENSG00000125384	P43116	0.6445	0.4674	cervix, uterine
PTGER3	ENSG00000050628	P43115	0.7204	0.4691	endometrium
PTGFR	ENSG00000122420	P43088	0.6227	0.4171	adipose tissue
PTH2R	ENSG00000144407	P49190	0.8732	0.7647	cerebral cortex
PTPRD	ENSG00000153707	P23468	0.6791	0.4507	cerebellum
PTPRH	ENSG00000080031	Q9HD43	0.7303	0.5359	small intestine
PTPRN	ENSG00000054356	Q16849	0.7354	0.6422	pituitary gland
PTPRO	ENSG00000151490	Q16827	0.6773	0.434	kidney
PTPRR	ENSG00000153233	Q15256	0.856	0.7111	cerebellum
PTPRT	ENSG00000196090	O14522	0.8515	0.6733	cerebral cortex
PTPRZ1	ENSG00000106278	P23471	0.6511	0.5129	amygdala
PVRIG	ENSG00000213413	Q6DKI7	0.8874	0.5625	spleen
QRFPR	ENSG00000186867	Q96P65	0.9068	0.7554	hypothalamus
RAET1E	ENSG00000164520	Q8TD07	0.828	0.6719	esophagus
RAET1G	ENSG00000203722	Q6H3X3	0.7884	0.5641	esophagus
RDH8	ENSG00000080511	Q9NYR8	1	1	kidney
RGR	ENSG00000148604	P47804	0.8858	0.7879	cerebral cortex
RGS9BP	ENSG00000186326	Q6ZS82	0.9115	0.6528	skeletal muscle
RHAG	ENSG00000112077	Q02094	0.8669	0.7284	spleen
RHBDL2	ENSG00000158315	Q9NX52	0.6836	0.5013	esophagus
RHBDL3	ENSG00000141314	P58872	0.6482	0.4579	cerebral cortex
RHCG	ENSG00000140519	Q9UBD6	0.8103	0.545	esophagus
RHD	ENSG00000187010	Q02161	0.87	0.5627	salivary gland
RHO	ENSG00000163914	P08100	0.9424	0.9299	cerebral cortex
RNF148	ENSG00000235631	Q8N7C7	0.7923	0.5921	cerebellum

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RNF175	ENSG00000145428	Q8N4F7	0.6971	0.4973	cerebral cortex
RNF182	ENSG00000180537	Q8N6D2	0.7571	0.5487	cerebellum
RNF222	ENSG00000189051	A6NCQ9	0.9192	0.8943	esophagus
RNF223	ENSG00000237330	E7ERA6	0.8643	0.8014	esophagus
RNF225	ENSG00000269855	M0QZC1	0.9065	0.8865	esophagus
RNFT2	ENSG00000135119	Q96EX2	0.7117	0.5322	cerebellum
ROBO2	ENSG00000185008	Q9HCK4	0.6406	0.4936	cerebral cortex
ROR2	ENSG00000169071	Q01974	0.5841	0.4226	colon
ROS1	ENSG00000047936	P08922	0.9881	0.9638	lung
RPRM	ENSG00000177519	Q9NS64	0.5866	0.417	cervix, uterine
RPRML	ENSG00000179673	Q8N4K4	0.8648	0.7156	basal ganglia
RRH	ENSG00000180245	O14718	0.8631	0.4221	cerebellum
RTL1	ENSG00000254656	A6NKG5	0.9374	0.8457	hypothalamus
RTP1	ENSG00000175077	P59025	0.9441	0.8899	cerebral cortex
RTP2	ENSG00000198471	Q5QGT7	1	1	skeletal muscle
RTP3	ENSG00000163825	Q9BQQ7	0.993	0.9768	liver
RTP5	ENSG00000188011	Q14D33	0.8361	0.7338	hypothalamus
RXFP1	ENSG00000171509	Q9HBX9	0.8567	0.7037	cerebral cortex
RXFP2	ENSG00000133105	Q8WXD0	0.8799	0.8391	fallopian tube
RXFP3	ENSG00000182631	Q9NSD7	0.9786	0.9659	adrenal gland
RXFP4	ENSG00000173080	Q8TDU9	0.9643	0.9402	colon
RYR2	ENSG00000198626	Q92736	0.9627	0.871	heart muscle
RYR3	ENSG00000198838	Q15413	0.5951	0.4241	basal ganglia
S1PR4	ENSG00000125910	O95977	0.8022	0.4641	spleen
S1PR5	ENSG00000180739	Q9H228	0.6682	0.4864	spinal cord
SCARA5	ENSG00000168079	Q6ZMJ2	0.5492	0.4026	urinary bladder
SCIMP	ENSG00000161929	Q6UWF3	0.8173	0.4138	spleen
SCN11A	ENSG00000168356	Q9UI33	0.8948	0.6915	spleen
SCN1A	ENSG00000144285	P35498	0.8186	0.735	cerebral cortex
SCN2A	ENSG00000136531	Q99250	0.8486	0.6979	cerebellum
SCN2B	ENSG00000149575	O60939	0.7773	0.5859	cerebellum
SCN3A	ENSG00000153253	Q9NY46	0.7189	0.5172	cerebellum
SCN3B	ENSG00000166257	Q9NY72	0.6808	0.438	cerebral cortex
SCN4A	ENSG00000007314	P35499	0.8932	0.7638	skeletal muscle
SCN5A	ENSG00000183873	Q14524	0.9173	0.6151	heart muscle
SCN8A	ENSG00000196876	Q9UQD0	0.8201	0.5781	cerebellum
SCN9A	ENSG00000169432	Q15858	0.7594	0.4311	hypothalamus
SCNN1A	ENSG00000111319	P37088	0.548	0.4393	salivary gland
SCNN1B	ENSG00000168447	P51168	0.6311	0.5117	colon
SCNN1G	ENSG00000166828	P51170	0.6329	0.5589	kidney
SCTR	ENSG00000080293	P47872	0.9467	0.89	pancreas
SDC1	ENSG00000115884	P18827	0.5779	0.4185	skin
SDK2	ENSG00000069188	Q58EX2	0.8226	0.6812	hypothalamus
SDR42E1	ENSG00000184860	Q8WUS8	0.7108	0.456	skin
SERP2	ENSG00000151778	Q8N6R1	0.6979	0.5313	cerebral cortex
SERTM1	ENSG00000180440	A2A2V5	0.7674	0.6298	fallopian tube
SEZ6	ENSG00000063015	Q53EL9	0.8311	0.747	cerebellum
SFT2D3	ENSG00000173349	Q58719	0.6865	0.405	pancreas
SGCG	ENSG00000102683	Q13326	0.832	0.6114	heart muscle
SGCZ	ENSG00000185053	Q96LD1	0.8585	0.6925	ovary
SHISA6	ENSG00000188803	Q6ZSJ9	0.649	0.486	cerebellum
SHISA7	ENSG00000187902	A6NL88	0.8127	0.7759	basal ganglia

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SHISA8	ENSG00000234965	B8ZZ34	0.9488	0.8338	cerebellum
SHISA9	ENSG00000237515	B4DS77	0.8116	0.7384	basal ganglia
SHISAL1	ENSG00000138944	Q3SXP7	0.681	0.4924	endometrium
SHISAL2A	ENSG00000182183	Q6UWV7	0.7881	0.5214	spleen
SHISAL2B	ENSG00000145642	A6NKW6	0.9603	0.9284	hypothalamus
SI	ENSG00000090402	P14410	0.9904	0.9854	small intestine
SIGLEC11	ENSG00000161640	Q96RL6	0.8878	0.6231	ovary
SIGLEC12	ENSG00000254521	Q96PQ1	0.9394	0.7528	spleen
SIGLEC15	ENSG00000197046	Q6ZMC9	0.9911	0.9862	urinary bladder
SIGLEC5	ENSG00000105501	O15389	0.9532	0.9368	spleen
SIGLEC6	ENSG00000105492	O43699	0.8224	0.646	small intestine
SIGLEC7	ENSG00000168995	Q9Y286	0.8046	0.4169	spleen
SIGLEC8	ENSG00000105366	Q9NYZ4	0.743	0.4954	spinal cord
SIRPG	ENSG00000089012	Q9P1W8	0.8825	0.6602	spleen
SIT1	ENSG00000137078	Q9Y3P8	0.8928	0.6672	spleen
SLAMF1	ENSG00000117090	Q13291	0.7965	0.5653	spleen
SLAMF6	ENSG00000162739	Q96DU3	0.8351	0.5582	spleen
SLAMF7	ENSG00000026751	Q9NQ25	0.7907	0.5499	spleen
SLAMF9	ENSG00000162723	Q96A28	0.9425	0.8772	adipose tissue
SLC10A1	ENSG00000100652	Q14973	0.9978	0.9918	liver
SLC10A2	ENSG00000125255	Q12908	0.9943	0.9893	small intestine
SLC10A4	ENSG00000145248	Q96EP9	0.8394	0.614	midbrain
SLC10A6	ENSG00000145283	Q3KNW5	0.841	0.6839	skin
SLC12A1	ENSG00000074803	Q13621	0.9869	0.9366	kidney
SLC12A3	ENSG00000070915	P55017	0.9958	0.9901	kidney
SLC12A5	ENSG00000124140	Q9H2X9	0.8487	0.7987	cerebellum
SLC13A1	ENSG00000081800	Q9BZW2	0.9683	0.9669	small intestine
SLC13A2	ENSG00000007216	Q13183	0.9256	0.884	small intestine
SLC13A4	ENSG00000164707	Q9UKG4	0.8562	0.7569	cerebral cortex
SLC13A5	ENSG00000141485	Q86YT5	0.9022	0.6773	liver
SLC14A1	ENSG00000141469	Q13336	0.6315	0.4145	urinary bladder
SLC14A2	ENSG00000132874	Q15849	0.9361	0.9258	adipose tissue
SLC15A1	ENSG00000088386	P46059	0.8795	0.7362	small intestine
SLC15A5	ENSG00000188991	A6NIM6	0.9375	0.9375	amygdala
SLC16A12	ENSG00000152779	Q6ZSM3	0.6857	0.4072	thyroid gland
SLC17A1	ENSG00000124568	Q14916	0.9793	0.9721	kidney
SLC17A2	ENSG00000112337	O00624	0.9982	0.9965	liver
SLC17A3	ENSG00000124564	O00476	0.9728	0.9559	kidney
SLC17A4	ENSG00000146039	Q9Y2C5	0.903	0.8915	liver
SLC17A6	ENSG00000091664	Q9P2U8	0.9082	0.8513	hypothalamus
SLC17A7	ENSG00000104888	Q9P2U7	0.7704	0.5291	cerebral cortex
SLC17A8	ENSG00000179520	Q8NDX2	0.9479	0.8546	small intestine
SLC18A1	ENSG00000036565	P54219	0.9637	0.8965	adrenal gland
SLC18A3	ENSG00000187714	Q16572	0.8954	0.8381	basal ganglia
SLC19A3	ENSG00000135917	Q9BZV2	0.7705	0.4211	adipose tissue
SLC1A2	ENSG00000110436	P43004	0.7774	0.6405	basal ganglia
SLC1A6	ENSG00000105143	P48664	0.8923	0.7955	cerebellum
SLC22A1	ENSG00000175003	O15245	0.9571	0.6527	liver
SLC22A10	ENSG00000184999	Q63ZE4	0.998	0.9962	liver
SLC22A11	ENSG00000168065	Q9NSA0	0.998	0.9943	kidney
SLC22A12	ENSG00000197891	Q96S37	0.9979	0.9948	kidney
SLC22A13	ENSG00000172940	Q9Y226	0.9789	0.944	kidney

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SLC22A14	ENSG00000144671	Q9Y267	0.8723	0.5431	cerebellum
SLC22A16	ENSG00000004809	Q86VW1	0.9443	0.8789	endometrium
SLC22A2	ENSG00000112499	O15244	0.9918	0.9606	kidney
SLC22A24	ENSG00000197658	Q8N4F4	0.9837	0.9785	kidney
SLC22A25	ENSG00000196600	Q6T423	1	1	liver
SLC22A6	ENSG00000197901	Q4U2R8	0.9426	0.8424	kidney
SLC22A7	ENSG00000137204	Q9Y694	0.9716	0.9457	liver
SLC22A8	ENSG00000149452	Q8TCC7	0.987	0.9668	kidney
SLC22A9	ENSG00000149742	Q8IVM8	0.9886	0.9808	liver
SLC23A3	ENSG00000213901	Q6PIS1	0.8232	0.5588	small intestine
SLC24A2	ENSG00000155886	Q9UI40	0.7915	0.7538	cerebral cortex
SLC24A4	ENSG00000140090	Q8NFF2	0.8115	0.6285	midbrain
SLC26A10	ENSG00000135502	Q8NG04	0.9414	0.8737	cerebellum
SLC26A3	ENSG00000091138	P40879	0.9514	0.8919	colon
SLC26A4	ENSG00000091137	O43511	0.9328	0.6563	thyroid gland
SLC26A5	ENSG00000170615	P58743	0.8818	0.7215	cerebellum
SLC26A8	ENSG00000112053	Q96RN1	0.9001	0.7564	cerebellum
SLC26A9	ENSG00000174502	Q7LBE3	0.9174	0.86	stomach
SLC27A2	ENSG00000140284	O14975	0.7567	0.459	liver
SLC27A6	ENSG00000113396	Q9Y2P4	0.6736	0.4638	adrenal gland
SLC28A1	ENSG00000156222	O00337	0.9411	0.9056	liver
SLC28A2	ENSG00000137860	O43868	0.9682	0.9388	small intestine
SLC28A3	ENSG00000197506	Q9HAS3	0.7948	0.685	salivary gland
SLC2A14	ENSG00000173262	Q8TDB8	0.8233	0.5152	adrenal gland
SLC2A2	ENSG00000163581	P11168	0.9653	0.9472	liver
SLC30A10	ENSG00000196660	Q6XR72	0.9271	0.802	liver
SLC30A3	ENSG00000115194	Q99726	0.8956	0.7413	cerebral cortex
SLC30A8	ENSG00000164756	Q8IWU4	0.9525	0.7575	pancreas
SLC34A1	ENSG00000131183	Q06495	0.997	0.9946	kidney
SLC34A2	ENSG00000157765	O95436	0.8391	0.6956	lung
SLC34A3	ENSG00000198569	Q8N130	0.9051	0.7644	kidney
SLC35D3	ENSG00000182747	Q5M8T2	0.9487	0.9103	basal ganglia
SLC35F1	ENSG00000196376	Q5T1Q4	0.7235	0.4976	cerebral cortex
SLC35F2	ENSG00000110660	Q8IXU6	0.9183	0.8644	skin
SLC35F3	ENSG00000183780	Q8IY50	0.7873	0.5775	cerebellum
SLC35F4	ENSG00000151812	A4IF30	0.9186	0.7746	cerebellum
SLC35G1	ENSG00000176273	Q2M3R5	0.7156	0.4045	small intestine
SLC36A2	ENSG00000186335	Q495M3	0.9742	0.9648	skeletal muscle
SLC38A4	ENSG00000139209	Q969I6	0.9105	0.6666	liver
SLC38A8	ENSG00000166558	A6NNN8	0.8913	0.8174	amygdala
SLC39A12	ENSG00000148482	Q504Y0	0.8546	0.8098	cerebral cortex
SLC39A2	ENSG00000165794	Q9NP94	0.8842	0.812	skin
SLC39A4	ENSG00000147804	Q6P5W5	0.8474	0.6092	small intestine
SLC39A5	ENSG00000139540	Q6ZMH5	0.8671	0.7687	pancreas
SLC3A1	ENSG00000138079	Q07837	0.859	0.6149	kidney
SLC44A4	ENSG00000204385	Q53GD3	0.6719	0.5517	colon
SLC46A1	ENSG00000076351	Q96NT5	0.7397	0.4087	adrenal gland
SLC46A2	ENSG00000119457	Q9BY10	0.9172	0.8199	skin
SLC47A2	ENSG00000180638	Q86VL8	0.8774	0.7711	kidney
SLC4A1	ENSG000000004939	P02730	0.946	0.8938	kidney
SLC4A10	ENSG00000144290	Q6U841	0.8472	0.7795	cerebral cortex
SLC4A11	ENSG00000088836	Q8NBS3	0.706	0.418	thyroid gland

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SLC4A4	ENSG00000080493	Q9Y6R1	0.6167	0.4004	pancreas
SLC4A8	ENSG00000050438	Q2Y0W8	0.7774	0.602	pituitary gland
SLC4A9	ENSG00000113073	Q96Q91	0.9813	0.8701	kidney
SLC51A	ENSG00000163959	Q86UW1	0.7634	0.4172	small intestine
SLC51B	ENSG00000186198	Q86UW2	0.8555	0.5823	small intestine
SLC52A1	ENSG00000132517	Q9NWF4	0.89	0.744	small intestine
SLC5A1	ENSG00000100170	P13866	0.8558	0.7111	small intestine
SLC5A10	ENSG00000154025	A0PJK1	0.9252	0.7081	kidney
SLC5A11	ENSG00000158865	Q8WVW8	0.8487	0.7541	spinal cord
SLC5A12	ENSG00000148942	Q1EHB4	0.9475	0.9131	kidney
SLC5A2	ENSG00000140675	P31639	0.9936	0.9738	kidney
SLC5A4	ENSG00000100191	Q9NY91	0.7273	0.4623	small intestine
SLC5A5	ENSG00000105641	Q92911	0.9076	0.8553	stomach
SLC5A7	ENSG00000115665	Q9GZV3	0.8539	0.7331	colon
SLC5A8	ENSG00000256870	Q8N695	0.9279	0.8441	thyroid gland
SLC5A9	ENSG00000117834	Q2M3M2	0.9427	0.8587	small intestine
SLC6A1	ENSG00000157103	P30531	0.6343	0.4589	cerebral cortex
SLC6A11	ENSG00000132164	P48066	0.8041	0.6978	midbrain
SLC6A12	ENSG00000111181	P48065	0.6914	0.5438	kidney
SLC6A13	ENSG0000010379	Q9NSD5	0.796	0.5954	kidney
SLC6A15	ENSG00000072041	Q9H2J7	0.7513	0.5994	cerebellum
SLC6A17	ENSG00000197106	Q9H1V8	0.7883	0.6932	cerebral cortex
SLC6A18	ENSG00000164363	Q96N87	0.9949	0.9913	kidney
SLC6A19	ENSG00000174358	Q695T7	0.9624	0.9351	small intestine
SLC6A2	ENSG00000103546	P23975	0.859	0.7225	adrenal gland
SLC6A20	ENSG00000163817	Q9NP91	0.8719	0.6457	small intestine
SLC6A3	ENSG00000142319	Q01959	0.9714	0.8467	midbrain
SLC6A4	ENSG00000108576	P31645	0.946	0.814	lung
SLC6A5	ENSG00000165970	Q9Y345	0.9439	0.9368	cerebellum
SLC6A7	ENSG00000011083	Q99884	0.899	0.8075	cerebellum
SLC7A10	ENSG00000130876	Q9NS82	0.8027	0.6743	adipose tissue
SLC7A11	ENSG00000151012	Q9UPY5	0.63	0.4702	basal ganglia
SLC7A13	ENSG00000164893	Q8TCU3	1	1	kidney
SLC7A3	ENSG00000165349	Q8WY07	0.845	0.6827	endometrium
SLC7A9	ENSG00000021488	P82251	0.9136	0.5972	small intestine
SLC8A1	ENSG00000183023	P32418	0.6777	0.4375	heart muscle
SLC8A2	ENSG00000118160	Q9UPR5	0.8022	0.6044	cerebellum
SLC8A3	ENSG00000100678	P57103	0.7723	0.6112	skeletal muscle
SLC9A2	ENSG00000115616	Q9UBY0	0.8239	0.6318	colon
SLC9A3	ENSG00000066230	P48764	0.8074	0.6262	colon
SLC9A4	ENSG00000180251	Q6A114	0.9693	0.9209	stomach
SLC9A5	ENSG00000135740	Q14940	0.744	0.4137	cerebellum
SLC9C2	ENSG00000162753	Q5TAH2	0.981	0.9527	fallopian tube
SLCO1A2	ENSG00000084453	P46721	0.8043	0.7425	hippocampal formation
SLCO1B1	ENSG00000134538	Q9Y6L6	0.9984	0.9969	liver
SLCO1B3	ENSG00000111700	Q9NPD5	0.9687	0.9183	liver
SLCO1C1	ENSG00000139155	Q9NYB5	0.8438	0.7821	basal ganglia
SLCO4C1	ENSG00000173930	Q6ZQN7	0.9158	0.8424	kidney
SLCO5A1	ENSG00000137571	Q9H2Y9	0.8988	0.7538	skeletal muscle
SLITRK1	ENSG00000178235	Q96PX8	0.8578	0.7875	cerebral cortex
SLITRK2	ENSG00000185985	Q9H156	0.7748	0.6447	basal ganglia

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SLITRK3	ENSG00000121871	O94933	0.7512	0.5757	fallopian tube
SLITRK4	ENSG00000179542	Q8IW52	0.8654	0.7019	adrenal gland
SLITRK5	ENSG00000165300	O94991	0.7519	0.5736	cerebral cortex
SLITRK6	ENSG00000184564	Q9H5Y7	0.8474	0.6578	urinary bladder
SMCO2	ENSG00000165935	A6NFE2	0.8776	0.7093	esophagus
SMCO3	ENSG00000179256	A2RU48	0.7385	0.5721	kidney
SMIM13	ENSG00000224531	P0DJ93	0.847	0.5643	skin
SMIM18	ENSG00000253457	P0DKX4	0.8321	0.7796	cerebellum
SMIM2	ENSG00000139656	Q9BVV6	0.9062	0.9063	colon
SMIM22	ENSG00000267795	K7EJ46	0.6129	0.4946	colon
SMIM23	ENSG00000185662	A6NLE4	1	1	cervix, uterine
SMIM24	ENSG00000095932	O75264	0.8306	0.6255	small intestine
SMIM28	ENSG00000262543	A0A1B0GU29	0.991	0.986	colon
SMIM3	ENSG00000256235	Q9BZL3	0.708	0.4962	adipose tissue
SMIM6	ENSG00000259120	P0DI80	0.7229	0.5605	kidney
SMLR1	ENSG00000256162	H3BR10	0.9746	0.9539	liver
SNORC	ENSG00000182600	Q6UX34	0.6868	0.406	spinal cord
SOGA3	ENSG00000214338	Q5TF21	0.7834	0.5599	spinal cord
SORCS3	ENSG00000156395	Q9UPU3	0.7995	0.697	basal ganglia
SPACA3	ENSG00000141316	Q8IXA5	0.9871	0.9361	pancreas
SPATA9	ENSG00000145757	Q9BWV2	0.9056	0.8257	adipose tissue
SPEM2	ENSG00000184560	Q0P670	0.9688	0.9688	breast
SPN	ENSG00000197471	P16150	0.786	0.4488	spleen
SPNS3	ENSG00000182557	Q6ZMD2	0.8849	0.7488	spinal cord
SPPL2C	ENSG00000185294	Q8IUH8	0.9759	0.9403	cerebellum
SSTR4	ENSG00000132671	P31391	0.948	0.9021	cerebellum
SSTR5	ENSG00000162009	P35346	0.9367	0.8741	pituitary gland
STAB2	ENSG00000136011	Q8WWQ8	0.9187	0.6395	spleen
STEAP1B	ENSG00000105889	Q6NZ63	0.6547	0.4009	spinal cord
STOML3	ENSG00000133115	Q8TAV4	0.9196	0.8472	fallopian tube
STRA6	ENSG00000137868	Q9BX79	0.8656	0.6643	cervix, uterine
STX1B	ENSG00000099365	P61266	0.8113	0.5745	cerebellum
STYK1	ENSG00000060140	Q6J9G0	0.6264	0.5154	prostate
SUCNR1	ENSG00000198829	Q9BXA5	0.9052	0.7854	thyroid gland
SV2A	ENSG00000159164	Q7L0J3	0.6219	0.4022	cerebellum
SV2B	ENSG00000185518	Q7L1I2	0.8503	0.6858	cerebellum
SV2C	ENSG00000122012	Q496J9	0.9163	0.8381	basal ganglia
SVOP	ENSG00000166111	Q8N4V2	0.9699	0.95	cerebellum
SVOPL	ENSG00000157703	Q8N434	0.8676	0.6357	salivary gland
SYNDIG1	ENSG00000101463	Q9H7V2	0.6676	0.4729	cerebellum
SYNDIG1L	ENSG00000183379	A6NDD5	0.9032	0.652	basal ganglia
SYNGR3	ENSG00000127561	Q43761	0.7077	0.5612	hypothalamus
SYNGR4	ENSG00000105467	O95473	0.9533	0.7614	cerebellum
SYNPR	ENSG00000163630	Q8TBG9	0.8446	0.7911	basal ganglia
SYP	ENSG00000102003	P08247	0.6477	0.4304	cerebral cortex
SYT1	ENSG00000067715	P21579	0.7294	0.5434	cerebral cortex
SYT12	ENSG00000173227	Q8IV01	0.7991	0.5778	cerebellum
SYT13	ENSG0000019505	Q7L8C5	0.737	0.6057	cerebral cortex
SYT14	ENSG00000143469	Q8NB59	0.8711	0.7897	pituitary gland
SYT2	ENSG00000143858	Q8N9I0	0.9138	0.7227	cerebellum
SYT3	ENSG00000213023	Q9BQG1	0.8065	0.689	cerebellum
SYT5	ENSG00000129990	O00445	0.7731	0.6886	cerebral cortex

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SYT6	ENSG00000134207	Q5T7P8	0.8891	0.7647	hypothalamus
SYT8	ENSG00000149043	Q8NBV8	0.8319	0.7243	urinary bladder
SYT9	ENSG00000170743	Q86SS6	0.8437	0.6675	cerebellum
TAAR1	ENSG00000146399	Q96RJ0	1	1	fallopian tube
TACR1	ENSG00000115353	P25103	0.6837	0.4932	adipose tissue
TACR2	ENSG00000075073	P21452	0.7779	0.5533	colon
TACR3	ENSG00000169836	P29371	0.9453	0.8839	urinary bladder
TACSTD2	ENSG00000184292	P09758	0.6687	0.523	esophagus
TAS1R1	ENSG00000173662	Q7RTX1	0.7989	0.6518	spleen
TAS1R2	ENSG00000179002	Q8TE23	1	1	skin
TAS1R3	ENSG00000169962	Q7RTX0	0.7485	0.4049	spleen
TAS2R1	ENSG00000169777	Q9NYW7	0.9688	0.9688	basal ganglia
TAS2R10	ENSG00000121318	Q9NYW0	0.6199	0.4368	adrenal gland
TAS2R13	ENSG00000212128	Q9NYV9	1	1	cerebellum
TAS2R3	ENSG00000127362	Q9NYW6	0.8865	0.7373	cerebellum
TAS2R30	ENSG00000256188	P59541	0.9688	0.9688	cerebellum
TAS2R38	ENSG00000257138	P59533	1	1	small intestine
TAS2R46	ENSG00000226761	P59540	0.902	0.8341	cerebellum
TAS2R50	ENSG00000212126	P59544	0.9837	0.9785	cerebellum
TECRL	ENSG00000205678	Q5HYJ1	0.9769	0.9584	heart muscle
TEDDM1	ENSG00000203730	Q5T9Z0	0.9183	0.8644	cerebellum
TENM2	ENSG00000145934	Q9NT68	0.9495	0.8425	heart muscle
TENM4	ENSG00000149256	Q6N022	0.7156	0.436	ovary
TEX38	ENSG00000186118	Q6PEX7	0.8148	0.4081	pituitary gland
TFR2	ENSG00000106327	Q9UP52	0.9643	0.8723	liver
TGFBR3L	ENSG00000260001	H3BV60	0.9326	0.6601	pituitary gland
THSD7B	ENSG00000144229	Q9C0I4	0.7062	0.5439	adipose tissue
TIGIT	ENSG00000181847	Q495A1	0.8507	0.5544	spleen
TIMD4	ENSG00000145850	Q96H15	0.8826	0.6597	spleen
TLCD2	ENSG00000185561	A6NGC4	0.5898	0.4102	adrenal gland
TLR10	ENSG00000174123	Q9BXR5	0.8935	0.6191	spleen
TM4SF19	ENSG00000145107	Q96DZ7	0.8477	0.7261	adipose tissue
TM4SF20	ENSG00000168955	Q53R12	0.9923	0.9855	small intestine
TM4SF4	ENSG00000169903	P48230	0.9259	0.8575	liver
TM4SF5	ENSG00000142484	O14894	0.9322	0.9018	liver
TMC1	ENSG00000165091	Q8TDI8	0.9347	0.8943	urinary bladder
TMC2	ENSG00000149488	Q8TDI7	0.9195	0.7355	cerebellum
TMC3	ENSG00000188869	Q7Z5M5	0.898	0.7965	vagina
TMC5	ENSG00000103534	Q6UXY8	0.7832	0.6727	small intestine
TMC7	ENSG00000170537	Q7Z402	0.6838	0.4708	spinal cord
TMCO5A	ENSG00000166069	Q8N6Q1	1	1	stomach
TMEFF1	ENSG00000241697	Q8IYR6	0.8178	0.7346	spinal cord
TMEFF2	ENSG00000144339	Q9UIK5	0.7204	0.6359	hypothalamus
TMEM114	ENSG00000232258	B3SHH9	0.978	0.9323	hypothalamus
TMEM132B	ENSG00000139364	Q14DG7	0.7703	0.5622	cerebral cortex
TMEM132C	ENSG00000181234	Q8N3T6	0.6529	0.4026	cervix, uterine
TMEM132D	ENSG00000151952	Q14C87	0.9078	0.825	cerebral cortex
TMEM132E	ENSG00000181291	Q6IEE7	0.8656	0.6522	cerebellum
TMEM145	ENSG00000167619	Q8NBT3	0.8388	0.6224	cerebellum
TMEM150B	ENSG00000180061	A6NC51	0.8425	0.6092	small intestine
TMEM151A	ENSG00000179292	Q8N4L1	0.7856	0.6987	spinal cord
TMEM151B	ENSG00000178233	Q8IW70	0.8271	0.654	cerebellum

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TMEM154	ENSG00000170006	Q6P9G4	0.7948	0.6227	esophagus
TMEM156	ENSG00000121895	Q8N614	0.8434	0.5216	spleen
TMEM163	ENSG00000152128	Q8TC26	0.7006	0.4622	cerebellum
TMEM169	ENSG00000163449	Q96HH4	0.7776	0.5315	cerebellum
TMEM171	ENSG00000157111	Q8WVE6	0.7866	0.652	colon
TMEM178B	ENSG00000261115	H3BS89	0.6796	0.4807	cerebral cortex
TMEM179	ENSG00000258986	Q6ZVK1	0.7476	0.6587	pituitary gland
TMEM184A	ENSG00000164855	Q6ZMB5	0.6816	0.5286	esophagus
TMEM190	ENSG00000160472	Q8WZ59	0.8984	0.7845	fallopian tube
TMEM196	ENSG00000173452	Q5HYL7	0.861	0.7818	hypothalamus
TMEM200A	ENSG00000164484	Q86VY9	0.6863	0.435	endometrium
TMEM200C	ENSG00000206432	A6NKL6	0.6991	0.4245	salivary gland
TMEM207	ENSG00000198398	Q6UWW9	1	1	kidney
TMEM210	ENSG00000185863	A6NLX4	0.9786	0.9659	salivary gland
TMEM211	ENSG00000206069	Q6ICI0	0.9603	0.9136	salivary gland
TMEM212	ENSG00000186329	A6NML5	0.9798	0.9663	fallopian tube
TMEM213	ENSG00000214128	A2RRL7	0.9546	0.9152	kidney
TMEM215	ENSG00000188133	Q68D42	0.9076	0.8553	cervix, uterine
TMEM217	ENSG00000172738	Q8N7C4	0.9101	0.7129	adrenal gland
TMEM229A	ENSG00000234224	B2RXF0	0.7703	0.6957	spinal cord
TMEM232	ENSG00000186952	C9JQI7	0.7741	0.4475	fallopian tube
TMEM233	ENSG00000224982	B4DJY2	0.9113	0.6351	skeletal muscle
TMEM235	ENSG00000204278	A6NFC5	0.8266	0.8022	spinal cord
TMEM239	ENSG00000198326	Q8WW34	0.9062	0.9063	breast
TMEM244	ENSG00000203756	Q5VVB8	0.9701	0.9212	pituitary gland
TMEM252	ENSG00000181778	Q8N6L7	0.7819	0.6137	kidney
TMEM253	ENSG00000232070	P0C7T8	0.8315	0.4339	small intestine
TMEM26	ENSG00000196932	Q6ZUK4	0.8377	0.6028	spleen
TMEM266	ENSG00000169758	Q2M3C6	0.9307	0.7627	cerebellum
TMEM270	ENSG00000175877	Q6UE05	0.9006	0.8384	fallopian tube
TMEM30B	ENSG00000182107	Q3MIR4	0.6797	0.5177	thyroid gland
TMEM40	ENSG00000088726	Q8WWA1	0.8446	0.7586	esophagus
TMEM45B	ENSG00000151715	Q96B21	0.6524	0.506	small intestine
TMEM52B	ENSG00000165685	Q4KMG9	0.9756	0.8869	kidney
TMEM61	ENSG00000143001	Q8N0U2	0.7623	0.4747	pituitary gland
TMEM63C	ENSG00000165548	Q9P1W3	0.7216	0.4869	cerebellum
TMEM72	ENSG00000187783	A0PK05	0.9636	0.9052	kidney
TMEM82	ENSG00000162460	A0PJX8	0.932	0.9166	liver
TMEM88B	ENSG00000205116	A6NKF7	0.8445	0.764	spinal cord
TMEM92	ENSG00000167105	Q6UXU6	0.8144	0.6211	small intestine
TMIE	ENSG00000181585	Q8NEW7	0.6817	0.4376	pituitary gland
TMIGD1	ENSG00000182271	Q6UXZ0	0.9739	0.9688	small intestine
TMIGD2	ENSG00000167664	Q96BF3	0.8122	0.5306	spleen
TMPRSS11B	ENSG00000185873	Q86T26	0.9249	0.9074	esophagus
TMPRSS11D	ENSG00000153802	O60235	0.9193	0.915	vagina
TMPRSS11E	ENSG00000087128	Q9UL52	0.8835	0.8607	esophagus
TMPRSS11F	ENSG00000198092	Q6ZWK6	0.924	0.9039	esophagus
TMPRSS13	ENSG00000137747	Q9BYE2	0.8273	0.6626	skin
TMPRSS15	ENSG00000154646	P98073	0.996	0.9928	small intestine
TMPRSS2	ENSG00000184012	O15393	0.6925	0.5755	prostate
TMPRSS4	ENSG00000137648	Q9NRS4	0.7954	0.7045	esophagus
TMPRSS5	ENSG00000166682	Q9H3S3	0.6262	0.4203	spinal cord

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
TMPRSS6	ENSG00000187045	Q8IU80	0.9345	0.788	liver
TMPRSS7	ENSG00000176040	Q7RTY8	1	1	pituitary gland
TMPRSS9	ENSG00000178297	Q7Z410	0.8902	0.624	spleen
TNF	ENSG00000232810	P01375	0.8333	0.5721	spleen
TNFRSF11A	ENSG00000141655	Q9Y6Q6	0.6687	0.4204	salivary gland
TNFRSF13B	ENSG00000240505	O14836	0.912	0.7522	spleen
TNFRSF13C	ENSG00000159958	Q96RJ3	0.8653	0.5196	spleen
TNFRSF17	ENSG00000048462	Q02223	0.8645	0.7154	spleen
TNFRSF18	ENSG00000186891	Q9Y5U5	0.6867	0.4385	cervix, uterine
TNFRSF8	ENSG00000120949	P28908	0.816	0.5995	adipose tissue
TNFRSF9	ENSG00000049249	Q07011	0.944	0.8963	spleen
TNFSF11	ENSG00000120659	O14788	0.9505	0.7957	small intestine
TNFSF14	ENSG00000125735	Q43557	0.7283	0.4245	liver
TNFSF15	ENSG00000181634	Q95150	0.7614	0.6706	salivary gland
TNFSF18	ENSG00000120337	Q9UNG2	1	1	esophagus
TNFSF8	ENSG00000106952	P32971	0.8072	0.4803	spleen
TNFSF9	ENSG00000125657	P41273	0.6988	0.4278	cervix, uterine
TNMD	ENSG00000000005	Q9H2S6	0.9036	0.7414	adipose tissue
TPBGL	ENSG00000261594	P0DKB5	0.8006	0.5435	basal ganglia
TPO	ENSG00000115705	P07202	0.8903	0.56	thyroid gland
TRABD2A	ENSG00000186854	Q86V40	0.8179	0.5502	ovary
TRAT1	ENSG00000163519	Q6PIZ9	0.8555	0.6536	spleen
TRDN	ENSG00000186439	Q13061	0.8566	0.6494	skeletal muscle
TREM1	ENSG00000124731	Q9NP99	0.8308	0.4849	lung
TREML1	ENSG00000161911	Q86YW5	0.8246	0.5072	spleen
TREML2	ENSG00000112195	Q5T2D2	0.9619	0.902	spleen
TRHDE	ENSG00000072657	Q9UKU6	0.64	0.4173	cerebellum
TRHR	ENSG00000174417	P34981	1	1	pituitary gland
TRPA1	ENSG00000104321	Q75762	0.9337	0.9021	urinary bladder
TRPC3	ENSG00000138741	Q13507	0.8383	0.6124	pituitary gland
TRPC4	ENSG00000133107	Q9UBN4	0.7854	0.4917	endometrium
TRPC5	ENSG00000072315	Q9UL62	0.9233	0.8898	cerebral cortex
TRPC6	ENSG00000137672	Q9Y210	0.7402	0.4443	lung
TRPC7	ENSG00000069018	Q9HCX4	0.9742	0.962	pituitary gland
TRPM1	ENSG00000134160	Q7Z4N2	0.9571	0.8828	skin
TRPM2	ENSG00000142185	O94759	0.6896	0.4051	cerebellum
TRPM3	ENSG00000083067	Q9HCF6	0.7819	0.5818	cerebellum
TRPM5	ENSG00000070985	Q9NZQ8	0.9048	0.8356	small intestine
TRPM6	ENSG00000119121	Q9BX84	0.8399	0.5254	colon
TRPM8	ENSG00000144481	Q7Z2W7	0.9742	0.9533	prostate
TRPV3	ENSG00000167723	Q8NET8	0.9569	0.8734	skin
TRPV4	ENSG00000111199	Q9HBA0	0.7071	0.5006	salivary gland
TSHR	ENSG00000165409	P16473	0.9723	0.7459	thyroid gland
TSPAN16	ENSG00000130167	Q9UKR8	0.913	0.8885	amygdala
TSPAN19	ENSG00000231738	P0C672	0.8803	0.7411	lung
TSPAN32	ENSG00000064201	Q96QS1	0.8633	0.6918	heart muscle
TSPO2	ENSG00000112212	Q5TGU0	0.9499	0.8765	spleen
TTYH1	ENSG00000167614	Q9H313	0.628	0.4757	basal ganglia
UGT2A3	ENSG00000135220	Q6UWM9	0.9119	0.8918	small intestine
UGT3A1	ENSG00000145626	Q6NUS8	0.9535	0.9401	kidney
UGT3A2	ENSG00000168671	Q3SY77	0.9703	0.9127	skin
UGT8	ENSG00000174607	Q16880	0.7692	0.5469	spinal cord

Gene symbol	Ensembl	Uniprot ID	Tau score	Gini score	Exemplary tissue/cellular localization of address target
UMODL1	ENSG00000177398	Q5DID0	0.9944	0.9905	fallopian tube
UNC5A	ENSG00000113763	Q6ZN44	0.8644	0.7438	cerebellum
UNC5D	ENSG00000156687	Q6UXZ4	0.8161	0.719	pituitary gland
UNC79	ENSG00000133958	Q9P2D8	0.8482	0.751	cerebellum
UNC80	ENSG00000144406	Q8N2C7	0.8425	0.7327	cerebellum
UNC93A	ENSG00000112494	Q86WB7	0.9474	0.8875	skin
UPK1A	ENSG00000105668	O00322	0.8966	0.7984	urinary bladder
UPK1B	ENSG00000114638	O75841	0.911	0.7294	urinary bladder
UPK2	ENSG00000110375	O00526	0.9681	0.8269	urinary bladder
UPK3B	ENSG00000243566	Q9BT76	0.8058	0.6621	adipose tissue
USH2A	ENSG00000042781	O75445	0.9853	0.97	liver
UTS2R	ENSG00000181408	Q9UKP6	0.941	0.8312	thyroid gland
VSIG1	ENSG00000101842	Q86XK7	0.9562	0.8105	stomach
VSIG10L	ENSG00000186806	Q86VR7	0.8816	0.7676	esophagus
VSIG2	ENSG00000019102	Q96IQ7	0.7017	0.4572	stomach
VSIG8	ENSG00000243284	P0DPA2	0.8588	0.6674	skin
VSTM1	ENSG00000189068	Q6UX27	0.9317	0.8411	pituitary gland
VSTM2B	ENSG00000187135	A6NLU5	0.7787	0.7502	cerebellum
VSTM5	ENSG00000214376	A8MXK1	0.7864	0.5312	hypothalamus
VTCN1	ENSG00000134258	Q7Z7D3	0.8401	0.7564	breast
WSCD2	ENSG00000075035	Q2TBF2	0.8128	0.5399	cerebellum
XCR1	ENSG00000173578	P46094	0.933	0.8323	skin
XG	ENSG00000124343	P55808	0.8147	0.6858	skin
XKR3	ENSG00000172967	Q5GH77	1	1	spleen
XKR4	ENSG00000206579	Q5GH76	0.7925	0.6118	colon
XKR7	ENSG00000260903	Q5GH72	0.954	0.8965	cerebellum
XKR9	ENSG00000221947	Q5GH70	0.7779	0.4034	small intestine
XKRX	ENSG00000182489	Q6PP77	0.8727	0.6825	skin
ZACN	ENSG00000186919	Q401N2	0.9783	0.9744	colon
ZDHHC17	ENSG00000186908	Q8IUH5	0.8693	0.773	cervix, uterine
ZP1	ENSG00000149506	P60852	0.9836	0.9712	pituitary gland
ZP2	ENSG00000103310	Q05996	0.994	0.9796	cerebellum
ZP4	ENSG00000116996	Q12836	1	1	ovary
ZPLD1	ENSG00000170044	Q8TCW7	0.9773	0.9605	kidney

ANDbody Structures

In general, an ANDbody can be any macromolecule, such as a polypeptide or protein that contains both an effector target binding site or binding domain, and an address target binding site or binding domain. The binding sites may be present on the same polypeptide chain or different polypeptide chains that are linked together, e.g., through disulfide bonds.

In some embodiments, the binding site for the effector target and the binding site for the address target of the ANDbody each comprise an antibody heavy chain and/or a light chain domain. In some embodiments the ANDbody comprises a first antibody variable domain which has binding specificity for the effector target and a second antibody variable domain that has binding specificity for the address target. In other embodiments the ANDbody comprises a first antigen binding site of an antibody, which first antigen binding site has binding specificity for the effector target, and a second antigen binding site of an antibody, which second antigen binding site has binding specificity for the

address target.

In some embodiments, the ANDbody may have the structure of an antibody molecule. The term "antibody" as used herein includes full-length antibodies and antigen binding antibody fragments (e.g., scFvs). In some embodiments, an antibody molecule has specificity for more than one, e.g., 2, 3, 4 antigens, e.g., the antibody molecule comprises a plurality of variable domain sequences, wherein a first variable domain sequence of the plurality has binding specificity for a first epitope (e.g., the effector target) and a second variable domain sequence of the plurality has binding specificity for a second epitope (e.g., the address target)

In some embodiments, the ANDbody is an antibody molecule that has an arm or domain that binds the effector target and an arm or domain that binds the address target. In embodiments, the ANDbody is an antibody molecule that comprises light chains that bind one of the effector target and address target, and heavy chains that bind the other of the effector target and address target.

In some embodiments, the ANDbody has the structure of an scFv, BsIgG, a BsAb fragment, a BiTE, a dual-affinity re-targeting protein (DART), a tandem diabody (TandAb), a diabody, an Fab2, a di-scFv, chemically linked F(ab')₂, an Ig molecule with 2, 3 or 4 different antigen binding sites, a DVI-IgG four-in-one, an ImmTac, an HSAbody, an IgG-IgG, a Cov-X-Body, an scFv1-PEG-scFv₂, an appended IgG, an DVD-IgG, an affibody, an affilin, an affimer, an affitin, an alphabody, an anticalin, an avimer, a DARPin, a Fynomer, a monobody, a nanoCLAMP, a bis-Fab, an Fv, a Fab, a Fab'-SH, a linear antibody, an scFv, an antibody with only a heavy chain (Humabody), an ScFab, an IgG antibody fragment, a single-chain variable region antibody, a single-domain heavy chain antibody, a bispecific triplebody, a BiKE, a CrossMAb, a dsDb, an scDb, tandem a dAb / VHH, a triple dAb VHH, a tetravalent dAb / VHH, a Fab-scFv, a Fab-Fv, or a DART-Fc, an adnectin, a Kunitz-type inhibitor, or a receptor decoy.

The affinity of the effector target binding site and address target binding site of an ANDbody for their respective binding partners may differ. In some embodiments the affinity of the first binding site to the therapeutic effector target it binds is weaker than the affinity of the second binding site to the address target. In some embodiments the affinity of the first binding site to the therapeutic effector target it binds is more than 2-fold, 3-fold, 4-fold, 5-fold, 10-fold, 15-fold, 20-fold, 50-fold, 100-fold, 200-fold, 500-fold, 1000-fold weaker than the affinity of the second binding site to the address target.

The terms "binding affinity" and "binding activity" refer to the tendency of a macromolecule, e.g., a polypeptide molecule, to bind or not to bind to a target. For purposes of the present invention, which combines two binding sites, the relative affinities of the two binding sites can be determined by, for example, measuring their respective affinities when each binding site is present on a common scaffold, such as in the form of a single chain antibody. Such a comparison allows a comparison of the affinities of two binding sites while eliminating any interference from other binding sites present on the macromolecule of the present invention.

Binding affinity may be quantified by determining the dissociation constant (K_d) for a polypeptide and its binder. A lower K_d is indicative of a higher affinity for a binding partner. Similarly, the specificity of binding of a polypeptide to its binding partner may be defined in terms of the

comparative dissociation constants (K_d) of the polypeptide for its binding partner as compared to the dissociation constant with respect to the polypeptide and another, non-target molecule.

The value of this dissociation constant can be determined by known methods. For example, the K_d may be established using a double-filter nitrocellulose filter binding assay such as that disclosed by Wong & Lohman (Proc. Natl. Acad. Sci. USA 90, 5428-5432, 1993). Other standard assays to evaluate the binding ability of ligands such as antibodies towards targets are known in the art, including for example, ELISAs, Western blots, RIAs, and flow cytometry analysis. The binding kinetics (e.g., binding affinity) of the antibody also can be assessed by standard assays known in the art, such as by BiacoreTM system analysis.

As an alternative to K_d , EC_{50} or IC_{50} may be used to determine relative affinities. In this context EC_{50} indicates the concentration at which a polypeptide achieves 50% of its maximum binding to a fixed quantity of binding partner. IC_{50} indicates the concentration at which a polypeptide inhibits 50% of the maximum binding of a fixed quantity of competitor to a fixed quantity of binding partner. In both cases, a lower level of EC_{50} or IC_{50} indicates a higher affinity for a target. The EC_{50} and IC_{50} values of an ANDbody binding site for its binding partner can both be determined by well-known methods, for example ELISA.

In some embodiments the K_d of therapeutic effector target binder might be higher than about 1pM, about 10pM, about 100pM, about 1nM, about 10nM, about 100nM, about 500nM, or about 1uM (e.g., may be between 1pM and 10pM, between 10 pM and 100pM, between 100 pM and 1nM, between 1 nM and 10 nM, between 10 nM and 100 nM, between 100 nM and 500nM, or between 500 nM and 1uM). In some embodiments the K_d of the address target binder might be less than about 1uM, about 500nM, about 100nM, about 10nM, about 1nM, about 100pM, about 10pM, or about 1pM (e.g., may be between 1uM and 500nM, between 500 nM and 100nM, between 100 nM and 10nM, between 10 nM and 1nM, between 1 nM and 100pM, between 100 pM and 10 pM, or between 10pM and 1pM). In some embodiments, the K_d for the therapeutic effector target binder may be about 6-fold, about 5-fold, about 4-fold, about 3-fold, or about 2-fold higher than the K_d for the address target binder.

In some embodiments the EC_{50} of therapeutic effector target binder might be higher than about 1pM, about 10pM, about 100pM, about 1nM, about 10nM, about 100nM, about 500nM, or about 1uM (e.g., may be between 1pM and 10pM, between 10 pM and 100pM, between 100 pM and 1nM, between 1 nM and 10 nM, between 10 nM and 100 nM, between 100 nM and 500nM, or between 500 nM and 1uM). In some embodiments the EC_{50} of the address target binder might be less than about 1uM, about 500nM, about 100nM, about 10nM, about 1nM, about 100pM, about 10pM, or about 1pM (e.g., may be between 1uM and 500nM, between 500 nM and 100nM, between 100 nM and 10nM, between 10 nM and 1nM, between 1 nM and 100pM, between 100 pM and 10 pM, or between 10pM and 1pM). In some embodiments, the EC_{50} for the therapeutic effector target binder may be about 6-fold, about 5-fold, about 4-fold, about 3-fold, or about 2-fold higher than the EC_{50} for the address target binder.

In some embodiments the IC_{50} of therapeutic effector target binder might be higher than about

1pM, about 10pM, about 100pM, about 1nM, about 10nM, about 100nM, about 500nM, or about 1uM (e.g., may be between 1pM and 10pM, between 10 pM and 100pM, between 100 pM and 1nM, between 1 nM and 10 nM, between 10 nM and 100 nM, between 100 nM and 500nM, or between 500 nM and 1uM). In some embodiments the IC₅₀ of the address target binder might be less than about 1uM, about 500nM, about 100nM, about 10nM, about 1nM, about 100pM, about 10pM, or about 1pM (e.g., may be between 1uM and 500nM, between 500 nM and 100nM, between 100 nM and 10nM, between 10 nM and 1nM, between 1 nM and 100pM, between 100 pM and 10 pM, or between 10pM and 1pM). In some embodiments, the IC₅₀ for the therapeutic effector target binder may be about 6-fold, about 5-fold, about 4-fold, about 3-fold, or about 2-fold higher than the IC₅₀ for the address target binder.

The cellular or tissue density of the effector target and address target bound by an ANDbody may differ. In embodiments, the density of the therapeutic effector target on a cell bound by the effector target binding site of an ANDbody is more than about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 10-fold, about 15-fold, about 20-fold, about 50-fold, about 100-fold, about 200-fold, about 500-fold, about 1000-fold, about 10,000-fold, about 100,000-fold less than the density of the address target on a cell bound by the address target binding site.

In some embodiments, the affinity of the first binding site to the therapeutic effector target it binds is about one-half ($\frac{1}{2}$) X K_d less than the affinity of the second binding site to the address target it binds and the density of the therapeutic effector target on a cell bound by the first binding site is about one-half ($\frac{1}{2}$) X K_d less than the density of the address target on a cell bound by the second binding site.

In some embodiments, the ANDbody has both the affinity and density parameters as described hereinabove.

In some embodiments the first binding site and second binding site in the ANDbody are directly joined to each other. By directly joined is meant that the first binding site coding sequences about the second binding site coding sequences and no sequences derived from other sequences (such as linkers) are present. In some embodiments the first binding site and second binding site in the ANDbody are not directly joined to each other.

An ANDbody, as disclosed herein, can be linked to an additional moiety or moieties, e.g., an extracellular component, an intracellular component, a soluble factor (e.g., an enzyme, hormone, cytokine, growth factor, toxin, venom, pollutant, etc.), or a transmembrane protein (e.g., a cell surface receptor).

Exemplary effector target and address target sequences for which ANDbodies of the present technology may have affinity are provided in Table 3 and in the Sequence Listing. In some instances, the sequences comprise full-length protein sequences and/or Fc fusion sequences with or without the signal peptide regions. In some embodiments, ANDbodies of the present technology include binding domains that bind address target or effector target proteins. In embodiments, binding domains of the present ANDbodies may bind protein sequences that include a signal peptide. In other embodiments, binding domains of the present ANDbodies may bind proteins that lack a signal protein. In some

- embodiments, binding domains of the present ANDbodies may bind full-length proteins. In other embodiments, binding domains of the present ANDbodies may bind protein fusions, such as full-length protein sequences, or peptide fragments thereof, with or without signal peptide regions, fused to other proteins, such as, for example, Fc sequences. In other embodiments, binding domains of the
- 5 present ANDbodies may bind proteins that comprise less than the full-length protein sequence, such as a peptide fragment of the address target or effector target.

Table 3: Exemplary Effector Target and Address Target Sequences

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
RAGE	H	Q15109	Uniprot	full length	MAAGTAVGAWVLVLSLWGAVVG AQNITARIGEPLVLKCKGAPKKPP QRLEWKLNTGRTEAWKVLSPQG GGPWDSVARVLPNGSLFLPAVGI QDEGIFRCQAMNRRNGKETKSNY RVRVYQIPGKPEIVDSASELTAGV PNKVGTCVSEGSYPAGTLSWHL DGKPLVPNEKGVSVKEQTRRH ETGLFTLQSELMVTPARGGDPRP TFSCSFSPGLPRHRALRTAPIQPR VWEPVPLEEVQLVVEPEGGA GGTVTLTCEVPAQPSPIHWMKD GVPLPLPSPVLILPEIGPDQGT YSCVATHSSHGPQESRAVSISIE PGEEGPTAGSVGGSGGLTLALAL GILGGLGTAALLIGVILWQRRQRR GEERKAPENQEEEEERAE EEPEAGESSTGGP	AA 1-22 is the signal peptide	SEQ ID NO: 1
RAGE	M	Q62151	Uniprot	full length	MPAGTAARAWVLVLALWGAVAG QONITARIGEPLVLKCKGAPKKPP QQLEWKLNTGRTEAWKVLSPQG GPWDSVARILPNSLLPATGIVD EGTFRCRATNRRGKEVKSNYRV RVYQIPGKPEIVDPASELTASVPN KVGTCVSEGSYPAGTLSWHL KLLIPDGKETLVKEETRRHPETGL FTLRSELTVIPTQGGTHPTFSCSF SLGLPRRRPLNTAPIQLRVREPG PPEGIQLLVEPEGGIVAPGGTVTL TCAISAQPPPVHWDGAPLPLA PSPVLLPEVGHEDGTYSCVAT HPSHGPQESPPVSIRVTETGDEG PAEGSVGESGLGLTLALALGILGGL GVVALLVGAILWRKRQPRREERK APESQDEEEERAE PENGAGGP	AA 1-22 is the signal peptide	SEQ ID NO: 2
RAGE-Fc, extracellular domain	H	Q15109 (RAGE - H) DB01281 (Abatacept)	uniprot (RAGE) DrugBank (Abatacept)	A23-A342 (RAGE)	aqnitari geplvlkckg apkkppqrle wklntrtea wkvlsppggg pwsdvarvlp ngslflpavgi qdegifrcq amnrrngketk snrvrvyqi pgkpeivdsaseltagvpnk vgtcvsegsy pagtlnswld gkplvpnekg vsvkeqtrrh petglftlqs elmvtpargg	Sequence is to full RAGE-Fc; RAGE is lowercas	SEQ ID NO: 3

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					dprptfscsf spglprhral rtapiqprvw epvpleevql vvepeggava pggvtltce vpaqpspqih wmkdgvplpl ppspvliipe igpqdqgtys cvathsshgp qesravsis iepggeegpta gsvggsglgt la QEPKSSDKTHTSPSPAPELLGG SSVFLFPPKPKDTLMISRTPEVTC VVVDVSHED PEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIA VEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK	e and from the accessio n ID at left, and the modified human IgG1 Fc region is in CAPS and is taken from the sequenc e for Abatacep t(DrugBa nk Online)	
RAGE -Fc, extrac ellular domai n	M	Q62151 (RAGE - M) DB01281 (Abatacep t)	uniprot (RAGE) DrugBan k (Abatacep t)	A23- A340 (RAGE)	gqnitarigeplvlsckgapkppqglewklnt grteawkvlsppqgpdwsvarilpngsllpat givdegtrfratnrrgkevksnyrvryqipgk peivdpaseltasvpnkvgtcvsegsypagtl swhldgkllipdgketlvkeetrrhpctglftrsel tvipqtggthptfscsfslgprrrplntapiqlrvre pgppegilqlvepeggivaaggvtltcaisaq pppqvhwikdgaplplapsplllpevghe gtyscvathpshgqpqesppvsirtetgdegp aegsvgesglgt QEPKSSDKTHTSPSPAPELLGG SSVFLFPPKPKDTLMISRTPEVTC VVVDVSHED PEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPA PIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIA VEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK	lower case is mouse RAGE- FC extracellu lar without signal peptide and the modified human IgG1 Fc region is in CAPS and is taken from the sequenc e for Abatacep t (DrugBan k Online)	SEQ ID NO: 4
Notch 2	H	Q04721	uniprot	full length	MPALRPALLWALLALWLCCAAPA HA LQCRDGYEPCVNEGMCVITYHNG TGYCKCPEGFLGEYCQHRDPCE KNRCQNGGTCVAQAMLGKATCR CASGFTGEDCQYSTSHPCFVSR PCLNGGTCHMLSRDTECTCQV GFTGKECQWTDACLSHPCANGS TCTTVANQFSCCKLTGFTGQKCE TDVNECDIPGHCQHGGTCLNLPG	1-25 is signal peptide; 26-1677 is extracellu lar; 1678- 1698 is transme mbrane;	SEQ ID NO: 5

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					SYQCQCPQGFTGQYCDLSLYVPC APSPCVNGGTCRQTGDFTFECN CLPGFEGSTCERNIDDCPNHRCQ NGGVCVDGVNTYNCRCPPQWT GQFCTEDVDECLLQPNACQNGG TCANRNGGYGCVCVNGWSGDD CSENIDDCAFASCTPGSTCIDRVA SFSCMCPEGKAGLLCHLDDACIS NPCHKGALCDTNPLNGQYICTCP QGYKGADCTEDVDECAMANSNP CEHAGKCVNTDGAHFHCECLKGY AGPRCEMDINECHSDPCQNDAT CLDKIGGFTCLCMPGFKGVHCEL EINECQSNPCVNNGQCVDKVNR FQCLCPPGFTGPVCQIDIDDCSST PCLNGAKCIDHPNGYECQCATGF TGVLC EENIDNCDPDPCHHGQC QDGIDSYTCICNPGYMGAI CSDQI DECYSSPCLNDGRCIDL VNGYQC NCQPGTSGVNCEINFDDCASNPC IHGICMDGINRYSCVCS PGFTGQ RCNIDIDECASNPCRK GATCINGV NGFRCICPEGPHHPSCYSQVNEC LSNPCIHGNCTGGLSGYKCLCDA GWVGINCEVDKNECLSNPCQNG GTC DNLVNGYRCTCKKGFKGYN CQVNIDECASNPCLNQGTCFDDI SGYTCHCVLPYTGKNCQTVLAPC SPNPCENAAVCKESP NFESYTCL CAPGWQGGQRCTIDIDE CISKPCM NHGLCHNTQGSYMCEC PPGFSG MDCEEDIDDCLANPCQNGGSCM DGVNTFSCLCLPGFTGDKCQTD MNECLSEPCKNGGTCS DYVNSY TCKCQAGFDGVHCENNINECTES SCFNNGT CVDGINSFSCLCPVGF TGSFCLHEINECSSHPCLNEGTC VDGLGTYRCSCPLGYTGKNCQTL VNLCSRSPCKNKGTCVQKKAES QCLCPSGWAGAYCDVPNVSCDI AASRRGVLVEHLCQHSGVCINAG NTHYCQCP LGYTGSYCEEQLDE CASNPCQH GATCSDFIGGYRCE CVPGYQGVNCEYEVDECQNQPC QNGGTCIDL VNHFKCSCPPGTRG LLCEENIDDCARGPHCLNGGQC MDRIGGYSCRCLPGFAGERCEG DINECLSNPCSSEGLDCIQLTND YLCVCRSAFTGRHCETFDVDCPQ MPCLNGGTCAVASNMPDGFICR CPPGFSGARCQSSCGQVKCRKG EQCVHTASGPRFCPSPRDCES GCASSPCQHGGSCHPQRQPPYY SCQCAPPFSGSRCELYTAPPSTP PATCLSQYCADKARDGVCDEAC	1699-2471 is cytoplasmic	

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					NSHACQWDGGDCSLTMENPWA NCSSPLPCWDYINNQCDELNTV ECLFDNFECQGNSTCKYDKYCA DHFKDNHCDQGCNSEECGWDG LDCAADQPENLAEGTLVIVVLMPP EQLLQDARSFLRALGTLHTNLRI KRDSQGELMVYPYGEKSAAMK KQRMTRRSLPGEQEVEVAGSKV FLEIDNRQCVQDSDFCFKNTDAA AALLASHAIQGTLSYPLVSVVSES LTPERTQ LLYLLAVAVVILFIILLGVIMAKRKR KHGSLWLPEGFTLRRDASNHKR REPVGQDAVGLKNLSVQVSEANL IGTGTSEHWVDEGPQPKVKAE DEALLSEDDPIDRRPWTQQHLE AADIRRTPSLALTPPQAEQEVVVL DVNVVRGPDGCTPLMLASLRGGS SDLSDEDEDAEDSSANIITDLVYQ GASLQAQTDRTGEMALHLAARYS RADAARKRLLDAGADANAQDNMG RCPLHAAVAADAQGVFQILIRNRV TDLARMNDGTTPLILAAARLAVEG MVAELINCQADVNAVDDHGKSAL HWAAAVNNVEATLLLLKNGANRD MQDNKEETPLFLAAREGSYEAAK ILLDHFANRDITDHMDRLPRDVAR DRMHHDIVRLLEYNVTPSPPGT VLTSALSPVICGPNRSFLSLKHTP MGKKSRRPSAKSTMPTSLPNLAK EAKDAKGSRRKSLSEKVQLSES SVTLSPVDSLESPTTYVSDTTSSP MITSPGILQASPNPMLATAAPPAP VHAQHLSFSLHEMQPLAHGAS TVLPVSQLLSHHHIVSPGSGSA GSLSRHPVPVPADWMNRMEVN ETQYNEMFGMVLAPAEGTHPGIA PQSRPPEGKHITTPREPLPIVTF QLIPKGSIAQPAGAPQPQSTCPP AVAGPLPTMYQIPEMARLPSVAF PTAMMPQQDGQVAQTILPAYHPF PASVGKYPTPPSQHSYASSNAAE RTPSHSGHLQGEHPYLTPSPESP DQWSSSSPHSASDWSVDVTSPT PGGAGGGQRGPGTHMSEPPHN NMQVYA		
Notch 2	M	O35516	uniprot	full length	MPALRPAALRALLWLWLOGAGP AHA LQCRGGQEPVCNEGTCVTHNG TGFCRCPEGFLGEYCQHRDPCE KNRCQNGGTCVPQGMLGKATCR CAPGFTGEDCQYSTSHPCFVSR PCQNGGTCHMLSRDTECTCQV GFTGKQCQWTDACLSHPCENG TCTSVASQFSCKCPAGLTGQKCE	1-25 is signal peptide; 26-1679 is extracellular; 1680-1700 is transmembrane	SEQ ID NO: 6

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					ADINECDIPGRCQHGGTCLNLPG SYRCQCPQGFTGQHCDSPYVPC APSPCVNGGTCRQTGDFTFECN CLPGFEGSTCERNIDDCPNHKCQ NGGVCVDGVNTYNCRCPPQWT GQFCTEDVDECLLPNACQNGG TCTNRNGGYGCVCVNGWSGDD CSENIDDCAYASCTPGSTCIDRVA SFSLCPEGKAGLLCHLDDACIS NPCHKGALCDTNPLNGQYICTCP QGYKGADCTEDVDECAMANSNP CEHAGKCVNTDGAHFHCECLKGY AGPRCEMDINECHSDPCQNDAT CLDKIGGFTCLCMPGFKGVHCEL EVNECQSNPCVNNGQCVDKVN FQCLCPPGFTGPVCQIDIDDCSST PCLNGAKCIDHPNGYECQCATGF TGILCDENIDNCDPDPCHHGQCQ DGIDSYTCICNPGYMGAIQSDQID ECYSSPCLNDGRICDLVNGYQCN CQPGTSGLNCEINFDDCASNPCM HGVCVDGINRYSCVCSGFTGQ RCNIDIDECASNPCRKGATCINDV NGFRCICPEGPHHPSCYSQVNEC LSNPCIHGNTGGLSGYKCLCDA GWVGVNCEVDKNECLSNPCQNG GTCNNLVNGYRCTCKKGFKGYN CQVNIDECASNPCLNQGTCTFDDV SGYTCHCMLPYTGKNCQTVLAP CSPNPCENAAVCKEAPNFESFSC LCAPGWQGRCTVDVDECISKP CMNNGVCHNTQGSYVCECPPGF SGMDCEEDINDCLANPCQNGGS CVDHVNTFSCQCHPGFIGDKCQT DMNECLSEPCKNGGTCSDYVNS YTCTCPAGFHGVHCENNIDECTE SSCFNGGTCVDGINSFSLCPVG FTGPFCLHDINECSSNPCLNAGT CVDGLGTYRCICPLGYTGKNCQT LVNLCSRSPCKNKGTVCQEKARP HCLCPPGWDGAYCDVLNVSCKA AALQKGVPEHLQHSIGICINAG NTHHCQCPLGYTGSYCEEQLDE CASNPCQHGATCNDFIGGYRCE CVPGYQGVNCEYEVEDECQNQPC QNGGTCIDLNVNHFKCSCPPGTRG LLCEENIDECAGGPHCLNGGQCV DRIGGYTCRCLPGFAGERCEGDI NECLSNPCSSEGLDCVQLKNY NCICRSFTGRHCETFLDVCPQK PCLNGGTCAVASNMPDGFICRCP PGFSGARCQSSCGQVKCRRGEQ CIHTDSGPRCFCLNPKDCESGCA SNPCQHGGTCYPQRQPPHYSCR CPPSFGGSHCELYTAPTSTPAT	mbrane; 1701- 2473 is cytoplas mic	

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					CQSQYCADKARDGICDEACNSH ACQWDGGDCSLTMEDPWANCT STLRWCWEYINNQCDEQCNTAECL FDNFECQRNSKTCKYDKYCADH FKDNHCDQGCNSEECGWGLD CASDQPENLAEGTLIIVVLLPPEQ LLQDSRSFLRALGTLHTNLRIKQ DSQGALMVYPYFGEKSAAMKKQ KMTRRSLPEEQEQEQEVIGSKIFL EIDNRQCVQDSQCFKNTDAAAA LLASHAIQGTLSYPLVSVFSELES PRNAQ LLYLLAVAVVILFFILLGVIMAKRK RKHGFLWLPFGFTLRDSSNHNK RREPVGQDAVGLKNLSVQVSEA NLIGSGTSEHWVDDEGPQPKKAK AEDEALLSEDDPIDRRPWTQQHL EAADIRHTPSLALTPPAEQEVVDV LDVNVVRGPDGCTPLMLASLRGG SSDLSDEDEDAEDSSANIITDLVY QGASLQAQTDRTGEMALHLAAR YSRADAAKRLLDAGADANAQDN MGRCPHAAVAADAQGVFQILIR NRVTDLARMNDGTTPLILAAARLA VEGMVAELINCQADVNAVDDHGK SALHWAAAVNNVEATLLLLKNGA NRDMQDNKEETPLFLAAREGSYE AAKILLDHFANRDITDHMDRLPRD VARDRMHHDIVRLLEYNVTPSP PGTVLTSALSPVLCGPNSFLSLK HTPMGKKARRPNTKSTMPSTLPN LAKEAKDAKGSRRKKCLNEKVQL SESSVTLSPVDSLESPHTYVSDA TSSPMITSPGILQASPTPLAAAA PAAPVHTQHLSFSNLHDMQPLA PGASTVLPSVSQLLSHHHIAPPGS SSAGSLGRLHPVPVPADWMNRV EMNETQYSEMFGMVLAPAEAGH PGIAAPQSRPPEGKHMSTQREPL PPIVTFQLIPKGSIAQAAGAPQTQ SSCPPAVAGPLPSMYQIPEMPRL PSVAFPTMMPQQEQQAQTIVP TYHPFPASVGKYPTPPSQHSYAS SNAAERTPSHGGHLQGEHPYLT SPESPDQWSSSSPHSASDWSDV TTSPTPGGGGGGQRGPGTHMSE PPHSNMQVYA		
Notch 2-Fc, extracellular domain	H	Q04721 (Notch2) DB01281 (Abatacept)	uniprot (Notch2) DrugBank (Abatacept)	A26-A1677 (Notch2)	lqcrdgyepcvnegmcvtyhngtgyckpe gflgeycqhrdpceknrcqnggtcvaqamlg katcrasgftgedcqystshpcfsrplngg tchmlsrctyectcqvgftgkccqwtadclshp cangstcttvanqfsccltqgtgkccetdvnc dipghcqhggtclnlpgsyqcqcpqgftgqyc dslyvpcapspcvnggtcrqtgdtfecncplpg fegstcernidcpnhrcqnggvcvdivntyn	Extracellular domain of Notch2 with abatacept Fc	SEQ ID NO: 7

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					crcppqwtgqfctedvdecllqpnacqnggtc anrnnggygcvcvngwsgddcseniddcfa sctpgstcidrvasfscmcpgekagllchdda cisnpchkgalcdtnplngqyictcpqgykga dctedvdecamansnpcehagkcvntdgaf hceclkgayagprcemdinechsdpcqndat cldkiggftclcmpgfkghceleinecqsnp vnngqcvdkvnrfqclcppgftgpcqjiddc sstpclngakcidhpngeyecqcatgftglcee nidncdpdpchhgqcdgidsyticnpgy mgaicsdqidecysspcldngrcidlvngyqc ncqpgtsgvnceinfddcasnpihgicmdgi nryscvcspgftgqrcnididecasnprkcat cingvngfricpegphhpscysqvneclsn cihgncgtglsykcldagwvngincevdkne clsnpcqnggtcdnlvngyrctckkgfkgync qvnidecasnplnggtcfddisgytchcvlpy tgkncqtlapcsnpncenaavckespnfes ytlcapgwqgqrcitidideciskpcmnhglc hntqgsymcecpvgfsgmdceediddclan pcqnggscmdgvntfscclpghtgdkcqt mneclsepcknggtcsdyvnsytckcagfd gvhcenninectesscfnggtcvdginsfclc pvgtgtsfclheinecsshpclnegtcvdglgty rcscplgytgkncqtlvnlcsrspcknkgtcvqk kaesqclcpsgwagaycdvpnvscdiaasrr gvlvehlcqhsgvcinagthycqplgytgs yceeqldecasnpqhgcatsdfgggyrcecv pgyqgvnceyevdecqnpqnggtcidlv nhfkscppgtrgllceeniddcargphclngg qcndriggyscrclpgfagercegdineclsn pcssegslcdiqltndylcvcrsaftgrhctfvd vcpqmpclnggtcavasmpdgifrcppgf sgarcqsscgvkcrkgeqcvhtasgprcf psprdcsgcasspcqhggschpqrqppyy scqcappfsgsrcelytappstppatclsqyca dkardgvcdeacnshacqwdggdcsltme npwancssplpcwdyinnqcdeicntveclfd nfecqgnsktckydycadhfkdnhcdqgc seecgwdgldcaadqpenlaegtllvivlmp peqlldarsflralgtllhnlrkrdsqgelmv pyygeksaamkkqrmtrslpgeqevag skvfleidnrqcvqdsdhcfkntdaaaallash aiqgtlsyplsvvsesltptqQEPKSSD KTHTSPPSPAPPELLGGSSVFLFPP KPKDTLMISRTPEVTCVVVDVSH EDPEVKFNWYVDGVEVHNAKTK PREEQYNSTYRVVSVLTVLHQD WLNKGKEYCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSRDEL KNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTTPVLDSDGSFF LYSKLTVDKSRWQQGNVFCSSV MHEALHNHYTQKSLSLSPGK		
Notch	M	O35516	uniprot	A26-	lqcrggqepcvnegtcvtyhngtgfcrcpegfl	Extracell	SEQ

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
2-Fc, extracellular domain		(Notch2) DB01281 (Abatacept)	(Notch2) DrugBank (Abatacept)	A1679 (Notch2)	geycqhrdpceknrcqnggtcvpqgmigkat crcapgtgedcqystshpcfvsrcqnggtc hmlsrqtyectcqvgftgkqcqwtadacishpc engstctsvasqfsckcpagltgkceadine cdipgrcqhggtclnlpgsyrcqcpqgftgqhc dspyvpcapspcvnggtcrqtdgffecncpl gfegstcerniddcpnhkcnnggvcdvgnvnt yncrcppqwtgqfctedvdecllqpnacqng gtctnrnggygcvcvngwsgddcseniddca yasctpgstcidvasfscclpegkagllchidd acisnpchkgalcdtnplngqyictcpqgykg adctedvdecamansnpcehagkcvntdg afhceclkgagprcemdinechsdpcqnd atcldkiggtclcmppgfkghcelevnecsqn pcvnnngqcvdkvnrfqclcppgftgpcqdid dcsstpcngakcidhpngeyccatgftgile denidncdpdpchhgqcdgidsyticnpg ymgaicsdqidecysspcldngrcldlvngyq cncqpgtsglnceinfddcasnpcmhgvcd ginryscvcsppgftgqrcnididecasnprkg atcindvngfricpepghhpscsysqvnecl npcihgntgglsykcldagwvgncevd kneclsnpcqnggtcnnlvngyrctckkgfkg yncqvndeasnpclnqgtcfddvsgytchc mlpytgkncqtlapcspnpcenaavckeap nfesfscclapgwqgkrctvdvdeciskpcm nngvchntqgsyvcecpfgsgmdceedin dclanpcqnggscvdhvnfscqchpgfigdk cqtdmneclsepcknggtcsdyvnsytctcp agfhgvhcennidectesscnggtcvdgins fscclpvgftgpfclhdinecssnpclnagtcvd glgtyrcicplgytgkncqtlvnlsrspcknkg cvqekarphclcppgwdgaycdvlnvscka aalqkgvpvehlcqhsqcinagnthhcqcp gytgsyceeqldecasnpqhgatecdfigg yrcecvpgyqgvnceyevdecqnpqcnq gtcidlvnhfkscppgtrgllceenidecaggp hclnggqcvdriggytcrclpgfagercegdin eclsnpcssegsldcvqlknynycicrsaftgr hctfldvcpqkpcldnggtcavasnmppdgfic rcppgfsqarqsscggqvkrrgeqcihtdsg prcfclnkdcesgcasnpqhggctypqrrq pphyscrppsfggshcelytaptstppatcq sqycadkardgicdeacnshacqwdggdcs ltmedpwantstlrcweyinnqcdeqcntae clfdnfecqrnsktckydycadhfkdnhcdq gcensecgwdglcdasdpnlaegtliivll ppeqlqdsrsflralgtllhnlrikqdsqgalmv ypyfgekzaamkkqkmtrslpeegeqeqe vigskifleidnrqcvqdsdqcfkntdaaaalla shaiqgtlsyplsvfselesprnaqQEPKS SDKTHTSPSPAPELLGGSSVFL FPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQ	ular domain of Notch2 with abatacept Fc	ID NO: 8

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					DWLNGKEYKCKVSNKALPAPIEK TISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDG SFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK		
Jagged-2-Fc	H	Q9Y219 (Jagged2) DB01281 (Abatacept)	Uniprot (Jagged2) DrugBank (Abatacept)	A27-A1080 (Jagged2)	arpmgyfelqlsalrnvngellsgaccdgdrtr raggcghdecptyvrvclkeyqakvtptgpc yghgatpvlggnsfypagaagdrararara ggdqdpglvvipqfawprstflveawdwn dtpneelliervshagminpedrwsllhfsgh vahlelqirvrdenyysatcnkfcprndffgh ytcdqygnkacmdgwmgkeckeavckqg cnllhggctvpgecrsygwqgrfdecvpyp gcvhgscevewqncetnwgllcdkdlnc gshhpctnggtcinaepdqyrctcpdgysgrn cekaehactsnpcanggschevpsgfehc psgwsqptcaldidecasnpcaaggtcvdq dgfecicpeqwgatcqlaneceqkpcnaf scknliggyycdpcpgwkginchinvnrcrg cqhggtckdlvngyqcvcprgfggrhcelerd ecasspchsnglcedladgfhchcpqgfspl cevdvdlcepspcrngarcynlegdyycacp ddfggkncsvprepcpggacrvldgcgsdag pgmpgtaasgvcgphgrcvspqpgnfsic dsfgtgytcheniddclgpcprnggtcidevda frfcpsgwegelcdtnpndclpdpchsrgrc ydlvndfycacddgwkgtchsrqcdaytc snggtcydsgdtfrcacppgwkgtcavakn ssclpncvnggtcvgsgasfscicrdgwegr tcthtntdcnplpcynggicvdivnwfrceca pgfagpdcridedcqqspcaygatcvdeing yrcscppragprcqviggrscwsgtptfph gsswvedcnsrclcdgrdcskvwgwkpc lagqpealsaqcplgqrclkapgqclrppe awgecgaeppstpcprsgldnncarlthf nrhvpqgttvgaicsgirsipatravardrll cdrassgasavevavsfspardlpdssligga ahaivaaitqrgnssllavtevkvetvtggsst QEPKSSDKTHTSPPSPAPELLGG SSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTTPVLD SDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLS PGK	Lower Case is Jagged-2 extracellular domain sequence without the signal peptide AA 24-1080. Upper case is Fc from Abatacept	SEQ ID NO: 9
UMOD	H	P07911	Uniprot	full length	MGQPSTWMLMVVVASWFITTA ATDTSEARWCSECHSNATCTED EAVTTCTCQEGFTGDGLTCVDLD ECAIPGAHNCSANSSCVNTPGSF SCVCPEGFRLSPGLGCTDVDECA	1-24 signal peptide; 25-614 uromodul	SEQ ID NO: 10

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					EPGLSHCHALATCVNVVGSYLCV CPAGYRGDGDWHCECSPGSCGP GLDCVPEGDALVCADPCQAHRTL DEYWRSTEYGEYACDIDLRGW YRFVGQGGARMAETCVPVLRN TAAPMWLNGTHPSSDEGIVSRKA CAHWSGHCCLDASVQVKACA GGYYVYNLTAPPECHLAYCTDPS SVEGTCEECSIDEDCKSNNGRW HCQCKQDFNITDISLLEHRLECGA NDMKVSLGKCQLKSLGFDKVF YLSDSRCSGFNDRDNRDWSV TPARDGPCGTVLRNETHATYSN TLYLADEIIIRDNIKINFACSYPLD MKVSLKTALQPMVSALNIRVGGT GMFTVRMALFQTPSYTQPYQGS SVTLSTEAFLYVGTMLDGGDLR FALLMTNICYATPSSNATDPLKYFII QDRCPHTRDSTIQVVENGESSQ GRFSVQMFRFAGNYDLVYLHCE VYLCDTMNEKCKPTCSGTRFRS GSVIDQSRVLNLPITRKGQVQATV SRAFSSLGLLKVWLPILLSATLTL TFQ	in; note: 25-587 is secreted form; 615-640 is cleaved in mature form	
UMOD	M	Q91X17	Uniprot	full length	MGIPLTWMLLVMMVTSWFTLAEA SNSTEARRCSECHNNATCTVDG VVTTCSCQTGTGDGLVCEDMD ECATPWTHNCSNSSCVNTPGSF KCSCQDGFRLTPELSCTDVDECS EQGLSNCHALATCVNTEGDYLCV CPEGFTGDGWYCECSPGSCEPG LDCLPQGPDPGLVCQDPCNTYET LTEYWRSTEYGVGYSCDAGLHG WYRFTGQGGVRMAETCVPVLRN NTAAPMWLNGSHPSSEGIVSRT ACAHWSQCCRWSTEIQVKACP GGFYIYNLTAPPECNLAYCTDPSS VEGTCEECDVEDCISDNNGRWR CQCKQDSNITDVSQLLEYRLECGA NDIKMSLRKCKQLQSLGFMNVFMY LNDRCQSGFSESDEDERDWMSIVT PARNGPCGTVLRNETHATYSNT LYLANAIIIRDIIIRMFECYPLDM KVSLKTSLQPMVSALNISLGGTGK FTVRMALFQSPYTTQPHQGPSV MLSTEAFLYVGTMLDGGDLRFRV LLMTNICYATPSSNSTDPVKYFIIQ DSCPRTEDTTIQVTENGESSQAR FSVQMFRFAGNYDLVYLHCEVYL CDSTSEQCKPTCSGTRFRSGNFI DQTRVLNLPITRQGVQASVSKA ASSNLRLLSIWLLLFPSATLIFMVQ	1-24 signal peptide; 25-618 uromodul in; note: 25-588 is secreted form; 619-642 is cleaved in mature form	SEQ ID NO: 11
MEP1 B	H	Q16820	Uniprot	full length	MDLWNLWFLFDALLVISGLATP ENFDVDGGMDQDIFDINEGLGLD LFEGDIRLDRAQIRNSIIGEKYRW	1-22 signal peptide;	SEQ ID NO: 12

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					PHTIPYVLEDSLEMNAKGVLNAF ERYRLKTCIDFKPWAGETNYISVF KSGSGCWSSVGNRRVGKQELSIG ANCDRIATVQHEFLHALGFWHEQ SRSDRDDYVRIMWDRILSGREHN FNTYSDDISDSLNVPHYDYTSVMH YSKTAFAQNGTEPTIVTRISDFEDVI GQRMDFSDSLKLNQLYNCSSS LSFMDSCSFELENVCGMIQSSGD NADWQRVVSQVPRGPESDHSNM GQCQSGGFFMHFDSSSVNVGAT AVLESRTLYPKRGFQCQLQFYLYN SGSESDQLNIYIREYSADNVDGNL TLVEEIKEIPTGSWQLYHVTLKVT KKFRVVFEGRKSGASLGGLSID DINLSETRCPHHIWHIRNFTQFIG SPNGTLYSPPFYSSKGYAFQIYLN LAHVTNAGIYFHLISGANDDQLQ WPCPWQQATMTLLDQNPDIRQR MSNQRSITTDPMFTTDNGNYFW DRPSKVGTVALFSNGTQFRRG GYGTSAFITHERLKSRDFIKGDDV YILLTVEDISHLNSTQIQLTPAPSV QDLCSKTTCKNDGVCTVRDGKA ECRCQSGEDWWYMERCEKRG STRDTIVIAVSSTVAVFALMLITLV SVYCTRKKYRERMSSNRPNLTP QNQHAF	23-652 extracellular; 653-673 transmembrane; 674-701 cytosol	
MEP1 B	M	Q61847	Uniprot	full length	MDARHQPWFLVFATFLLVSGLPA PEKFVKDIDGGIDQDIFDINQGLG LDFEGDIKLEANGKNSIIGDHR WPHTIPYVLEDSLEMNAKGVLNA FERYRLKTCIDFKPWSGEANYISV FKGSGCWSSVGNHAGKQELSIG TNCRIATVQHEFLHALGFWHEQ SRADRDDYVIVWDRIQPGKEHN FNIYNDVSDSLNVPHYDYTSVMH YSKTAFAQNGTESTIVTRISEFEDVI GQRMDFSYDYLKLNQLYNCTSS LSFMDSCDFELENICGMIQSSGD SADWQRVVSQVLSGPESDHSKMG QCKDSGFFMHFNSTILNEGATAM LESRLLYPKRGFQCLEFYLYNSG SGNDQLNIYTREYTTGQQGGVLT LQRQIKEVPIGWSQLHYVTLQVTK KFRVVFEGLRGPGTSSGGLSIDI NLSETRCPHHIWHIQNFTQILGGQ DTSVYSPPFYSSKGYAFQIYMDL RSSTNVGIYFHLISGANDDQLQW PCPWQQATMTLLDQNPDIRQRM FNQRSITTDPTMTSDNGSYFWDR PSKVGVTDFPNGTQFSRGIGYG TTVFITRERLKSREFIKGDDIYILLT VEDISHLNSTSAVPDPVPTLAVHN ACSEVVCQNGGICVVQDGRAEC	1-20 signal peptide; 21-654 extracellular; 655-678 transmembrane; 679-704 cytosol	SEQ ID NO: 13

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					KCPAGEDWWYMGKRCEKRGST RDTVIIAVSSTVTVFVAVMLIITLVSV YCTRRKYRKARANTAAMTLENQ HAF		
IL11RA	H	Q14626	Uniprot	full length	MSSSCSGLSRVLVAVATALVSAS SPCPQAWGPPGVQYQGQGRSV KLCCPGVTAGDPVSWFRDGEPK LLQGPDSGLGHELVLAQADSTDE GTICQTLTGALGGTVTLQLGY PARPVVSCQAADYENFSCTWSP SQISGLPTRYLTSYRKKTVLGADS QRRSPSTGPWPCPDPLGAARC VVHGAEFWSQYRINVTEVNPLGA STRLLDVSLQSLRPDPPQGLRVE SVPGYPRRLRASWTYPASWPCQ PHFLLKFRLLQYRPAQHPAWSTVE PAGLEEVITDAVAGLPHAVRVSA RDFLDAGTWSWSPAWGTPST GTIPKEIPAWGQLHTQPEVEPQV DSPAPPRPSLQPHPRLLDHRDSV EQVAVLASLGILSFLGLVAGALAL GLWLRRLRRGGKDGSPKPGFLAS VIPVDRRPGAPNL	1-22 is signal peptide; 23-422 is full IL11Ra; 371-391 is transmembrane; 392-422 is cytoplasmic)	SEQ ID NO: 14
IL11RA	M	Q64385	Uniprot	full length	MSSSCSGLTRVLVAVATALVSSS SPCPQAWGPPGVQYQGQGRPV MLCCPGVSAGTPVSWFRDGDSP LLQGPDSGLGHLVLAQVDSPDE GTVCQTLTGVSQGMVTLKLGFP PARPEVSCQAVDYENFSCTWSP GQVSGLPTRYLTSYRKKTLPAGE SQRESPSTGPWPCPDPLEASR CVVHGAEFWSEYRINVTEVNPLG ASTCLLDVRLQSLRPDPPQGLRV ESVPGYPRRLHASWTYPASWRR QPHFLLKFRLLQYRPAQHPAWSTV EPIGLEEVITDAVAGLPHAVRVSA RDFLDAGTWSAWSPAWGTPST GPLQDEIPDWSQGHGQQLAVV AQEDSPAPARPSLQPDPRPLDHR DPLEQVAVLASLGIFSLGLAVGA LALGLWLRRLRRSGKDGPKPGLL APMIPVEKLPGIPNLQRTPENFS	1-23 is signal peptide; 24-432 is full IL11Ra; 373-393 is transmembrane; 394-432 is cytoplasmic)	SEQ ID NO: 15
IL11RA, extracellular domain	H	Q14626	Uniprot	A23-391	SSPCPQAWGPPGVQYQGQGRS VKLCCPGVTAGDPVSWFRDGEK KLLQGPDSGLGHELVLAQADSTD EGTYICQTLTGALGGTVTLQLGY PPARPVVSCQAADYENFSCTWS PSQISGLPTRYLTSYRKKTVLGAD SQRRSPSTGPWPCPDPLGAAR CVVHGAEFWSQYRINVTEVNPLG ASTRLLDVSLQSLRPDPPQGLRV ESVPGYPRRLRASWTYPASWPC QPHFLLKFRLLQYRPAQHPAWSTV EPAGLEEVITDAVAGLPHAVRVSA RDFLDAGTWSWSPAWGTPST		SEQ ID NO: 16

Name	Species (M/H)	Accession #	Accession Location	Positions	AA sequence	Notes	SEQ ID NO:
					GTIPKEIPAWGQLHTQPEVEPQV DSPAPPRPSLQPHPRLLDHRDSV EQVAVLA		
IL11RA, extracellular domain	M	Q64385	Uniprot	A24-A393	SPCPQAWGPPGVQYQGQGRPV MLCCPGVSAGTPVSWFRDGD LLQGPDGSLGHLVLAQVDS PTYVCQTLGVSQGMVTLKLGFP PARPEVSCQAVDYENFSCWSP GQVSGLPTRYLTSYRKKTLP SQRESPSTGPWPCQDPLEASR CVVHGAEFWSEYRINVTEVNPLG ASTCLLDVRLQSLRPDPQGLRV ESVPGYPRRLHASWTYPASWRR QPHFLKFRLLQYRPAQHPAWSTV EPIGLEEVITDAVAGLPHAVR RVSARDFLDAGTWSA SPEAWGTPSTGPLQDEIPDWSQGHGQ QLEAVVAQEDSPAPARPSLQPD PRPLDHRDPLEQVAV		SEQ ID NO: 17
IL11	H	P20809	Uniprot	full length	MNCVCRLVLVLSLWPD TAVAPGPPGPPRVSPDPRAEL DSTVLLTRSLADTRQLAAQLRDK FPADGDHNLDSLPTLAMSAGAL GALQLPGVLTRLRADLLSYLRH VQWLRRAGGSSKLTLEPELGT LQARLDRLRLQLLLMSRLALPQ PPPDPPAPPLAPPSSAWGGIRAA HAILGGLHLTDWAVRGLLLKTRL	1-22 is signal peptide; 23-199 is IL11	SEQ ID NO: 18

Production of ANDbody Compositions

Production of ANDbody polypeptides

5

ANDbody polypeptides of the invention may be produced by any suitable means. For example, all or part of the ANDbody may be expressed by a host cell comprising a nucleotide which encodes the ANDbody. Such methods of making a therapeutic polypeptide are routine in the art. See, in general, Smales & James (Eds.), *Therapeutic Proteins: Methods and Protocols* (Methods in Molecular Biology),

10 Humana Press (2005); and Crommelin, Sindelar & Meibohm (Eds.), *Pharmaceutical Biotechnology: Fundamentals and Applications*, Springer (2013).

Methods for producing an ANDbody may involve expression in mammalian cells, although recombinant proteins can also be produced using insect cells, yeast, bacteria, or other cells under the control of appropriate promoters. Mammalian expression vectors may comprise nontranscribed

15 elements such as an origin of replication, a suitable promoter and enhancer, and other 5' or 3' flanking nontranscribed sequences, and 5' or 3' nontranslated sequences such as necessary ribosome binding sites, a polyadenylation site, splice donor and acceptor sites, and termination sequences. DNA sequences derived from the SV40 viral genome, for example, SV40 origin, early promoter, enhancer, splice, and polyadenylation sites may be used to provide the other genetic elements required for

expression of a heterologous DNA sequence. Appropriate cloning and expression vectors for use with bacterial, fungal, yeast, and mammalian cellular hosts are described in Green & Sambrook, *Molecular Cloning: A Laboratory Manual* (Fourth Edition), Cold Spring Harbor Laboratory Press (2012).

Various mammalian cell culture systems can be employed to express and manufacture an ANDbody described herein. Examples of mammalian expression systems include CHO cells, COS cells, HeLA and BHK cell lines. Processes of host cell culture for production of protein therapeutics are described in, e.g., Zhou and Kantardjieff (Eds.), *Mammalian Cell Cultures for Biologics Manufacturing* (Advances in Biochemical Engineering/Biotechnology), Springer (2014). Purification of protein therapeutics is described in Franks, *Protein Biotechnology: Isolation, Characterization, and Stabilization*, Humana Press (2013); and in Cutler, *Protein Purification Protocols* (Methods in Molecular Biology), Humana Press (2010). Formulation of protein therapeutics is described in Meyer (Ed.), *Therapeutic Protein Drug Products: Practical Approaches to formulation in the Laboratory, Manufacturing, and the Clinic*, Woodhead Publishing Series (2012).

Antibody production techniques are known. See, for example, Zhiqiang (Editor), *Therapeutic Monoclonal Antibodies: From Bench to Clinic*. 1st Edition. Wiley 2009; Greenfield (Ed.) *Antibodies: A Laboratory Manual*. (Second edition) Cold Spring Harbor Laboratory Press 2013; Ferrara et al. 2012. Using Phage and Yeast Display to Select Hundreds of Monoclonal Antibodies: Application to Antigen 85, a Tuberculosis Biomarker. *PLoS ONE* 7(11): e49535, for methods of making recombinant antibodies, including antibody engineering, use of degenerate oligonucleotides, 5'-RACE, phage display, and mutagenesis; antibody testing and characterization; antibody pharmacokinetics and pharmacodynamics; antibody purification and storage; and screening and labeling techniques.

Production of ANDbody RNAs

In some embodiments, ANDbodies RNAs may be produced, e.g., for delivery to a subject. Generally, therapeutic mRNAs are made by *in vitro* transcription. Modification such as incorporation of modified bases, 5'cap analogues, and polyA tails can optimize activity and function. For example, translation and stability of mRNA can be accomplished, by cap and poly A tail modifications. E.g., incorporation of cap analogs such as ARCA (anti-reverse cap analogs) and a poly(A) tail of 100–200 bp into *in vitro* transcribed (IVT) mRNAs improves expression and stability (Kaczmarek et al. *Genome Medicine* (2017) 9:60). New types of cap analogs, such as 1,2-dithiodiphosphate-modified caps, can further improve efficiency of translation (Strenkowska et al. *Nucleic Acids Res.* 2016;44:9578–90). Codon optimization can also improve efficacy of protein synthesis and limit mRNA destabilization by rare codons (Presnyak et al. *Cell.* 2015;160:1111–24. 93; Thess et al. *Mol Ther.* 2015;23: 1456–64). Modifying 3' and 5' untranslated regions (UTRs), which contain sequences responsible for recruiting RNA-binding proteins (RBPs) and miRNAs, can enhance the level of protein product (Kaczmarek). Further, UTRs can be modified to encode regulatory elements (e.g., K-turn motifs and miRNA binding sites), in order to control RNA expression in a cell-specific manner (Wroblewska et al. *Nat Biotechnol.* 2015;33:839–41). RNA base modifications (e.g., pseudouridine incorporated mRNA, e.g., N1-methyl-pseudouridine) contribute to masking mRNA immune-stimulatory activity and increase mRNA

translation by enhancing translation initiation (Andries et al. J Control Release. 2015;217:337–44; Svitkin et al. Nucleic Acids Res. 2017;45:6023–36). mRNA compositions and methods of their manufacture are known and are disclosed, e.g., in WO2016011306; WO2016014846; WO2016022914; WO2016077123; WO2016164762; WO2016201377; WO2017049275; US9937233; US8710200; US10022425; US9878056; US9572897; Jemielity et al. RNA. 2003;9:1108–22. 90; Mockey et al. Biochem Biophys Res Commun. 2006;340:1062–8. 91; Strenkowska et al. Nucleic Acids Res. 2016;44:9578–90. 92; Presnyak et al. Cell. 2015;160:1111–24. 93; Kaczmarek et al. Genome Medicine (2017) 9:60.

Production Of ANDbodies With Altered Affinities

ANDbodies with binding sites with altered affinities can be made using methods known in the art, e.g., an ANDbody can be engineered to have a target binding site that has decreased affinity for the effector target. See, e.g., US Patent No. 10,654,928. In general, an ANDBody may be modified to alter the affinity of an effector target binding site to its effector target or to alter the affinity of an address target binding site to its address target. The modification can increase or decrease affinity for the binding site's binding partner.

Assessment of Targets and Addresses

Expression of a therapeutic target can be assessed at either the RNA or protein level using methods known in the art. In embodiments, expression of the therapeutic target is assessed by measuring RNA expression, e.g., using an RNA sequence dataset as a proxy for protein expression levels. RNA datasets include those a genotype-Tissue Expression (GTEx) dataset (see, e.g., <https://www.genome.gov/Funded-Programs-Projects/Genotype-Tissue-Expression-Project>) or a Human Protein Atlas (HPA) dataset (<https://www.proteinatlas.org/>).

A non-limiting list of tissues in which expression of the therapeutic target can be assessed includes, e.g., the minor salivary gland, thyroid, lung, breast (mammary tissue), pancreas, adrenal gland, liver, kidney (cortex), kidney (medulla), adipose-visceral (omentum), small intestine – terminal ileum, fallopian tube, ovary, uterus, skin not sun exposed (suprapubic); cervix—endocervix, cervix—ectocervix, vagina, skin sun exposed (lower leg), cells eneanterior cingulate cortex (BA24), caudate (basal ganglia), putamen (basal ganglia), nucleus acumbens (basal ganglia), hypothalamus, amygdala, hippocampus, cerebellum/cerebellar hemisphere, substantia nigra, pituitary, spinal cord (cervical), artery-aorta, heart-atrial appendage, artery-coronary- heart, left ventricle, esophagus-mucosa, esophagus-muscularis, esophagus-gastroesophageal junction, spleen, stomach, colon-transverse, colon—sigmoid, testis, whole blood, cells – (EBV-transformed lymphocytes, artery-tibial, or nerve-tibial tissues).

Address markers can be assessed using methods well known in the art, e.g., gene expression can be assessed at the mRNA level using Northern blots, cDNA or oligonucleotide microarrays, or sequencing (e.g., RNA-Seq), or at the level of protein expression using protein microarrays, Western blots, flow cytometry, immunohistochemistry, etc. Modifications can be assessed, e.g., using antibodies

that are specific for a particular modified form of a protein, *e.g.*, phospho-specific antibodies, or mass spectrometry.

Uses of ANDbodies

5 ANDbodies and their pharmaceutical compositions provided herein are suitable for administration to a subject in need thereof, wherein the subject is a human or a non-human animal, for example, suitable for human therapeutic or veterinary use.

 Veterinary use includes use for treatment of mammals, including commercially relevant mammals, *e.g.*, pet and live-stock animals, such as cattle, pigs, horses, sheep, goats, cats, dogs, mice, 10 and/or rats; and/or birds, including commercially relevant birds such as parrots, poultry, chickens, ducks, geese, hens or roosters and/or turkeys; zoo animals, *e.g.*, a feline; non-mammal animals, *e.g.*, reptiles, fish, amphibians, etc.

 The invention is further directed to a subject or subject cell comprising the ANDbody composition described herein. In some embodiments, the subject or subject cell is a plant, insect, 15 bacteria, fungus, vertebrate, mammal (*e.g.*, human), or other organism or cell.

 In some embodiments, a subject or a subject cell is contacted with (*e.g.*, delivered to or administered to) the ANDbody composition. In some embodiments, the subject is a mammal, such as a human. The amount of the ANDbody composition, expression product, or both in the subject can be measured at any time after administration.

20 ***Pharmaceutical Compositions***

Polypeptide Pharmaceutical Compositions

 The ANDbody compositions described herein (*e.g.*, ANDbody polypeptide or RNA compositions) may be administered to a subject in need thereof. The invention includes pharmaceutical 25 compositions that include an ANDbody composition in combination with one or more pharmaceutically acceptable excipients.

 Formulation of protein therapeutics is routine. See, for example, Ribeiro et al., Insights on the Formulation of Recombinant Proteins. *Adv Biochem Eng Biotechnol.* 2020;171:23-54. doi: 10.1007/10_2019_119. PMID: 31844925.

30 RNA pharmaceutical compositions

 Nucleic acids (*e.g.*, RNA) encoding an ANDBody can alternatively or additionally be administered to a subject. Generally, therapeutic mRNAs are made by *in vitro* transcription. Modification such as incorporation of modified bases, 5'cap analogues, and polyA tails can optimize activity and function. For example, translation and stability of mRNA can be accomplished, by cap and poly A tail 35 modifications. *E.g.*, incorporation of cap analogs such as ARCA (anti-reverse cap analogs) and a poly(A) tail of 100–200 bp into *in vitro* transcribed (IVT) mRNAs improves expression and stability (Kaczmarek et al. *Genome Medicine* (2017) 9:60). New types of cap analogs, such as 1,2-dithiodiphosphate-modified caps, can further improve efficiency of translation (Strenkowska et al. *Nucleic Acids Res.* 2016;44:9578–90). Codon optimization can also improve efficacy of protein

synthesis and limit mRNA destabilization by rare codons (Presnyak et al. Cell. 2015;160:1111–24. 93; Thess et al. Mol Ther. 2015;23: 1456–64). Modifying 3' and 5' untranslated regions (UTRs), which contain sequences responsible for recruiting RNA-binding proteins (RBPs) and miRNAs, can enhance the level of protein product (Kaczmarek). Further, UTRs can be modified to encode regulatory elements (e.g., K-turn motifs and miRNA binding sites), in order to control RNA expression in a cell-specific manner (Wroblewska et al. Nat Biotechnol. 2015;33:839–41). RNA base modifications (e.g., pseudouridine incorporated mRNA, e.g., N1-methyl-pseudouridine) contribute to masking mRNA immune-stimulatory activity and increase mRNA translation by enhancing translation initiation (Andries et al. J Control Release. 2015;217:337–44; Svitkin et al. Nucleic Acids Res. 2017;45:6023–36). mRNA compositions and methods of their manufacture are known and are disclosed, e.g., in WO2016011306; WO2016014846; WO2016022914; WO2016077123; WO2016164762; WO2016201377; WO2017049275; US9937233; US8710200; US10022425; US9878056; US9572897; Jemielity et al. RNA. 2003;9:1108–22. 90; Mockey et al. Biochem Biophys Res Commun. 2006;340:1062–8. 91; Strenkowska et al. Nucleic Acids Res. 2016;44:9578–90. 92; Presnyak et al. Cell. 2015;160:1111–24. 93; Kaczmarek et al. Genome Medicine (2017) 9:60.

In embodiments, the RNA is a circular RNA. See, for example, WO2019118919, describing the expression of a therapeutic RNA, such as an antibody RNA, from a circular RNA. In some embodiments, the invention includes a circular polyribonucleotide that comprises (a) an internal ribosome entry site (IRES), (b) an expression sequence encoding a ANDbody described herein and lacking a poly-A sequence, and (c) a termination element. A circular RNA encoding an ANDbody described herein may be delivered naked (i.e., without formulation with a carrier) or with a carrier.

Carriers

Lipid nanoparticles

Formulations of the compositions described herein (e.g., polypeptide or RNA ANDbody compositions) for *in vivo* delivery with a carrier include lipid nanoparticle (LNP) formulations. See, e.g., US Pat. 9,764,036; US Pat. 9,682,139; Kauffman et al. Nano Lett. 2015;15: 7300–6. 37; Fenton et al. Adv Mater. 2016;28:2939–43). LNPs, in some embodiments, comprise one or more ionic lipids, such as non-cationic lipids (e.g., neutral or anionic, or zwitterionic lipids); one or more conjugated lipids (such as PEG-conjugated lipids or lipids conjugated to polymers described in Table 5 of WO2019217941; incorporated herein by reference in its entirety); one or more sterols (e.g., cholesterol); and, optionally, one or more targeting molecules (e.g., conjugated receptors, receptor ligands, antibodies); or combinations of the foregoing.

Lipids that can be used in nanoparticle formations (e.g., lipid nanoparticles) include, for example those described in Table 4 of WO2019217941, which is incorporated herein by reference—e.g., a lipid-containing nanoparticle can comprise one or more of the lipids in Table 4 of WO2019217941. Lipid nanoparticles can include additional elements, such as polymers, such as the polymers described in Table 5 of WO2019217941, incorporated by reference.

In some embodiments, conjugated lipids, when present, can include one or more of PEG-

diacylglycerol (DAG) (such as 1-(monomethoxy-polyethyleneglycol)-2,3- dimyristoylglycerol (PEG-DMG)), PEG-dialkylxypropyl (DAA), PEG-phospholipid, PEG- ceramide (Cer), a pegylated phosphatidylethanolamine (PEG-PE), PEG succinate diacylglycerol (PEGS-DAG) (such as 4-0-(2',3'-di(tetradecanoyloxy)propyl)-0-(w- methoxy(polyethoxy)ethyl) butanedioate (PEG-S-DMG)), PEG

5 dialkoxypopylcarbam, N- (carbonyl-methoxypoly ethylene glycol 2000)- 1 ,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt, and those described in Table 2 of WO2019051289 (incorporated by reference), and combinations of the foregoing.

In some embodiments, sterols that can be incorporated into lipid nanoparticles include one or more of cholesterol or cholesterol derivatives, such as those in W02009/127060 or US2010/0130588,

10 which are incorporated by reference. Additional exemplary sterols include phytosterols, including those described in Eygeris et al (2020), dx.doi.org/10.1021/acs.nanolett.0c01386, incorporated herein by reference.

In some embodiments, the lipid particle comprises an ionizable lipid, a non-cationic lipid, a conjugated lipid that inhibits aggregation of particles, and a sterol. The amounts of these components

15 can be varied independently and to achieve desired properties. For example, in some embodiments, the lipid nanoparticle comprises an ionizable lipid is in an amount from about 20 mol % to about 90 mol % of the total lipids (in other embodiments it may be 20-70% (mol), 30-60% (mol) or 40-50% (mol); about 50 mol % to about 90 mol % of the total lipid present in the lipid nanoparticle), a non-cationic lipid in an amount from about 5 mol % to about 30 mol % of the total lipids, a conjugated lipid in an amount

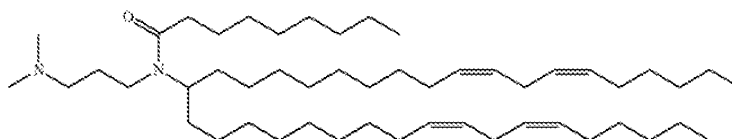
20 from about 0.5 mol % to about 20 mol % of the total lipids, and a sterol in an amount from about 20 mol % to about 50 mol % of the total lipids. The ratio of total lipid to nucleic acid can be varied as desired. For example, the total lipid to nucleic acid (mass or weight) ratio can be from about 10: 1 to about 30: 1.

In some embodiments, the lipid to nucleic acid ratio (mass/mass ratio; w/w ratio) can be in the range of from about 1 : 1 to about 25: 1, from about 10: 1 to about 14: 1, from about 3 : 1 to about 15: 1,

25 from about 4: 1 to about 10: 1, from about 5: 1 to about 9: 1, or about 6: 1 to about 9: 1. The amounts of lipids and nucleic acid can be adjusted to provide a desired N/P ratio, for example, N/P ratio of 3, 4, 5, 6, 7, 8, 9, 10 or higher. Generally, the lipid nanoparticle formulation's overall lipid content can range from about 5 mg/ml to about 30 mg/mL.

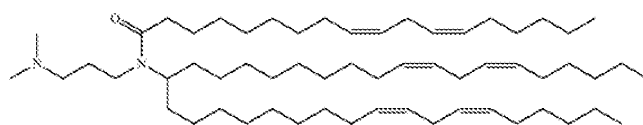
Some non-limiting example of lipid compounds that may be used (e.g., in combination with

30 other lipid components) to form lipid nanoparticles for the delivery of compositions described herein, e.g., nucleic acid (e.g., RNA) described herein includes,



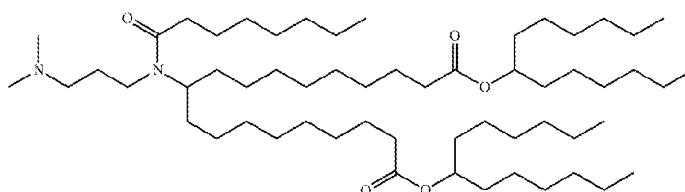
(i)

In some embodiments an LNP comprising Formula (i) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.



(ii)

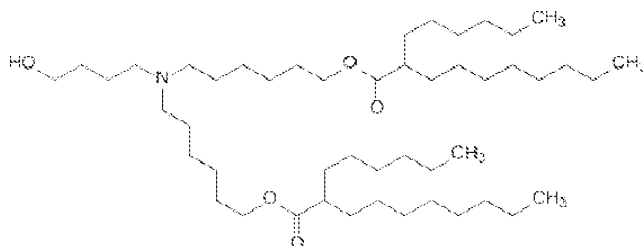
In some embodiments an LNP comprising Formula (ii) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.



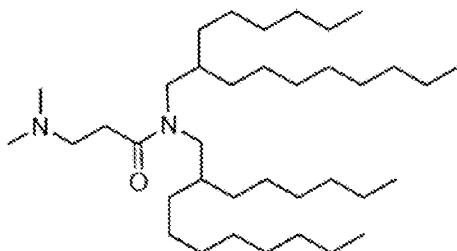
(iii)

- 5 In some embodiments an LNP comprising Formula (iii) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.

(iv)

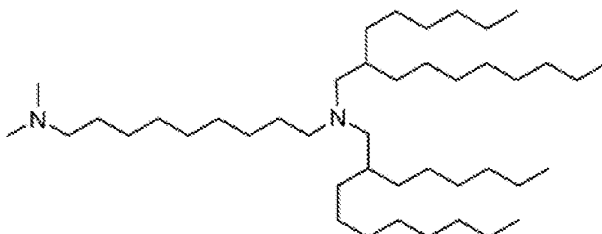


(v)



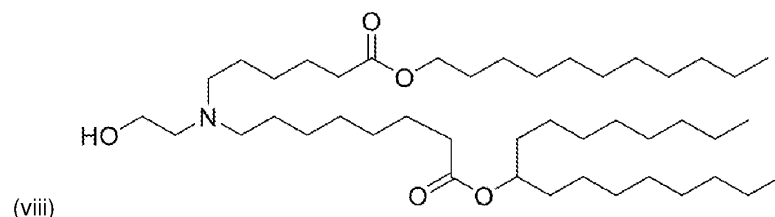
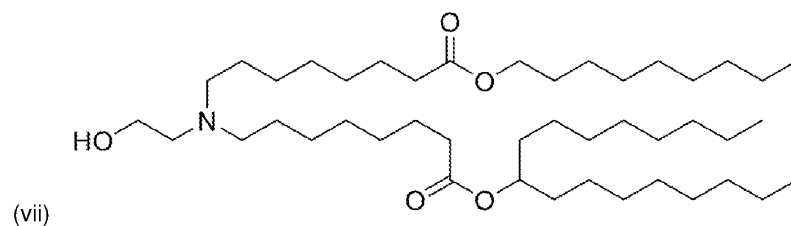
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In some embodiments an LNP comprising Formula (v) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.

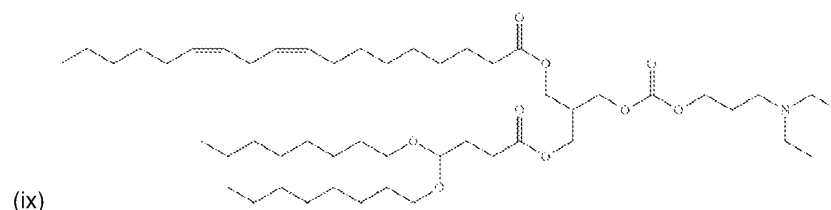


(vi)

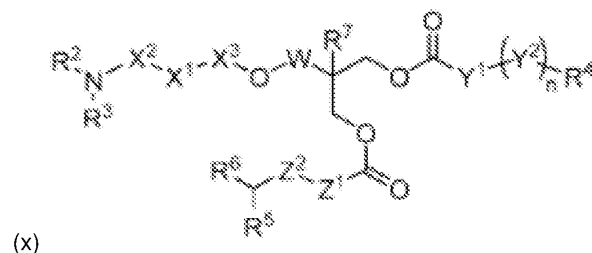
In some embodiments an LNP comprising Formula (vi) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.



- 5 In some embodiments an LNP comprising Formula (viii) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.

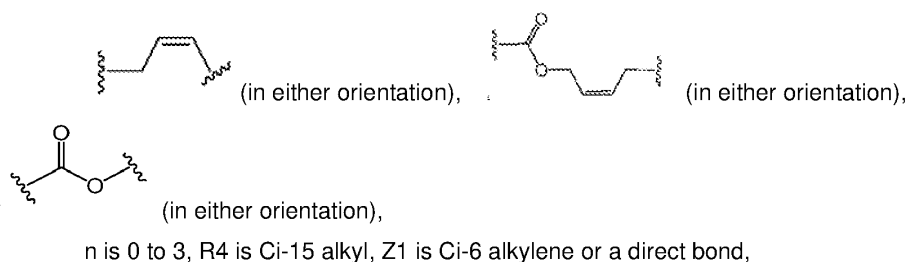


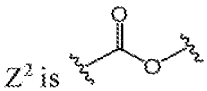
- 10 In some embodiments an LNP comprising Formula (ix) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.



wherein

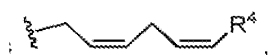
- 15 X1 is O, NR¹, or a direct bond, X2 is C2-5 alkylene, X3 is C(=O) or a direct bond, R¹ is H or Me, R³ is C1-3 alkyl, R² is C1-3 alkyl, or R² taken together with the nitrogen atom to which it is attached and 1-3 carbon atoms of X2 form a 4-, 5-, or 6-membered ring, or X1 is NR¹, R¹ and R² taken together with the nitrogen atoms to which they are attached form a 5- or 6-membered ring, or R² taken together with R³ and the nitrogen atom to which they are attached form a 5-, 6-, or 7-membered ring, Y¹ is C2-12 alkylene, Y² is selected from



5 Z^2 is  (in either orientation) or absent, provided that if Z₁ is a direct bond, Z₂ is absent;

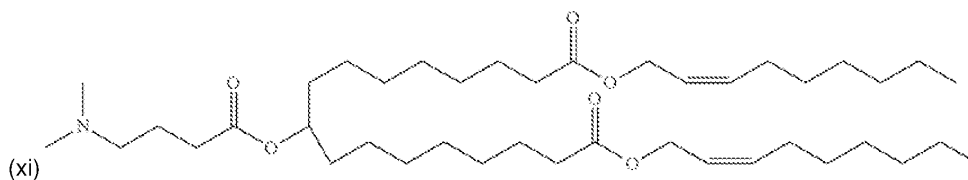
R₅ is C₅₋₉ alkyl or C₆₋₁₀ alkoxy, R₆ is C₅₋₉ alkyl or C₆₋₁₀ alkoxy, W is methylene or a direct bond, and R₇ is H or Me, or a salt thereof, provided that if R₃ and R₂ are C₂ alkyls, X₁ is O, X₂ is linear C₃ alkylene, X₃ is C(=O), Y₁ is linear C₆ alkylene, (Y₂)_n-R₄ is

10



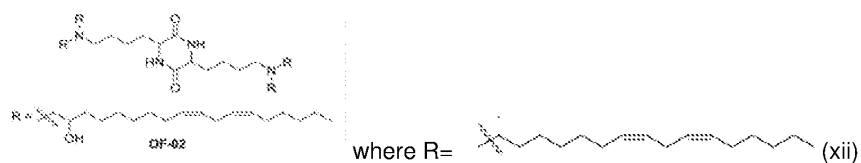
R₄ is linear C₅ alkyl, Z₁ is C₂ alkylene, Z₂ is absent, W is methylene, and R₇ is H, then R₅ and R₆ are not C_x alkoxy.

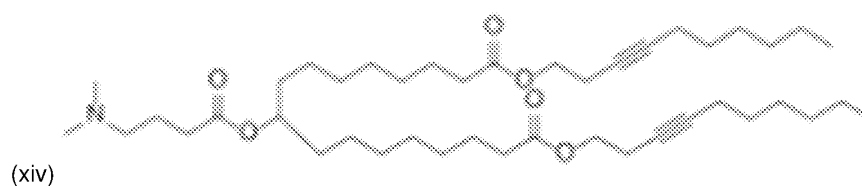
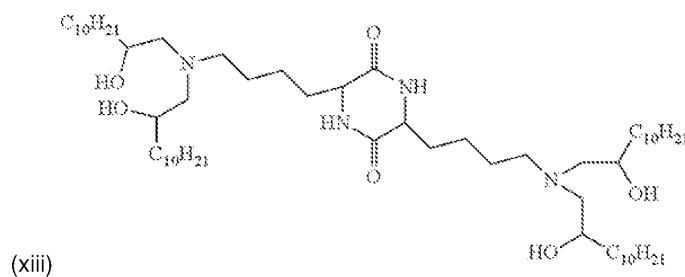
In some embodiments an LNP comprising Formula (xi) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.



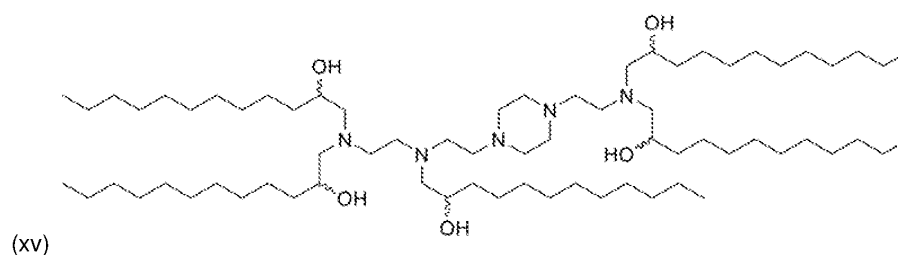
In some embodiments an LNP comprising Formula (xi) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.

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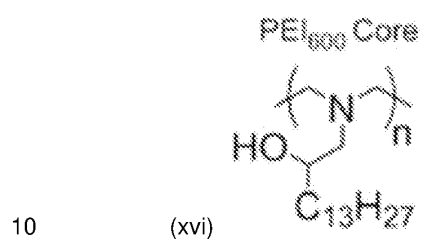




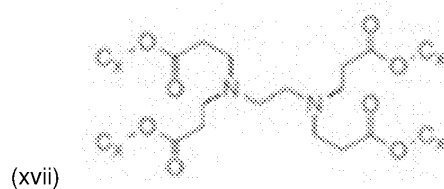
In some embodiments an LNP comprises a compound of Formula (xiii) and a compound of
5 Formula (xiv).

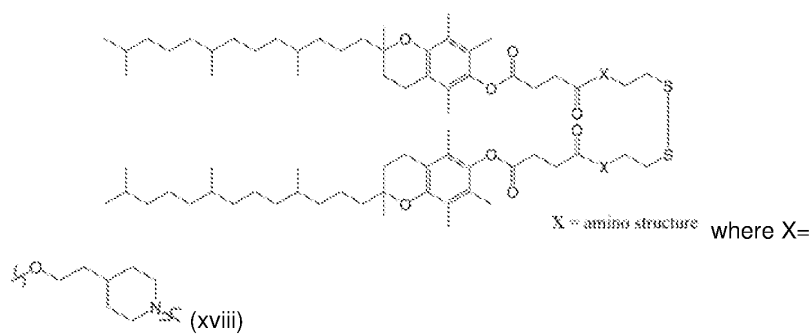


In some embodiments an LNP comprising Formula (xv) is used to deliver an ANDbody RNA composition described herein to the liver and/or hepatocyte cells.

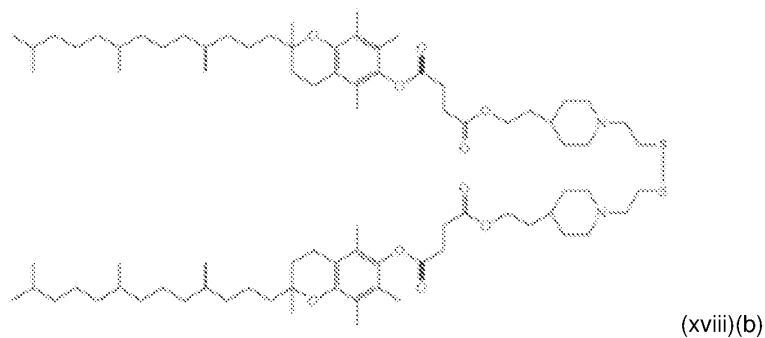


In some embodiments an LNP comprising a formulation of Formula (xvi) is used to deliver an
ANDbody RNA composition described herein to the lung endothelial cells.

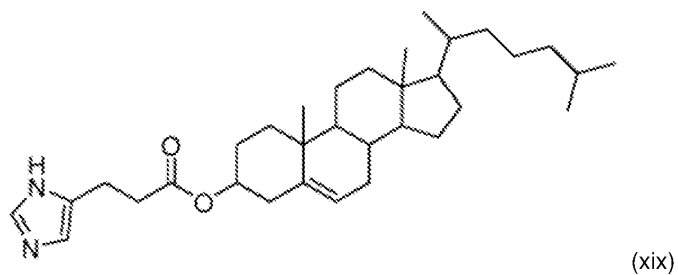




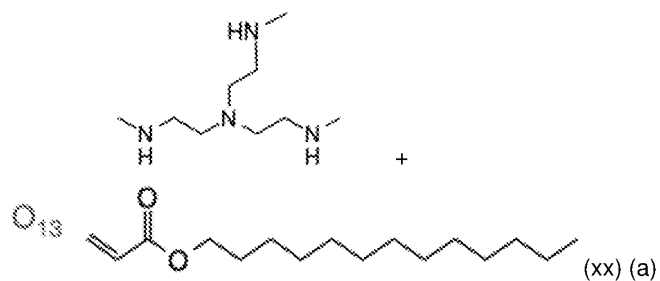
(a)

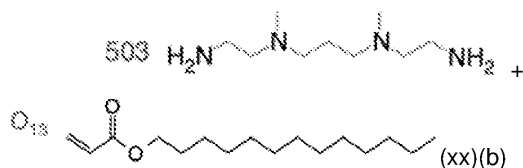


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10 In some embodiments, a lipid compound used to form lipid nanoparticles for the delivery of compositions described herein, *e.g.*, nucleic acid (*e.g.*, RNA) described herein is made by one of the following reactions:





In some embodiments, a composition described herein (*e.g.*, a nucleic acid or a protein) is provided in an LNP that comprises an ionizable lipid. In some embodiments, the ionizable lipid is heptadecan-9-yl 8-((2-hydroxyethyl)(6-oxo-6-(undecyloxy)hexyl)amino)octanoate (SM-102); *e.g.*, as described in Example 1 of US9,867,888 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is 9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-(((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate (LP01), *e.g.*, as synthesized in Example 13 of WO2015/095340 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is Di((Z)-non-2-en-1-yl) 9-((4-dimethylamino)butanoyl)oxy)heptadecanedioate (L319), *e.g.* as synthesized in Example 7, 8, or 9 of US2012/0027803 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is 1,1'-((2-(4-(2-((2-(Bis(2-hydroxydodecyl)amino)ethyl)(2-hydroxydodecyl) amino)ethyl)piperazin-1-yl)ethyl)azanediyl)bis(dodecan-2-ol) (C12-200), *e.g.*, as synthesized in Examples 14 and 16 of WO2010/053572 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is Imidazole cholesterol ester (ICE) lipid (3S, 10R, 13R, 17R)-10, 13-dimethyl-17- ((R)-6-methylheptan-2-yl)-2, 3, 4, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 3-(1H-imidazol-4-yl)propanoate, *e.g.*, Structure (I) from WO2020/106946 (incorporated by reference herein in its entirety).

In some embodiments, an ionizable lipid may be a cationic lipid, an ionizable cationic lipid, *e.g.*, a cationic lipid that can exist in a positively charged or neutral form depending on pH, or an amine-containing lipid that can be readily protonated. In some embodiments, the cationic lipid is a lipid capable of being positively charged, *e.g.*, under physiological conditions. Exemplary cationic lipids include one or more amine group(s) which bear the positive charge. In some embodiments, the lipid particle comprises a cationic lipid in formulation with one or more of neutral lipids, ionizable amine-containing lipids, biodegradable alkyne lipids, steroids, phospholipids including polyunsaturated lipids, structural lipids (*e.g.*, steroids), PEG, cholesterol and polymer conjugated lipids. In some embodiments, the cationic lipid may be an ionizable cationic lipid. An exemplary cationic lipid as disclosed herein may have an effective pKa over 6.0. In embodiments, a lipid nanoparticle may comprise a second cationic lipid having a different effective pKa (*e.g.*, greater than the first effective pKa), than the first cationic lipid. A lipid nanoparticle may comprise between 40 and 60 mol percent of a cationic lipid, a neutral lipid, a steroid, a polymer conjugated lipid, and a therapeutic agent, *e.g.*, a nucleic acid (*e.g.*, RNA) described herein, encapsulated within or associated with the lipid nanoparticle. In some embodiments, the nucleic acid is co-formulated with the cationic lipid. The nucleic acid may be adsorbed to the surface of an LNP, *e.g.*, an LNP comprising a cationic lipid. In some embodiments, the nucleic acid may be

encapsulated in an LNP, e.g., an LNP comprising a cationic lipid. In some embodiments, the lipid nanoparticle may comprise a targeting moiety, e.g., coated with a targeting agent. In embodiments, the LNP formulation is biodegradable. In some embodiments, a lipid nanoparticle comprising one or more lipid described herein, e.g., Formula (i), (ii), (iii), (vii) and/or (ix) encapsulates at least 1%, 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 92%, at least 95%, at least 97%, at least 98% or 100% of an RNA molecule.

Exemplary ionizable lipids that can be used in lipid nanoparticle formulations include, without limitation, those listed in Table 1 of WO2019051289, incorporated herein by reference. Additional exemplary lipids include, without limitation, one or more of the following formulae: X of

US2016/0311759; I of US20150376115 or in US2016/0376224; I, II or III of US20160151284; I, IA, II, or IIA of US20170210967; I-c of US20150140070; A of US2013/0178541; I of US2013/0303587 or US2013/0123338; I of US2015/0141678; II, III, IV, or V of US2015/0239926; I of US2017/0119904; I or II of WO2017/117528; A of US2012/0149894; A of US2015/0057373; A of WO2013/116126; A of US2013/0090372; A of US2013/0274523; A of US2013/0274504; A of US2013/0053572; A of W02013/016058; A of W02012/162210; I of US2008/042973; I, II, III, or IV of US2012/01287670; I or II of US2014/0200257; I, II, or III of US2015/0203446; I or III of US2015/0005363; I, IA, IB, IC, ID, II, IIA, IIB, IIC, IID, or III-XXIV of US2014/0308304; of US2013/0338210; I, II, III, or IV of W02009/132131; A of US2012/01011478; I or XXXV of US2012/0027796; XIV or XVII of US2012/0058144; of US2013/0323269; I of US2011/0117125; I, II, or III of US2011/0256175; I, II, III, IV, V, VI, VII, VIII, IX, X, XI, XII of US2012/0202871; I, II, III, IV, V, VI, VII, VIII, X, XII, XIII, XIV, XV, or XVI of US2011/0076335; I or II of US2006/008378; I of US2013/0123338; I or X-A-Y-Z of US2015/0064242; XVI, XVII, or XVIII of US2013/0022649; I, II, or III of US2013/0116307; I, II, or III of US2013/0116307; I or II of US2010/0062967; I-X of US2013/0189351; I of US2014/0039032; V of US2018/0028664; I of US2016/0317458; I of US2013/0195920; 5, 6, or 10 of US10,221,127; III-3 of WO2018/081480; I-5 or I-8 of WO2020/081938; 18 or 25 of US9,867,888; A of US2019/0136231; II of WO2020/219876; 1 of US2012/0027803; OF-02 of US2019/0240349; 23 of US10,086,013; cKK-E12/A6 of Miao et al (2020); C12-200 of WO2010/053572; 7C1 of Dahlman et al (2017); 304-O13 or 503-O13 of Whitehead et al; TS-P4C2 of US9,708,628; I of WO2020/106946; I of WO2020/106946.

In some embodiments, the ionizable lipid is MC3 (6Z,9Z,28Z,3 IZ)-heptatriaconta- 6,9,28,3 I-tetraen-19-yl-4-(dimethylamino) butanoate (DLin-MC3-DMA or MC3), e.g., as described in Example 9 of WO2019051289A9 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is the lipid ATX-002, e.g., as described in Example 10 of WO2019051289A9 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is (13Z,16Z)-A,A-dimethyl-3- nonyldocosa-13, 16-dien-1-amine (Compound 32), e.g., as described in Example 11 of WO2019051289A9 (incorporated by reference herein in its entirety). In some embodiments, the ionizable lipid is Compound 6 or Compound 22, e.g., as described in Example 12 of WO2019051289A9 (incorporated by reference herein in its entirety).

Exemplary non-cationic lipids include, but are not limited to, distearoyl-sn-glycero-phosphoethanolamine, distearoylphosphatidylcholine (DSPC), dioleoylphosphatidylcholine (DOPC),

dipalmitoylphosphatidylcholine (DPPC), dioleoylphosphatidylglycerol (DOPG), dipalmitoylphosphatidylglycerol (DPPG), dioleoyl-phosphatidylethanolamine (DOPE), palmitoyloleoylphosphatidylcholine (POPC), palmitoyloleoylphosphatidylethanolamine (POPE), dioleoyl-phosphatidylethanolamine 4-(N-maleimidomethyl)-cyclohexane-1-carboxylate (DOPE-mal),

5 dipalmitoyl phosphatidyl ethanolamine (DPPE), dimyristoylphosphoethanolamine (DMPE), distearoyl-phosphatidyl-ethanolamine (DSPE), monomethyl-phosphatidylethanolamine (such as 16-O-monomethyl PE), dimethyl-phosphatidylethanolamine (such as 16-O-dimethyl PE), 18-l-trans PE, 1-stearoyl-2-oleoyl-phosphatidylethanolamine (SOPE), hydrogenated soy phosphatidylcholine (HSPC), egg phosphatidylcholine (EPC), dioleoylphosphatidylserine (DOPS), sphingomyelin (SM), dimyristoyl

10 phosphatidylcholine (DMPC), dimyristoyl phosphatidylglycerol (DMPG), distearoylphosphatidylglycerol (DSPG), dierycophosphatidylcholine (DEPC), palmitoyloleoylphosphatidylglycerol (POPG), dielaidoyl-phosphatidylethanolamine (DEPE), lecithin, phosphatidylethanolamine, lysolecithin, lysophosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, sphingomyelin, egg sphingomyelin (ESM), cephalin, cardiolipin, phosphatidic acid, cerebrosides, dicetylphosphate,

15 lysophosphatidylcholine, dilinoleoylphosphatidylcholine, or mixtures thereof. It is understood that other diacylphosphatidylcholine and diacylphosphatidylethanolamine phospholipids can also be used. The acyl groups in these lipids are preferably acyl groups derived from fatty acids having C10-C24 carbon chains, e.g., lauroyl, myristoyl, palmitoyl, stearoyl, or oleoyl. Additional exemplary lipids, in certain embodiments, include, without limitation, those described in Kim et al. (2020)

20 [dx.doi.org/10.1021/acs.nanolett.0c01386](https://doi.org/10.1021/acs.nanolett.0c01386), incorporated herein by reference. Such lipids include, in some embodiments, plant lipids found to improve liver transfection with mRNA (e.g., DGTS).

Other examples of non-cationic lipids suitable for use in the lipid nanoparticles include, without limitation, nonphosphorous lipids such as, e.g., stearylamine, dodecylamine, hexadecylamine, acetyl palmitate, glycerol ricinoleate, hexadecyl stearate, isopropyl myristate, amphoteric acrylic polymers,

25 triethanolamine-lauryl sulfate, alkyl-aryl sulfate polyethoxylated fatty acid amides, dioctadecyl dimethyl ammonium bromide, ceramide, sphingomyelin, and the like. Other non-cationic lipids are described in WO2017/099823 or US patent publication US2018/0028664, the contents of which are incorporated herein by reference in their entirety.

In some embodiments, the non-cationic lipid is oleic acid or a compound of Formula I, II, or IV of US2018/0028664, incorporated herein by reference in its entirety. The non-cationic lipid can comprise, for example, 0-30% (mol) of the total lipid present in the lipid nanoparticle. In some

30 embodiments, the non-cationic lipid content is 5-20% (mol) or 10-15% (mol) of the total lipid present in the lipid nanoparticle. In embodiments, the molar ratio of ionizable lipid to the neutral lipid ranges from about 2:1 to about 8:1 (e.g., about 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, or 8:1).

35 In some embodiments, the lipid nanoparticles do not comprise any phospholipids.

In some aspects, the lipid nanoparticle can further comprise a component, such as a sterol, to provide membrane integrity. One exemplary sterol that can be used in the lipid nanoparticle is cholesterol and derivatives thereof. Non-limiting examples of cholesterol derivatives include polar analogues such as 5 α -cholestanol, 5 β -coprostanol, cholesteryl-(2,-hydroxy)-ethyl ether, cholesteryl-(4'-

hydroxy)-butyl ether, and 6-ketocholestanol; non-polar analogues such as 5 α -cholestane, cholestenone, 5 α -cholestanone, 5 β -cholestanone, and cholesteryl decanoate; and mixtures thereof. In some embodiments, the cholesterol derivative is a polar analogue, e.g., cholesteryl-(4'-hydroxy)-butyl ether. Exemplary cholesterol derivatives are described in PCT publication W02009/127060 and US
 5 patent publication US2010/0130588, each of which is incorporated herein by reference in its entirety.

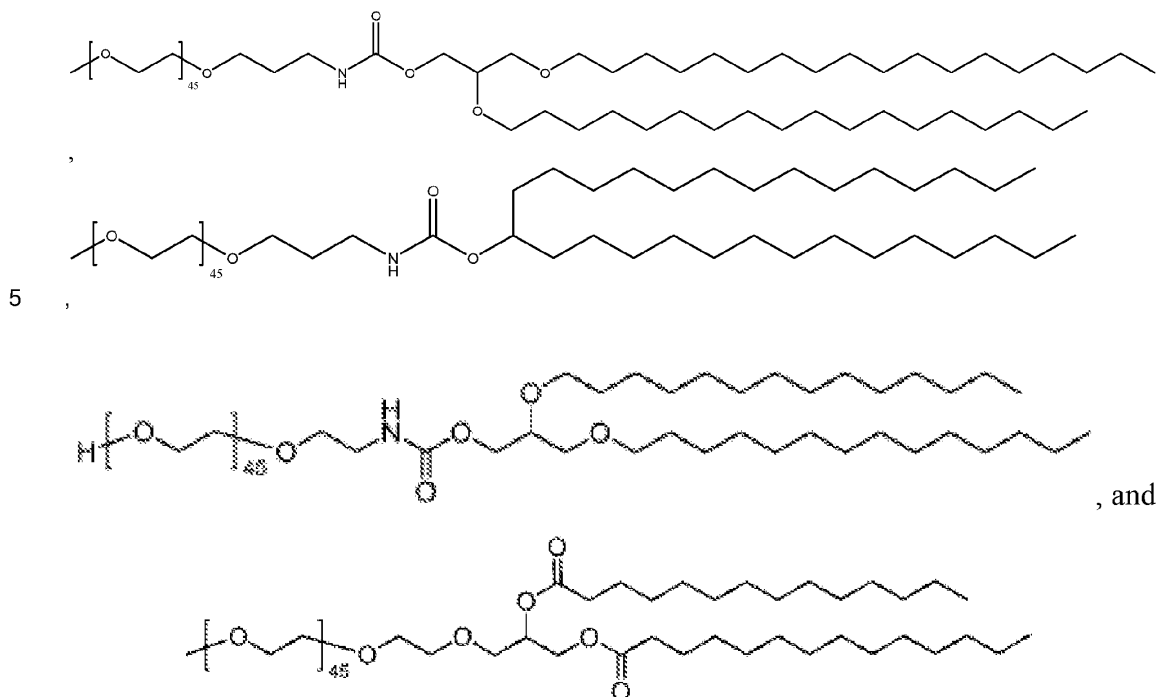
In some embodiments, the component providing membrane integrity, such as a sterol, can comprise 0-50% (mol) (e.g., 0-10%, 10-20%, 20-30%, 30-40%, or 40-50%) of the total lipid present in the lipid nanoparticle. In some embodiments, such a component is 20-50% (mol) 30-40% (mol) of the total lipid content of the lipid nanoparticle.

10 In some embodiments, the lipid nanoparticle can comprise a polyethylene glycol (PEG) or a conjugated lipid molecule. Generally, these are used to inhibit aggregation of lipid nanoparticles and/or provide steric stabilization. Exemplary conjugated lipids include, but are not limited to, PEG-lipid conjugates, polyoxazoline (POZ)-lipid conjugates, polyamide-lipid conjugates (such as ATTA-lipid conjugates), cationic-polymer lipid (CPL) conjugates, and mixtures thereof. In some embodiments, the
 15 conjugated lipid molecule is a PEG-lipid conjugate, for example, a (methoxy polyethylene glycol)-conjugated lipid.

Exemplary PEG-lipid conjugates include, but are not limited to, PEG-diacylglycerol (DAG) (such as 1-(monomethoxy-polyethyleneglycol)-2,3-dimyristoylglycerol (PEG-DMG)), PEG-dialkoxypentyl (DAA), PEG-phospholipid, PEG-ceramide (Cer), a pegylated phosphatidylethanolamine (PEG-PE),
 20 PEG succinate diacylglycerol (PEGS-DAG) (such as 4-O-(2',3'-di(tetradecanoyloxy)propyl)-1-O-(w-methoxy(polyethoxy)ethyl) butanedioate (PEG-S-DMG)), PEG dialkoxypentylcarbam, N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt, or a mixture thereof. Additional exemplary PEG-lipid conjugates are described, for example, in US5,885,613, US6,287,591,

25 US2003/0077829, US2003/0077829, US2005/0175682, US2008/0020058, US2011/0117125, US2010/0130588, US2016/0376224, US2017/0119904, and US/099823, the contents of all of which are incorporated herein by reference in their entirety. In some embodiments, a PEG-lipid is a compound of Formula III, III-a-I, III-a-2, III-b-1, III-b-2, or V of US2018/0028664, the content of which is incorporated herein by reference in its entirety. In some embodiments, a PEG-lipid is of Formula II of
 30 US20150376115 or US2016/0376224, the content of both of which is incorporated herein by reference in its entirety. In some embodiments, the PEG-DAA conjugate can be, for example, PEG-dilauryloxypropyl, PEG-dimyristyloxypropyl, PEG-dipalmitoyloxypropyl, or PEG-distearoyloxypropyl. The PEG-lipid can be one or more of PEG-DMG, PEG-dilaurylglycerol, PEG-dipalmitoylglycerol, PEG-disteryl-glycerol, PEG-dilaurylglycamide, PEG-dimyristylglycamide, PEG-dipalmitoylglycamide, PEG-disteryl-glycamide, PEG-cholesterol (1-[8'-(Cholest-5-en-3[beta]-oxy)carboxamido-3',6'-dioxaoctanyl]
 35 carbamoyl-[omega]-methyl-poly(ethylene glycol), PEG-DMB (3,4-Ditetradecoxybenzyl-[omega]-methyl-poly(ethylene glycol) ether), and 1,2-dimyristoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000]. In some embodiments, the PEG-lipid comprises PEG-DMG, 1,2-

dimyristoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000]. In some embodiments, the PEG-lipid comprises a structure selected from:



10 In some embodiments, lipids conjugated with a molecule other than a PEG can also be used in place of PEG-lipid. For example, polyoxazoline (POZ)-lipid conjugates, polyamide-lipid conjugates (such as ATTA-lipid conjugates), and cationic-polymer lipid (GPL) conjugates can be used in place of or in addition to the PEG-lipid.

Exemplary conjugated lipids, i.e., PEG-lipids, (POZ)-lipid conjugates, ATTA-lipid conjugates
 15 and cationic polymer-lipids are described in the PCT and LIS patent applications listed in Table 2 of WO2019051289A9, the contents of all of which are incorporated herein by reference in their entirety.

In some embodiments, the PEG or the conjugated lipid can comprise 0-20% (mol) of the total lipid present in the lipid nanoparticle. In some embodiments, PEG or the conjugated lipid content is 0.5-10% or 2-5% (mol) of the total lipid present in the lipid nanoparticle. Molar ratios of the ionizable lipid,
 20 non-cationic-lipid, sterol, and PEG/conjugated lipid can be varied as needed. For example, the lipid particle can comprise 30-70% ionizable lipid by mole or by total weight of the composition, 0-60% cholesterol by mole or by total weight of the composition, 0-30% non-cationic-lipid by mole or by total weight of the composition and 1-10% conjugated lipid by mole or by total weight of the composition. Preferably, the composition comprises 30-40% ionizable lipid by mole or by total weight of the
 25 composition, 40-50% cholesterol by mole or by total weight of the composition, and 10-20% non-

cationic-lipid by mole or by total weight of the composition. In some other embodiments, the composition is 50-75% ionizable lipid by mole or by total weight of the composition, 20-40% cholesterol by mole or by total weight of the composition, and 5 to 10% non-cationic-lipid, by mole or by total weight of the composition and 1-10% conjugated lipid by mole or by total weight of the composition. The composition may contain 60-70% ionizable lipid by mole or by total weight of the composition, 25-35% cholesterol by mole or by total weight of the composition, and 5-10% non-cationic-lipid by mole or by total weight of the composition. The composition may also contain up to 90% ionizable lipid by mole or by total weight of the composition and 2 to 15% non-cationic lipid by mole or by total weight of the composition. The formulation may also be a lipid nanoparticle formulation, for example comprising 8-30% ionizable lipid by mole or by total weight of the composition, 5-30% non-cationic lipid by mole or by total weight of the composition, and 0-20% cholesterol by mole or by total weight of the composition; 4-25% ionizable lipid by mole or by total weight of the composition, 4-25% non-cationic lipid by mole or by total weight of the composition, 2 to 25% cholesterol by mole or by total weight of the composition, 10 to 35% conjugate lipid by mole or by total weight of the composition, and 5% cholesterol by mole or by total weight of the composition; or 2-30% ionizable lipid by mole or by total weight of the composition, 2-30% non-cationic lipid by mole or by total weight of the composition, 1 to 15% cholesterol by mole or by total weight of the composition, 2 to 35% conjugate lipid by mole or by total weight of the composition, and 1-20% cholesterol by mole or by total weight of the composition; or even up to 90% ionizable lipid by mole or by total weight of the composition and 2-10% non-cationic lipids by mole or by total weight of the composition, or even 100% cationic lipid by mole or by total weight of the composition. In some embodiments, the lipid particle formulation comprises ionizable lipid, phospholipid, cholesterol and a PEG-ylated lipid in a molar ratio of 50: 10:38.5: 1.5. In some other embodiments, the lipid particle formulation comprises ionizable lipid, cholesterol and a PEG-ylated lipid in a molar ratio of 60:38.5:1.5.

In some embodiments, the lipid particle comprises ionizable lipid, non-cationic lipid (e.g. phospholipid), a sterol (e.g., cholesterol) and a PEG-ylated lipid, where the molar ratio of lipids ranges from 20 to 70 mole percent for the ionizable lipid, with a target of 40-60, the mole percent of non-cationic lipid ranges from 0 to 30, with a target of 0 to 15, the mole percent of sterol ranges from 20 to 70, with a target of 30 to 50, and the mole percent of PEG-ylated lipid ranges from 1 to 6, with a target of 2 to 5.

In some embodiments, the lipid particle comprises ionizable lipid / non-cationic-lipid / sterol / conjugated lipid at a molar ratio of 50:10:38.5:1.5.

In an aspect, the disclosure provides a lipid nanoparticle formulation comprising phospholipids, lecithin, phosphatidylcholine and phosphatidylethanolamine.

In some embodiments, one or more additional compounds can also be included. Those compounds can be administered separately, or the additional compounds can be included in the lipid nanoparticles of the invention. In other words, the lipid nanoparticles can contain other compounds in addition to the nucleic acid or at least a second nucleic acid, different than the first. Without limitations, other additional compounds can be selected from the group consisting of small or large organic or

inorganic molecules, monosaccharides, disaccharides, trisaccharides, oligosaccharides, polysaccharides, peptides, proteins, peptide analogs and derivatives thereof, peptidomimetics, nucleic acids, nucleic acid analogs and derivatives, an extract made from biological materials, or any combinations thereof.

5 In some embodiments, LNPs are directed to specific tissues by the addition of LNP targeting domains. For example, biological ligands may be displayed on the surface of LNPs to enhance interaction with cells displaying cognate receptors, thus driving association with and cargo delivery to tissues wherein cells express the receptor. In some embodiments, the biological ligand may be a ligand that drives delivery to the liver, e.g., LNPs that display GalNAc result in delivery of nucleic acid cargo to
 10 hepatocytes that display asialoglycoprotein receptor (ASGPR). The work of Akinc et al. *Mol Ther* 18(7):1357-1364 (2010) teaches the conjugation of a trivalent GalNAc ligand to a PEG-lipid (GalNAc-PEG-DSG) to yield LNPs dependent on ASGPR for observable LNP cargo effect (see, e.g., FIG. 6 of Akinc et al. 2010, supra). Other ligand-displaying LNP formulations, e.g., incorporating folate, transferrin, or antibodies, are discussed in WO2017223135, which is incorporated herein by reference
 15 in its entirety, in addition to the references used therein, namely Kolhatkar et al., *Curr Drug Discov Technol.* 2011 8:197-206; Musacchio and Torchilin, *Front Biosci.* 2011 16:1388-1412; Yu et al., *Mol Membr Biol.* 2010 27:286-298; Patil et al., *Crit Rev Ther Drug Carrier Syst.* 2008 25:1-61; Benoit et al., *Biomacromolecules.* 2011 12:2708-2714; Zhao et al., *Expert Opin Drug Deliv.* 2008 5:309-319; Akinc et al., *Mol Ther.* 2010 18:1357-1364; Srinivasan et al., *Methods Mol Biol.* 2012 820:105-116; Ben-Arie et al., *Methods Mol Biol.* 2012 757:497-507; Peer 2010 *J Control Release.* 20:63-68; Peer et al., *Proc Natl Acad Sci U S A.* 2007 104:4095-4100; Kim et al., *Methods Mol Biol.* 2011 721:339-353; Subramanya et al., *Mol Ther.* 2010 18:2028-2037; Song et al., *Nat Biotechnol.* 2005 23:709-717; Peer et al., *Science.* 2008 319:627-630; and Peer and Lieberman, *Gene Ther.* 2011 18:1127-1133.

25 In some embodiments, LNPs are selected for tissue-specific activity by the addition of a Selective ORgan Targeting (SORT) molecule to a formulation comprising traditional components, such as ionizable cationic lipids, amphipathic phospholipids, cholesterol and poly(ethylene glycol) (PEG) lipids. The teachings of Cheng et al. *Nat Nanotechnol* 15(4):313-320 (2020) demonstrate that the addition of a supplemental "SORT" component precisely alters the *in vivo* RNA delivery profile and mediates tissue-specific (e.g., lungs, liver, spleen) gene delivery and editing as a function of the
 30 percentage and biophysical property of the SORT molecule.

In some embodiments, the LNPs comprise biodegradable, ionizable lipids. In some embodiments, the LNPs comprise (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-(((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate, also called 3-((4,4-bis(octyloxy)butanoyl)oxy)-2-(((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl (9Z,12Z)-octadeca-
 35 9,12-dienoate) or another ionizable lipid. See, e.g., lipids of WO2019/067992, WO/2017/173054, WO2015/095340, and WO2014/136086, as well as references provided therein. In some embodiments, the term cationic and ionizable in the context of LNP lipids is interchangeable, e.g., wherein ionizable lipids are cationic depending on the pH.

In some embodiments, the average LNP diameter of the LNP formulation may be between 10s of nm and 100s of nm, e.g., measured by dynamic light scattering (DLS). In some embodiments, the average LNP diameter of the LNP formulation may be from about 40 nm to about 150 nm, such as about 40 nm, 45 nm, 50 nm, 55 nm, 60 nm, 65 nm, 70 nm, 75 nm, 80 nm, 85 nm, 90 nm, 95 nm, 100 nm, 105 nm, 110 nm, 115 nm, 120 nm, 125 nm, 130 nm, 135 nm, 140 nm, 145 nm, or 150 nm. In some embodiments, the average LNP diameter of the LNP formulation may be from about 50 nm to about 100 nm, from about 50 nm to about 90 nm, from about 50 nm to about 80 nm, from about 50 nm to about 70 nm, from about 50 nm to about 60 nm, from about 60 nm to about 100 nm, from about 60 nm to about 90 nm, from about 60 nm to about 80 nm, from about 60 nm to about 70 nm, from about 70 nm to about 100 nm, from about 70 nm to about 90 nm, from about 70 nm to about 80 nm, from about 80 nm to about 100 nm, from about 80 nm to about 90 nm, or from about 90 nm to about 100 nm. In some embodiments, the average LNP diameter of the LNP formulation may be from about 70 nm to about 100 nm. In a particular embodiment, the average LNP diameter of the LNP formulation may be about 80 nm. In some embodiments, the average LNP diameter of the LNP formulation may be about 100 nm. In some embodiments, the average LNP diameter of the LNP formulation ranges from about 1 mm to about 500 mm, from about 5 mm to about 200 mm, from about 10 mm to about 100 mm, from about 20 mm to about 80 mm, from about 25 mm to about 60 mm, from about 30 mm to about 55 mm, from about 35 mm to about 50 mm, or from about 38 mm to about 42 mm.

A LNP may, in some instances, be relatively homogenous. A polydispersity index may be used to indicate the homogeneity of a LNP, e.g., the particle size distribution of the lipid nanoparticles. A small (e.g., less than 0.3) polydispersity index generally indicates a narrow particle size distribution. A LNP may have a polydispersity index from about 0 to about 0.25, such as 0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.10, 0.11, 0.12, 0.13, 0.14, 0.15, 0.16, 0.17, 0.18, 0.19, 0.20, 0.21, 0.22, 0.23, 0.24, or 0.25. In some embodiments, the polydispersity index of a LNP may be from about 0.10 to about 0.20.

The zeta potential of a LNP may be used to indicate the electrokinetic potential of the composition. In some embodiments, the zeta potential may describe the surface charge of an LNP. Lipid nanoparticles with relatively low charges, positive or negative, are generally desirable, as more highly charged species may interact undesirably with cells, tissues, and other elements in the body. In some embodiments, the zeta potential of a LNP may be from about -10 mV to about +20 mV, from about -10 mV to about +15 mV, from about -10 mV to about +10 mV, from about -10 mV to about +5 mV, from about -10 mV to about 0 mV, from about -10 mV to about -5 mV, from about -5 mV to about +20 mV, from about -5 mV to about +15 mV, from about -5 mV to about +10 mV, from about -5 mV to about +5 mV, from about -5 mV to about 0 mV, from about 0 mV to about +20 mV, from about 0 mV to about +15 mV, from about 0 mV to about +10 mV, from about 0 mV to about +5 mV, from about +5 mV to about +20 mV, from about +5 mV to about +15 mV, or from about +5 mV to about +10 mV.

The efficiency of encapsulation of a protein and/or nucleic acid, describes the amount of protein and/or nucleic acid that is encapsulated or otherwise associated with a LNP after preparation, relative to the initial amount provided. The encapsulation efficiency is desirably high (e.g., close to 100%). The

encapsulation efficiency may be measured, for example, by comparing the amount of protein or nucleic acid in a solution containing the lipid nanoparticle before and after breaking up the lipid nanoparticle with one or more organic solvents or detergents. An anion exchange resin may be used to measure the amount of free protein or nucleic acid (e.g., RNA) in a solution. Fluorescence may be used to measure the amount of free protein and/or nucleic acid (e.g., RNA) in a solution. For the lipid nanoparticles described herein, the encapsulation efficiency of a protein and/or nucleic acid may be at least 50%, for example 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%. In some embodiments, the encapsulation efficiency may be at least 80%. In some embodiments, the encapsulation efficiency may be at least 90%. In some embodiments, the encapsulation efficiency may be at least 95%.

A LNP may optionally comprise one or more coatings. In some embodiments, a LNP may be formulated in a capsule, film, or tablet having a coating. A capsule, film, or tablet including a composition described herein may have any useful size, tensile strength, hardness or density.

Additional exemplary lipids, formulations, methods, and characterization of LNPs are taught by WO2020061457, which is incorporated herein by reference in its entirety.

In some embodiments, *in vitro* or ex vivo cell lipofections are performed using Lipofectamine MessengerMax (Thermo Fisher) or TransIT-mRNA Transfection Reagent (Mirus Bio). In certain embodiments, LNPs are formulated using the GenVoy_ILM ionizable lipid mix (Precision NanoSystems). In certain embodiments, LNPs are formulated using 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA) or dilinoleylmethyl-4-dimethylaminobutyrate (DLin-MC3-DMA or MC3), the formulation and *in vivo* use of which are taught in Jayaraman et al. Angew Chem Int Ed Engl 51(34):8529-8533 (2012), incorporated herein by reference in its entirety.

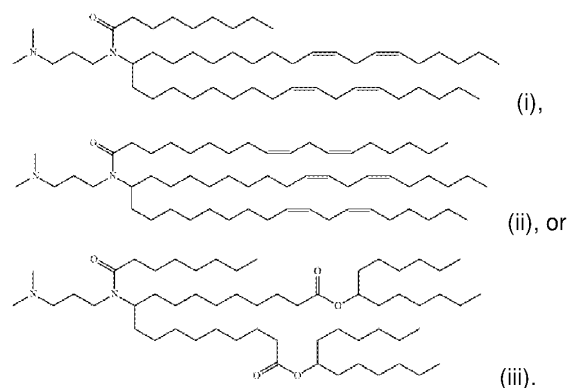
LNP formulations optimized for the delivery of CRISPR-Cas systems, e.g., Cas9-gRNA RNP, gRNA, Cas9 mRNA, are described in WO2019067992 and WO2019067910, both incorporated by reference.

Additional specific LNP formulations useful for delivery of nucleic acids are described in US8158601 and US8168775, both incorporated by reference, which include formulations used in patisiran, sold under the name ONPATPRO.

Exemplary dosing of LNPs comprising the RNA compositions described herein may include about 0.1, 0.25, 0.3, 0.5, 1, 2, 3, 4, 5, 6, 8, 10, or 100 mg/kg (RNA). Exemplary dosing of AAV comprising a nucleic acid encoding one or more components of the system may include an MOI of about 10¹¹, 10¹², 10¹³, and 10¹⁴ vg/kg.

In some embodiments, the invention includes a lipid nanoparticle (LNP) comprising the ANDbody polypeptide (or RNA encoding the same), nucleic acid molecule, or DNA encoding an ANDbody described herein. In embodiments, the LNP comprises a cationic lipid. In some embodiments, the LNP further comprises one or more neutral lipid, e.g., DSPC, DPPC, DMPC, DOPC, POPC, DOPE, SM, a steroid, e.g., cholesterol, and/or one or more polymer conjugated lipid, e.g., a pegylated lipid,

e.g., PEG-DAG, PEG-PE, PEG-S-DAG, PEG-cer or a PEG dialkoxypylcarbamate. In some embodiments, the cationic lipid of the LNP has a structure according to:



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For a review of LNP, see also, e.g., Li et al. 2017, *Nanomaterials* 7, 122; doi:10.3390/nano7060122.

10 **Other Carriers**

Viral vectors

The compositions described herein (e.g., polypeptide or RNA ANDbody compositions), can be delivered by a viral vector (e.g., a viral vector expressing an RNA). A viral vector may be administered to a cell or to a subject (e.g., a human subject or non-human animal). A viral vector may be locally or systemically administered.

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Examples of viral vectors include a retrovirus (e.g., Retroviridae family viral vector), adenovirus (e.g., Ad5, Ad26, Ad34, Ad35, and Ad48), parvovirus (e.g., adeno-associated viruses), coronavirus, negative strand RNA viruses such as orthomyxovirus (e.g., influenza virus), rhabdovirus (e.g., rabies and vesicular stomatitis virus), paramyxovirus (e.g., measles and Sendai), positive strand RNA viruses, such as picornavirus and alphavirus, and double stranded DNA viruses including adenovirus, herpesvirus (e.g., Herpes Simplex virus types 1 and 2, Epstein-Barr virus, cytomegalovirus, replication deficient herpes virus), and poxvirus (e.g., vaccinia, modified vaccinia Ankara (MVA), fowlpox and canarypox). Other viruses include Norwalk virus, togavirus, flavivirus, reoviruses, papovavirus, hepadnavirus, human papilloma virus, human foamy virus, and hepatitis virus, for example. Examples of retroviruses include: avian leukosis-sarcoma, avian C-type viruses, mammalian C-type, B-type viruses, D-type viruses, oncoretroviruses, HTLV-BLV group, lentivirus, alpharetrovirus, gammaretrovirus, spumavirus (Coffin, J. M., *Retroviridae: The viruses and their replication*, Virology (Third Edition) Lippincott-Raven, Philadelphia, 1996). Other examples include murine leukemia viruses, murine sarcoma viruses, mouse mammary tumor virus, bovine leukemia virus, feline leukemia virus, feline sarcoma virus, avian leukemia virus, human T-cell leukemia virus, baboon endogenous virus, Gibbon ape leukemia virus, Mason Pfizer monkey virus, simian immunodeficiency virus, simian

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sarcoma virus, Rous sarcoma virus and lentiviruses. Other examples of vectors are described, for example, in US Patent No. 5,801,030, the teachings of which are incorporated herein by reference.

Anellovirus vectors can also be used for delivering an ANDbody composition described herein.

Anellovectors are known in the art and described, e.g., in WO2020123773, WO2020123816,

- 5 WO2018232017, and WO2020123773. In certain embodiments, an anellovector composition comprises a genomic element that comprises a promoter operably linked to a nucleic acid sequence encoding an ANDbody described herein, the genetic element encapsulated by a proteinaceous exterior comprising an Anellovirus ORF1, e.g., an anellovirus capsid protein.

Cell and vesicle-based carriers

- 10 A composition described herein (e.g., polypeptide or RNA ANDbody compositions), described herein can be administered to a cell in a cell, vesicle or other membrane-based carrier. In one embodiment, the compositions and systems described herein can be formulated in liposomes or other similar vesicles. Liposomes are spherical vesicle structures composed of a uni- or multilamellar lipid bilayer surrounding internal aqueous compartments and a relatively impermeable outer lipophilic
- 15 phospholipid bilayer. Liposomes may be anionic, neutral or cationic. Liposomes are biocompatible, nontoxic, can deliver both hydrophilic and lipophilic drug molecules, protect their cargo from degradation by plasma enzymes, and transport their load across biological membranes and the blood brain barrier (BBB) (see, e.g., Spuch and Navarro, Journal of Drug Delivery, vol. 2011, Article ID 469679, 12 pages, 2011. doi:10.1155/2011/469679 for review). Vesicles can be made from several
- 20 different types of lipids; however, phospholipids are most commonly used to generate liposomes as drug carriers. Methods for preparation of multilamellar vesicle lipids are known in the art (see for example U.S. Pat. No. 6,693,086, the teachings of which relating to multilamellar vesicle lipid preparation are incorporated herein by reference). Although vesicle formation can be spontaneous when a lipid film is mixed with an aqueous solution, it can also be expedited by applying force in the
- 25 form of shaking by using a homogenizer, sonicator, or an extrusion apparatus (see, e.g., Spuch and Navarro, Journal of Drug Delivery, vol. 2011, Article ID 469679, 12 pages, 2011. doi:10.1155/2011/469679 for review). Extruded lipids can be prepared by extruding through filters of decreasing size, as described in Templeton et al., Nature Biotech, 15:647-652, 1997, the teachings of which relating to extruded lipid preparation are incorporated herein by reference.

- 30 Exosomes can also be used as drug delivery vehicles for the compositions and systems described herein. For a review, see Ha et al. July 2016. Acta Pharmaceutica Sinica B. Volume 6, Issue 4, Pages 287-296; <https://doi.org/10.1016/j.apsb.2016.02.001>.

Ex vivo differentiated red blood cells can also be used as a carrier for an agent (e.g., an inhibitor) described herein, e.g., an antibody or a nucleic acid described herein. See, e.g.,

- 35 WO2015073587; WO2017123646; WO2017123644; WO2018102740; WO2016183482; WO2015153102; WO2018151829; WO2018009838; Shi et al. 2014. Proc Natl Acad Sci USA. 111(28): 10131–10136; US Patent 9,644,180; Huang et al. 2017. Nature Communications 8: 423; Shi et al. 2014. Proc Natl Acad Sci USA. 111(28): 10131–10136.

Fusosome compositions, e.g., as described in WO2018208728, can also be used as carriers to deliver the [agent] or preparation described herein.

Plant nanovesicles and plant messenger packs (PMPs), e.g., as described in WO2011097480, WO2013070324, WO2017004526, or WO2020041784 can also be used as carriers to deliver the

5 compositions described herein.

Without further elaboration, it is believed that one skilled in the art can, based on the above description, utilize the present invention to its fullest extent. The following specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. All publications and sections thereof cited herein are herein incorporated by

10 reference for the purposes or subject matter referenced herein.

EXAMPLES

The invention will be further illustrated in the following non-limiting examples.

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15 **EXAMPLE 1. ANDBODY BINDING MOUSE AND HUMAN RAGE AND NOTCH2**

1.1 Vaccination to create anti-RAGE antibodies

Antibodies against human RAGE extracellular domain, an exemplary address target of the present technology, are created by immunization. The extracellular domain of human RAGE (NCBI
20 protein accession Q15109 positions N24-A344) (huRAGE) fused to the Fc region of human IgG1 (UniProt ID P01857 positions P100-K330) is expressed in HEK293F cells. Briefly, DNA sequences are codon optimized for mammalian expression and ordered in the pcDNA3.4-TOPO expression vector

(ThermoFisher Scientific). Proteins are transiently transfected into HEK293 cells and purified using rProtein A Sepharose Fast Flow resin according to manufacturer's instructions (GE Healthcare) similar to prior methods (Rothschilds et al. 2019). 50 ug of the huRAGE-Fc fusion protein is used to immunize female BALB/c mice by i.p. injection in CFA/IFA (Millipore Sigma, catalog # F5881-10ML and F5506-10ML) adjuvant. Subsequently, hybridomas are generated (Listek et al. 2020). Clones are initially screened for IgG reactivity specific for the huRAGE-Fc fusion protein used for immunization in an ELISA format followed by flow cytometry studies using cells stably (CHO) or transiently (HEK293F) transfected with full-length huRAGE. Anti-RAGE hybridoma clones are next evaluated based on murine cross-reactivity. Flow cytometry studies are done using cells stably (CHO) or transiently (HEK293F) transfected with full-length mouse RAGE (mRAGE), and clones are selected that bind to mRAGE. Positive clones expressing anti-RAGE mAbs cross-reactive between human and mouse are then further purified by limited dilution cloning. The hybridomas are grown in DMEM/2% ultra low IgG serum and the mAbs are purified by protein G chromatography according to manufacturer's instructions using (Millipore Sigma, P3296-1ML).

1.2 Selecting for inert anti-RAGE antibodies

Address target binding sites of the present technology are designed to not influence signaling upon binding the address target, such as the exemplary RAGE address target. Accordingly, anti-RAGE hybridoma clones produces as described above are further evaluated based on their inability to block RAGE ligand binding. Human RAGE ligands tested included HMGB1 (full-length, from Creative BioMart catalog # HMGB1-29332TH), Advanced Glycation Endproduct (fused to bovine serum albumin, Millipore Sigma catalog # 121800-10MG-M), S100A12 (full-length, from R&D Systems catalog # 1052-ER-050), S100A1 (full-length, from R&D Systems catalog # 9705-S1-100), S100A4 (R&D Systems catalog # 4137-S4-050), S100A10 (full-length, from Creative BioMart catalog # S100A10-157H), S100A11 (R&D Systems catalog #9015-S11-050), S100A13 (R&D Systems catalog #4327-SA-050), S100B (R&D Systems catalog #1820-SB-050), amyloid- β -peptide (DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA from NM_000484.2, Millipore Sigma catalog # AG912-1MG) and Mac-1 (F17-N1105 from NP_001139280 and Q23-N700 from UniProt P05107, R&D Systems catalog #4047-AM-050). ELISAs are used to quantify ability of ligands to bind in the presence of anti-RAGE antibodies. HuRAGE-Fc is adsorbed to ELISA plates, then after blocking, the plates are incubated with concentrations of 10 fM up to 10 uM of anti-RAGE antibody clones from the hybridomas (one condition per concentration and per clone). After washing the plates, ligands are each biotinylated according to manufacturer's instructions (ThermoFisher catalog #21435), and then incubated on the plates at concentrations ranging from 10 fM up to 10 uM. After washing, SA-linked HRP secondary antibodies are added, followed by TMB substrate and colorimetric readout quantified by absorbance. Ligand binding is compared within a given ligand with versus without anti-RAGE antibodies to isolate anti-RAGE clones that are inert and do not affect binding of one or more ligands.

The inability of anti-RAGE antibodies to inhibit IFN α -induced gene signature is also evaluated, and anti-RAGE hybridoma clones are chosen that do not change cellular signaling based on an IFN α -

induced gene signature assay. PBMCs from healthy human donors are stimulated for 4h with 50% sera from SLE patients. The assay is completed either in the presence of anti-RAGE antibodies or unrelated (negative) isotype control human IgG1 antibodies (Bio X Cell catalog # BE0297) at antibody concentrations ranging from 10 fM up to 10 uM. In addition a huRAGE-Fc fusion molecule is used as a positive control. Total RNA is purified and expression of type I IFN-inducible genes, including DDX58, G1P2, MXI, OAS3, RSAD2, IFIT1, IFI35 are measured by real-time qRT-PCR analysis as in prior methods (WO 2008/137552 A2, <https://patentimages.storage.googleapis.com/94/26/c8/7b9f27f693c4b6/WO2008137552A2.pdf>). The inhibition values of gene expression are normalized to the negative control Ab.

1.3 Vaccination to create anti-Notch2 antibodies

Antibodies against the extracellular domain of human Notch2 (huNotch2) fused to the Fc region of human IgG1, an exemplary effector target of the present technology, are created by immunization similar to RAGE as described above. After immunization and hybridoma generation, clones are screened exactly as above but for binding to full length human and mouse Notch2 (instead of RAGE). Positive clones expressing anti-Notch2 mAbs cross-reactive between human and mouse are then further purified by limited dilution cloning. The hybridomas are grown in DMEM/2% ultra low IgG serum and the mAbs are purified by protein G chromatography.

1.4 Selecting for active anti-Notch2 antibodies at wide IC₅₀ ranges

Effector target binding sites of the present technology, such as Notch2, are designed to not influence signaling upon binding the effector target, unless they are localized to a target tissue by an address target binding site, such as RAGE. Accordingly, the binding affinities of effector target (e.g., Notch2) binding sites are analyzed. Specifically, the IC₅₀s of Notch2 antibodies on the ligand human Jagged-2-Fc fusion protein (Creative BioMart, JAG2-382H) binding to surface Notch2 are evaluated using flow cytometry to choose antibodies at IC₅₀'s ranging from less than 1 nM up to 5 uM. Jagged-2-Fc is labeled with alexa fluor 647 (AF647) according to manufacturer's instructions (ThermoFisher, A20186) and methods previously described (Tzeng et al. 2015).

HEK293F cells are transiently transfected with full-length huNotch2. The cells are incubated with anti-Notch2 antibodies at concentrations increasing from 1 pM up to 50 uM. Subsequently (and without washing the cells), the cells are then incubated for 1 hour at 4 degrees Celsius with a constant concentration of AF647 labeled Jagged-2-Fc, ranging (for different IC₅₀ assays) from 1pM up to 50uM. For each IC₅₀ assay, one constant concentration of AF647 Jagged-2-Fc is chosen with varied anti-Notch2. Binding of AF647 Jagged-2-Fc with increasing anti-Notch2 antibody concentrations is quantified on the cells by flow cytometry using a ThermoFisher Attune NxT (B2R3Y3V6).

1.5 Expressing and purifying ANDbodies as bispecifics

DNA sequences from 10 RAGE antibodies and 10 Notch2 antibodies ranging in IC₅₀ (from < 1 nM up to 5 uM) are cloned using In-Fusion HD Cloning (Takara Bio, catalog # 638911) into human IgG1 framework with single matching point mutations in the CH3 domain Fc region according to the

'Controlled Fab-Arm Exchange' (cFAE) method (Labrijn et al. 2014). After separately expressing antibodies from transient HEK293 expressions and purifying each antibody using protein A affinity resin, parental antibodies (combinations of 1 RAGE antibody with 1 Notch2 antibody) are made into bispecific RAGE/Notch2 ANDbodies according to the cFAE method. Briefly, parental antibodies are
5 mixed under permissive redox conditions to enable recombination of half-molecules. Subsequently, the reductant is removed to allow for reoxidation of interchain disulfide bonds. Lastly, exchange efficiency is quantified using chromatography-based or mass spectrometry-based methods. Around 100 variant ANDbodies of RAGExNotch2 are made.

1.6 Affinity of ANDbody variants

10 To identify ANDbody™ variants that meet desired effector target and address target binding affinity criteria, SPR-based affinity measurements are carried out on BIAcore model 2000 or T100 (Biacore/GE Healthcare, Piscataway, NJ) at 25°C using HBS-EP+ buffer (Cytiva catalog # BR100669) with 0.1 mg/ml BSA (Millipore Sigma catalog # A9418) as a running buffer. A Sensor Chip Protein A (Cytiva catalog # 29127557) is used to capture mouse RAGE-Fc, human RAGE-Fc, mouse Notch2-Fc,
15 or human Notch2-Fc. ANDbody is injected in a 3-fold dilution series from 60 to 0.74 nM, and dissociation is monitored for 10 min for all proteins. Kinetic analysis is done by simultaneously fitting the association and dissociation phases of the sensorgram using the 1:1 Langmuir binding model in BIAevaluation software (Biacore) as supplied by the manufacturer. Double referencing is applied in each analysis to eliminate background responses from the reference surface and buffer only control.

20 This assay can quantitatively assess the affinities of every ANDbody variant for RAGE and Notch2. ANDbody variants with higher affinity for RAGE than Notch2 as well as variants with no affinity differences or higher affinity for Notch2 are used in subsequent *in vitro* and *in vivo* experiments.

1.7 *In vitro* assays for Notch2 antagonism on cells with or without RAGE expression

To analyze ANDbody characteristics, *in vitro*, HEK293F cells are transiently transfected with full
25 length huRAGE (R+) or full length huNotch2 (N+), or co-transfected with both (RN+). The many variant RAGExNotch2 ANDbodies are fluorophore-labeled with alexa fluor 647 (AF647) according to manufacturer's instructions (ThermoFisher, A20186) and methods previously described (Tzeng et al. 2015). Subsequently, ANDbodies are incubated with R+, N+, RN+, or combined R+ plus N+ cells at ANDbody concentrations ranging from 10 fM up to 10 uM. The parental anti-Notch2 mono-specific
30 antibodies (one from each variant) are fluorophore labeled with FITC according to manufacturer's instructions (ThermoFisher, 53027). In some conditions, the parental anti-Notch2 FITC labeled antibodies are incubated with the cells pre-bound with AF647 RAGExNotch2 (matching Notch2 variants) at concentrations of 10 fM up to 10 uM to saturate the remaining binding sites for Notch2. The binding EC₅₀s of both the AF647 labeled RAGExNotch2 ANDbody variants and the parental FITC
35 labeled parental anti-Notch2 antibodies are quantified using flow cytometry. When the FITC Notch2 antibody is added after the AF647 RAGExNotch2, the FITC signal from those cells is subtracted from the FITC signal from FITC Notch2 alone on cells (then normalized to the Notch2 alone signal) to quantify the %Notch2 bound by RAGExNotch2. These numbers at different concentrations of the

RAGExNotch2 ANDbody are used to create EC₅₀ curves. The assay is also run replacing the AF647-labeled ANDbody with AF647-labeled anti-Notch2 antibody.

A difference in observed EC₅₀s on N+ cells vs RN+ cells reveals an enhanced Notch2 blockade when RAGE is present and identifies cells expressing the RAGExNotch2 ANDbodies.

5 1.8 *Biodistribution (in vivo) for ANDbody and parental antibodies*

To analyze ANDbody distribution, *in vivo*, the biodistribution of the RAGExNotch2 ANDbody as well as each of the parental antibodies (anti-Notch2 or anti-RAGE used for the cFAE of the ANDbody) is quantified in female Balb/c and C57BL/6 mice.

10 To quantify the cellular biodistribution, the proteins (ANDbody and antibodies) are first individually labeled with AF647 according to manufacturer's instructions (ThermoFisher, A20186) and methods previously described (Tzeng et al. 2015). Then, each labeled antibody is injected individually at doses of 10ug, 100ug, and 500ug IV (tail vein). Saline (PBS) is also injected as a control at equal volume.

15 For cellular biodistribution, at time points of 12 hours, 1 day, 2 days, 3 days, 7 days, and 14 days after injection, mice are euthanized using CO₂ and tissues including heart, lung, spleen, blood, kidney, liver, and intestines are processed into single cell suspensions according to methods previously described (Tzeng et al. 2015). Briefly, blood is collected by cardiac puncture into EDTA-treated tubes (BD catalog # 365974), and other tissues are harvested, weighed, mechanically dissociated between frosted glass slides, and rendered into single-cell suspensions by filtration through 70-μm mesh screens
20 (Millipore Sigma, catalog # CLS431751-50EA). Splenocytes, whole blood, and lung are treated with ammonium-chloride-potassium (ACK) lysing buffer (ThermoFisher Scientific, catalog # A1049201). Heart is digested with collagenase and processed into single cell suspension according to previous methods (Covarrubias et al. 2019). Flow cytometry is performed on immune cells using markers for CD8 T cells (CD3e+ CD8+), CD4 T cells (CD3e+ CD4+ Foxp3-), regulatory T cells (CD4+ CD25+
25 FOXP3+), monocytes/macrophages (CD3e- CD11b+ CD11c-/lo NK1.1- Ly6G- SSClo), dendritic cells (CD3e- CD11chi), NK cells (NK1.1+ CD3e-), and NKT cells (NK1.1+ CD3e+) as previously described (Tzeng et al. 2015). Lung cells including epithelial (CD326+CD31-CD45-), endothelial (CD326-CD31+CD45-), and hematopoietic lineages (CD326-CD31-CD45+) are also analyzed as previously defined (Singer et al. 2016). Antibodies are purchased from Biolegend, and flow cytometry is
30 run on a ThermoFisher Attune NxT (B2R3Y3V6). Presence of the labeled ANDbody or other labeled antibody on the cell surface is defined by fluorescence of AF647 (and this fluorophore was avoided in the flow panels).

35 To quantify the tissue biodistribution, the proteins (ANDbody and antibodies) are first individually labeled with NHS-5/6-FAM (ThermoFisher Scientific, catalog # 46409) as per the manufacturer's instructions.

For tissue biodistribution, at time points of 12 hours, 1 day, 2 days, 3 days, 7 days, and 14 days after injection, mice are euthanized using CO₂ and tissues including lung, spleen, blood, kidney, liver, and intestines are harvested, weighed, and imaged on an IVIS Spectrum imaging system (Caliper Life

Sciences; excitation, 500nm; emission, 540nm). Images are analyzed using the Living Image software.

1.9 *In vivo bioactivity quantifying gene expression changes*

To analyze ANDbody activity, *in vivo*, bioactivity is quantified using using female Balb/c and C57BL/6 mice. To quantify bioactivity across tissues, the RAGExNotch2 ANDbody or each of the respective parental antibodies (anti-Notch2 or anti-RAGE used for the cFAE of the ANDbody) is injected at doses of 10ug, 100ug, and 500ug IV (tail vein). Saline (PBS) is also injected as a control at equal volume.

At time points of 12 hours, 1 day, 2 days, 3 days, 7 days, and 14 days after injection, tissues including lung, spleen, blood, kidney, liver, heart, and intestines are processed into single cell suspensions according to methods previously described (Tzeng et al. 2015). Briefly, blood is collected by cardiac puncture into EDTA-treated tubes (BD catalog # 365974), and other tissues are harvested, weighed, mechanically dissociated between frosted glass slides, and rendered into single-cell suspensions by filtration through 70-µm mesh screens (Millipore Sigma, catalog # CLS431751-50EA). Splenocytes and whole blood are treated with ammonium-chloride-potassium (ACK) lysing buffer (Thermofisher Scientific, catalog # A1049201).

qRT-PCR is performed using methods previously described (Nandagopal et al. 2018). RNA is prepared using the RNeasy kit (QIAGEN). cDNA is prepared from 500ng RNA using the iScript cDNA synthesis kit (Bio-Rad). 0.5 µL cDNA is used per 10 µL RT-qPCR reaction mix containing 1X iQSYBR Green Supermix (Bio-Rad) and 450 nM total forward and reverse primers. Reactions are performed on a BioRad CFX Real-Time PCR Detection System using a 2-step amplification protocol, with the following thermocycling parameters: 95 C, 3 min followed by 40 cycles of 95 C, 10 s (melting) and 55 C, 30 s (annealing + extension). All reactions are performed in duplicate.

Genes related to Notch2 signaling are mouse Hes1, Hey1, and HeyL, and the reference gene is SdhA. Primers used for amplification are the mouse Hes1 primer set (Forward, 5'-CAACACGACACCGGACAAAC-3' and Reverse, 5'-AAGAATAAATGAAAGTCTAAGCCAA-3'), mouse Hey1 primer set (Forward, 5'-GCCGAAGTTG CCCGTTATCT-3' and Reverse, 5'-CGCTGGGATG CGTAGTTGTT-3'), mouse HeyL primer set (Forward, 5'-GAGCTGAC TTCCCACAACCA-3' and Reverse, 5'-GAGAGG TGCCTTGCGTAGA-3'), and mouse SdhA primer set (Forward, 5'-AGTGGGCT GTCTTCCTTAAC-3' and Reverse, 5'-GGATTGCTTCT GTTTGCTTGG-3') previously described (Nandagopal et al. 2018). All primers are purchased from IDT DNA.

Hes1, Hey1, and HeyL gene expression is measured in the ANDbody treated mice, untreated mice, and anti-Notch2 treated mice, including in the lungs.

1.10 *In vivo bioactivity using weights and histology*

Using female Balb/c and C57BL/6 mice, histology is done on organs such as the spleen, kidney, liver, heart, intestines, teeth, and lungs to compare pathology with ANDbody treatment, with treatment with anti-Notch2 alone, or saline (PBS). Starting at 8 weeks of age, 10ug, 100ug, and 500ug of the ANDbody or of the corresponding Notch2 antibody (prior to cFAE) is injected IV (tail vein) 1x or

2x per week. Saline (PBS) is also injected as a control at equal volume 1x or 2x per week. Mice are weighed 2x per week starting prior to the first treatment. After 2 weeks, 4 weeks, and 6 weeks of treatment, mice are euthanized and organs are processed for histology.

Unless otherwise noted, organs are removed into cassettes and then placed directly into 10% neutral-buffered formalin (Sigma-Aldrich) for 12-24 hours prior to embedding in paraffin. Lungs are perfused with 10% neutral-buffered formalin prior to being placed in cassettes for soaking in neutral-buffered formalin. Intestines are thoroughly rinsed before being put in cassettes for soaking in 10% neutral-buffered formalin. Paraffin sections (1-2 μ m) are cut and de-waxed prior to histochemical staining. Sections are stained with hematoxylin/eosin (H&E; Merck, Darmstadt, Germany) and scored blindly according to immune infiltrates and tissue morphology.

In addition to lung morphology, weight loss (or not) of ANDbody treated mice over the course of treatment is compared with weight loss (or not) of mice treated with anti-Notch2, and weight loss (or not) of untreated mice.

EXAMPLE 2. ANDBODY BINDING MOUSE AND HUMAN UMOD AND NOTCH2

2.1 Yeast surface display to create anti-UMOD antibodies

Yeast surface display (Chao et al. 2006) is used to engineer antibodies to mouse UMOD (Creative BioMart, catalog # UMOD-17835M, untagged), an exemplary address target of the present technology. This is done by using methods described previously (Angelini et al. 2015) and summarized below. The yeast display starts with a synthetic antibody library from the Sidhu laboratory that is based off of natural frameworks, library 'G' (Van Deventer et al. 2015). scFvs displayed on the yeast surface are selected for binding to mouse UMOD. Subsequent sorts can be done against the human UMOD antigen (Creative BioMart, catalog # UMOD-001H, untagged), such that binders can be cross-reactive between human and mouse forms. To increase affinity of the scFv binders, affinity maturation is performed using error-prone PCR as described previously (Angelini et al. 2015) and the resulting library is re-sorted for binding to both mouse and human UMOD. Subsequent to engineering, many scFvs that are multi-species cross-reactive are cloned back into human IgG1 antibody format.

2.2 Selecting for inert anti-UMOD antibodies

Address target binding sites of the present technology are designed to not influence signaling upon binding the address target, such as the exemplary UMOD address target. Accordingly, anti-UMOD antibodies are further evaluated based on their inability to block UMOD ligand binding, in an assay such as the one described above for RAGE antibodies or an *in vivo* assay. Inert UMOD antibodies may be identified in such assays whereby kidney architecture is not affected or modified by the screened UMOD antibody.

2.3 Vaccination to create anti-Notch2 antibodies

Antibodies cross-reactive to mouse and human Notch2 are created, cloned, and expressed into the human IgG1 framework according to prior methods as described above.

2.4 *Selecting for active Notch2 antibodies at wide IC₅₀ ranges*

Antibodies against Notch2 will be selected at wide IC₅₀ ranges as described above.

2.5 *Expressing and purifying ANDbodies as bispecifics*

5 DNA sequences from 10 UMOD antibodies and 10 Notch2 antibodies ranging in IC₅₀ (from < 1 nM up to 5 uM) are made into about 100 variant ANDbodies as described above.

2.6 *Affinity of ANDbody variants for UMOD and Notch2*

10 ANDbody affinities for UMOD and Notch2 are evaluated similarly to above using a BIAcore (as described above). In this case, human and mouse versions of His-tagged UMOD are immobilized on a Sensor Chip NTA (Cytiva catalog # BR100034). Human and mouse notch2-Fc are immobilized as described above.

2.7 *Biodistribution (in vivo) for ANDbody and parental antibodies*

Cellular and tissue biodistribution studies are done using methods described above (as described above). However, the ANDbody used in this case is UMODxNotch2, and the parental antibodies correspond to anti-UMOD and anti-Notch2.

2.8 *In vivo bioactivity quantifying gene expression changes*

15 The *in vivo* bioactivity of UMODxNotch2 ANDbodies is quantified using gene expression methods described above.

2.9 *In vivo bioactivity using weights and histology*

20 The *in vivo* bioactivity of UMODxNotch2 ANDbodies is quantified using weight and histology methods described above.

EXAMPLE 3. ANDBODY BINDING MOUSE AND HUMAN MEP1B AND NOTCH2

3.1 *Yeast surface display to create anti-MEP1B antibodies*

25 Yeast surface display (Chao et al. 2006) is used to engineer antibodies to mouse MEP1B (Cusabio, CSB-MP730755MO), an exemplary address target of the present technology. Yeast display is performed as described above (0) to get cross-reactive mouse/human MEP1B binders (human MEP1B, Cusabio, CSB-MP618098HU). Subsequent to engineering, many scFv's cross-reactive to mouse and human MEP1B are cloned into human IgG1, transiently transfected into HEK293F cells, and purified using protein A resin as described above.

3.2 *Vaccination to create anti-Notch2 antibodies*

Antibodies cross-reactive to mouse and human Notch2 are created, cloned, and expressed into the human IgG1 framework according to prior methods described above.

3.3 *Selecting for active Notch2 antibodies at wide IC₅₀ ranges*

35 Antibodies against Notch2 are selected at wide IC₅₀ ranges as described above.

3.4 *Expressing and purifying ANDbodies as bispecifics*

DNA sequences from 10 MEP1B antibodies and 10 Notch2 antibodies ranging in IC₅₀ (from < 1 nM up to 5 uM) are made into about 100 variant ANDbodies as described above.

5 3.5 *Affinity of ANDbody variants for MEP1B and Notch2*

ANDbody affinities for MEP1B and Notch2 are evaluated similarly to above using a BIAcore. In this case, human and mouse versions of His-tagged MEP1B are immobilized on a Sensor Chip NTA (Cytiva catalog # BR100034). Human and mouse notch2-Fc are immobilized as described above.

10 3.6 *Biodistribution (in vivo) for ANDbody and parental antibodies*

Cellular and tissue biodistribution studies are done using methods described above. However, the ANDbody used in this case is MEP1BxNotch2, and the parental antibodies correspond to anti-MEP1B and anti-Notch2.

15 3.7 *In vivo bioactivity quantifying gene expression changes*

The *in vivo* bioactivity of MEP1BxNotch2 ANDbodies is quantified using the gene expression methods described above.

3.8 *In vivo bioactivity using weights and histology*

20 The *in vivo* bioactivity of MEP1BxNotch2 ANDbodies is quantified using weight and histology methods described above.

EXAMPLE 4. ANDBODY BINDING MOUSE AND HUMAN RAGE AND IL11Ra

4.1 *Vaccination to create anti-RAGE antibodies*

25 Methods are described above to vaccinate in order to create mouse/human cross-reactive anti-RAGE antibodies.

4.2 *Selecting for inert anti-RAGE antibodies*

Methods are described above to select for inert anti-RAGE antibodies.

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4.3 *Yeast surface display to create anti-IL11Ra antibodies*

Yeast surface display is used similar to above to create antibodies of varying affinities cross-reactive with mouse and human IL11Ra, an exemplary effector target of the present technology. The DNA sequences coding for extracellular domains of mouse IL11Ra (positions 24-372 of UniProt ID Q64385) and human IL11Ra (positions 24-370 of UniProt ID Q14626) are codon optimized for mammalian expression and ordered with a C-terminal His tag in the pcDNA3.4-TOPO expression vector (ThermoFisher Scientific). Proteins are transiently transfected into HEK293F cells and purified using TALON® Metal Affinity Resin according to manufacturer's instructions (Clontech) similar to prior methods (Rothschilds et al. 2019). These soluble recombinant mouse and human IL11Ra are used as the antigens for yeast surface display.

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ScFv's cross-reactive to mouse and human IL11Ra are cloned into human IgG1, transiently transfected into HEK293F cells, and purified using protein A resin as described above.

4.4 *Selecting for active anti-IL11Ra antibodies at wide IC₅₀ ranges*

5 The IC₅₀s of IL11Ra antibodies on the ligand human IL11 (R&D Systems, catalog # 218-IL-025/CF) binding to surface IL11Ra are evaluated using flow cytometry to choose antibodies at IC₅₀'s ranging from less than 1 nM up to 5 uM, as described above. In this current example, full length human IL11Ra is transiently transfected to the surface of HEK293F cells. The methods from the prior example are used by replacing IL11Ra antibodies in place of Notch2 antibodies, and IL11 in place of Jagged-2-Fc.

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4.5 *Expressing and purifying ANDbodies as bispecifics*

DNA sequences from 10 RAGE antibodies and 10 IL11Ra antibodies ranging in IC₅₀ (from < 1 nM up to 5 uM) are made into about 100 variant ANDbodies as described above.

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4.6 *Affinity of ANDbody variants for RAGE and IL11Ra*

ANDbody affinities for RAGE and IL11Ra are evaluated similarly to above using a BIAcore. In this case, human and mouse versions of His-tagged IL11Ra are immobilized on a Sensor Chip NTA (Cytiva catalog # BR100034), and human and mouse versions of RAGE-Fc are captured on a Sensor Chip Protein A (Cytiva catalog # 29127557).

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4.7 *In vitro assays for IL11Ra antagonism on cells with or without RAGE expression*

This assay is done as described above, except substituting full length human IL11Ra instead of Notch2, as well as substituting anti-IL11Ra antibodies for anti-Notch antibodies. The corresponding RAGExIL11Ra ANDbodies are also used.

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4.8 *Biodistribution (in vivo) for ANDbody and parental antibodies*

Cellular and tissue biodistribution studies are done using methods described above. However, the ANDbody used in this case is RAGExIL11Ra, and the parental antibodies correspond to anti-RAGE and anti-IL11Ra.

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4.9 *In vivo bioactivity of RAGExIL11Ra ANDbodies*

In response to mouse treatment with murine IL11, there is an increase in collagen content in both the ventricle and the kidney (Schafer et al. 2017). Accordingly, collagen content is measured to quantify amount of IL11Ra bioactivity after ANDbody treatment.

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Similar to prior methods (Schafer et al. 2017), 10-week-old male C57BL/6 mice are injected with 2 ug mouse IL11 daily subcutaneously or an identical volume of saline for 21 days. The mouse IL11 is recombinantly made by synthesizing codon-optimized DNA using the sequence for mouse IL11 (UniProt ID P47873) with a C-terminal His tag, doing HEK293F transient transfections, and purifying the His tagged IL11 with TALON resin as described above. Starting 3 days before the first IL11 injection

and then 2x per week thereafter, IL11- and saline-treated mice receive therapeutic injections IP constituting 250 ug of ANDbody RAGExIL11Ra, parental anti-IL11Ra alone, or saline (PBS) in equal volume.

At the end of 21 days of IL11 treatment, mice are euthanized and the amounts of total collagen in the lung, spleen, blood, kidney, liver, heart, and intestines are quantified on the basis of colorimetric detection of hydroxyproline using a Quickzyme Total Collagen assay kit (Quickzyme Biosciences) and similar to prior methods (Schafer et al. 2017).

EXAMPLE 5. ANDBODY BINDING MOUSE AND HUMAN UMOD AND IL11RA

5.1 Yeast surface display to create anti-UMOD antibodies

Anti-UMOD (e.g., address target) antibodies are selected for as above and cloned into human IgG1.

5.2 Selecting for inert anti-UMOD antibodies

Anti-UMOD antibodies are further evaluated based on their inability to block UMOD ligand binding, in an assay such as the ones described above.

5.3 Yeast surface display to create anti-IL11Ra antibodies

The same IL11Ra antibodies generated above in yeast surface display will be used here as described above. ScFv's cross-reactive to mouse and human IL11Ra are cloned into human IgG1, transiently transfected into HEK293F cells, and purified using protein A resin as described above.

5.4 Selecting for active IL11Ra antibodies at wide IC_{50} ranges

The method described above is used to select for IL11Ra antibodies at varied IC_{50} s.

5.5 Expressing and purifying ANDbodies as bispecifics

DNA sequences from 10 UMOD antibodies and 10 IL11Ra antibodies ranging in IC_{50} (from < 1 nM up to 5 uM) are made into about 100 variant ANDbodies as described above.

5.6 Affinity of ANDbody variants for UMOD and IL11Ra

ANDbody affinities for UMOD and IL11Ra are evaluated similarly to above using a BIAcore. In this case, human and mouse versions of His-tagged UMOD and His-tagged IL11Ra are immobilized on a Sensor Chip NTA (Cytiva catalog # BR100034). It is expected that some ANDbody variants have higher affinity for UMOD than for IL11Ra, although all variants are tested in future assays.

5.7 Biodistribution (in vivo) for ANDbody and parental antibodies

Cellular and tissue biodistribution studies are done using methods described above. However, the ANDbody used in this example is UMODxIL11Ra, and the parental antibodies correspond to anti-UMOD and anti-IL11Ra.

5.8 *In vivo* bioactivity of UMODxIL11Ra ANDbodies

The *in vivo* bioactivity of UMODxIL11Ra ANDbodies is quantified using the same methods described above.

EXAMPLE 6. ANDBODY BINDING MOUSE AND HUMAN MEP1B AND IL11RA

6.1 *Yeast surface display to create anti-MEP1B antibodies*

Anti-MEP1B (e.g., address target) antibodies are selected for as above and cloned into human IgG1.

6.2 *Yeast surface display to create anti-IL11Ra antibodies*

The same IL11Ra (e.g., effector target) antibodies generated above in yeast surface display will be used here. ScFv's cross-reactive to mouse and human IL11Ra are cloned into human IgG2, transiently transfected into HEK293F cells, and purified using protein A resin as described above.

6.3 *Selecting for active anti-IL11Ra antibodies at wide IC₅₀ ranges*

The method described above is used to select for IL11Ra antibodies at varied IC₅₀s.

6.4 *Expressing and purifying ANDbodies as fusion proteins into human IgG2*

The 10 highest affinity MEP1B scFv's and 10 IL11Ra antibodies ranging in affinity (from < 1 nM up to 5 μ M) are made as ANDbodies with human IgG2 Fc regions. To do this, the scFv sequences from MEP1B variants are cloned respectively onto the IgG2 IL11Ra antibody variants. The MEP1B scFvs are separated by a flexible linker (3xGGGGS) from either the N or C terminal of either the light or heavy chains of IL11Ra antibodies (each ANDbody has 2 MEP1B scFvs). Variants are made with 4 total MEP1B scFvs per ANDbody by cloning MEP1B scFvs (always separated by the linker) before the N terminal and after the C terminal of the heavy chain or the light chain, respectively. Other variants with 4 or more MEP1B scFvs per IL11Ra antibody on the MEP1BxIL11Ra ANDbody by mixing and matching the locations of the scFv on the IL11Ra antibodies: at N terminal of both heavy and light chains; at C terminal of both heavy and light chains; at N terminal of heavy chain and C terminal of light chain; at C terminal of heavy chain and N terminal of light chain; and other variants with scFvs in 3 or 4 different locations (resulting in 6 or 8 total scFvs per ANDbody, respectively).

6.5 *Affinity of ANDbody variants for MEP1B and IL11Ra*

ANDbody affinities for MEP1B and IL11Ra are evaluated similarly to above using a BIAcore. In this case, human and mouse versions of His-tagged MEP1B and His-tagged IL11Ra are immobilized on a Sensor Chip NTA (Cytiva catalog # BR100034).

6.6 *Biodistribution (in vivo) for ANDbody and parental antibodies*

Cellular and tissue biodistribution studies are done using methods described above. However, the ANDbody used in this case is MEP1BxIL11Ra, and the parental antibodies correspond to anti-

MEP1B and anti-IL11Ra.

6.7 *In vivo bioactivity of MEP1BxIL11Ra ANDbodies*

The *in vivo* bioactivity of MEP1BxIL11Ra ANDbodies is quantified using the same methods described above.

EXAMPLE 7. EXEMPLARY ADDRESS-RESTRICTED BINDER FOR SKIN

This example demonstrates the restricted expression of an anti-DSG1 antibody (address binder) in skin.

7.1 *Anti-DSG1 monoclonal antibody expression and purification*

Sequences encoding the variable heavy chain regions (HC: SEQ ID NO: 24 and SEQ ID NO: 26, shown in Table 4) of two anti-desmoglein-1 (anti-DSG1) antibodies named 3-09*5 and 3-07/1e (Yamagami et al., *J Immunol.*, 183(9): 5615-5621, 2009) were fused to a human IgG1 (hulgG1) backbone with the effector null mutations L234A, L235A, and P329G (LALA-PG) and cloned into a PCDNA3.4™ vector (ThermoFisher Scientific). The variable light chain regions (SEQ ID NO: 25 and SEQ ID NO: 27) were fused to a constant kappa light chain (for 3-09*5) (SEQ ID NO: 22) or a constant lambda light chain (for 3-07/1e) (SEQ ID NO: 23) and cloned into PCDNA3.4™.

To express and purify the antibodies, a 1:1 ratio of heavy chain to light chain DNA was transfected into EXPI293F™ cells (ThermoFisher Scientific) using the EXPIFECTAMINE™ 293 Transfection Kit (ThermoFisher Scientific) following manufacturer's recommendations. Transiently expressed antibodies were purified from conditioned media 5 days post-transfection by filtering out the transfected cells. Conditioned media was incubated with protein A agarose beads for 1 hour. The bound beads were washed with Phosphate Buffered Saline (PBS) pH 7.4 followed by elution of the bound antibody with 0.1M Glycine pH 2.5 and neutralized with 1/10 volume of Tris pH 8.5. The neutralized eluate was buffer exchanged into PBS. The resulting mAbs were designated as PRO003 (3-09*5 HC) (heavy chain sequence: SEQ ID NO: 28; light chain sequence: SEQ ID NO: 29) and PRO004 (3-07/1e HC) (heavy chain sequence: SEQ ID NO: 30; light chain sequence: SEQ ID NO: 31).

The purified mAbs were analyzed by analytical size exclusion chromatography (SEC) for monodispersity and by SDS-PAGE for purity.

Table 4. PRO003 and PRO004 sequences

Region	Sequence	SEQ ID number
Heavy chain signal peptide sequence	MGWSCIIILFLVATATGVHS	SEQ ID NO: 19
Light chain signal peptide sequence	METDTLLLWVLLLWVPGSTG	SEQ ID NO: 20
Constant heavy chain region	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTWSW NSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYIC NVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVF	SEQ ID NO: 21

	LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV NKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT LVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSK LTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPG	
Kappa light chain constant region	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 22
Lambda light chain constant region	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAW KADSSPVKAGVETTTPSKQSNKNKYAASSYLSTPEQWKS SYSCQVTHEGSTVEKTVAPTECS	SEQ ID NO: 23
3-09*5 variable heavy chain sequence	EVQLVESGGGLVQPGSRSLRLSCAASGFTFDDYAMHWVRQA PGKGLEWVSGISWNSGSDYADSVKGRFTISRDNANKNSLYLQ MNSLRVEDTALYYCAKDGSRVFVGSGGDFWGGQGMVTVS S	SEQ ID NO: 24
3-09*5 variable light chain sequence	ELQMTQSPSSLSASVGDRVTITCQASQDIGNYLNWYQQKPG KAPKLLIYDASYLETGVPSRFSGSGSGTDFTFTISLQPEDIA YYCQQYDNLPTFGPGTKVDIK	SEQ ID NO: 25
3-07/1e variable heavy chain sequence	QVQLVQSGGGLVQPGGSLRVSCAASGFTSNIFWMSWVRQA PGKGLEWVANIDEDGSEKNYVDSVKGRFTISRDNANKNSLYL QMNSLRAEDTAVYYCARESFYGSGTYFDWGGQGLTVTVS S	SEQ ID NO: 26
3-07/1e variable light chain sequence	ELVVTQPPSVSGAPGQRVTISCTGSSSNIGAGYDVHWYQQL PGTAPKLLIYGNKNRPSGVPDRFSGSKSGTSASLAITGLRAE DEADYYCQSFDSGLGWVFGGGTQTLTVL	SEQ ID NO: 27
PRO003 heavy chain	MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGSRSLRLSCA ASGFTFDDYAMHWVRQAPGKGLEWVSGISWNSGSDYADS VKGRFTISRDNANKNSLYLQMNSLRVEDTALYYCAKDGSRVF VGSGGDFWGGQGMVTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPG	SEQ ID NO: 28
PRO003 light chain	METDTLLLWVLLLWVPGSTGELQMTQSPSSLSASVGDRVTIT CQASQDIGNYLNWYQQKPGKAPKLLIYDASYLETGVPSRFS GSGSGTDFTFTISLQPEDIAYYCQQYDNLPTFGPGTKVDI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEK KVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 29
PRO004 heavy chain	MGWSCIILFLVATATGVHSQVQLVQSGGGLVQPGGSLRVSC AASGFTSNIFWMSWVRQAPGKGLEWVANIDEDGSEKNYVD SVKGRFTISRDNANKNSLYLQMNSLRAEDTAVYYCARESFYG SGTYFDWGGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTH TCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVY TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEAL HNHYTQKSLSLSPG	SEQ ID NO: 30
PRO004 light chain	METDTLLLWVLLLWVPGSTGELVVTQPPSVSGAPGQRVTISC TGSSSNIGAGYDVHWYQQLPGTAPKLLIYGNKNRPSGVPDR	SEQ ID NO: 31

	FSGSKSGTSASLAITGLRAEDEADYYCQSFDSGLGWVFGGG TQLTVLGQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADSSPVKAGVETTTTPSKQSNKYAASSYLSLTPEQ WKSHRSYSCQVTHEGSTVEKTVAPTECS	
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7.2 *Anti-DSG1 antibodies PRO003 and PRO004 bind to murine DSG1 expressed on cells*

Murine DSG1 (NCBI accession NP_034209.2) with a c-Myc epitope tag at the protein C terminus was transiently expressed in RAW 264.7 cells using LIPOFECTAMINE™ 3000 (ThermoFisher Scientific) according to the manufacturer's protocol. Expression of DSG1 was confirmed by fixing and permeabilizing the cells, followed by staining with an anti-c-Myc antibody (Life Technologies A-21281) and analysis by flow cytometry. PRO003 and PRO004 bound specifically to the cells transfected with mouse DSG1, confirming that they have the expected binding specificity and are suitable for studies in mice.

7.3 *Anti-DSG1 antibodies injected into mice accumulate preferentially in skin*

To demonstrate that binding to a skin address can cause accumulation of an antibody in the skin, the anti-DSG1 antibodies PRO003 and PRO004 were chemically conjugated to the near-infrared (IR) dye IRDYE® 800CW using according to the manufacturer's instructions (LI-COR® 928-38044).

The labeled antibodies were each administered to mice by tail vein injection at a dose level of 3 mg/kg. Each antibody was administered to two groups of 3 mice, which were euthanized at 3 days and 7 days after dosing. Following euthanization, 9 organs were collected (heart, lung, pancreas, kidney, small intestine, large intestine, skin, liver, stomach), and the near-IR fluorescence of each tissue was measured on a IVIS® imager (PERKINELMER®). To image the skin, a patch of skin was shaved and approximately 1 cm² was collected for imaging. Samples from each mouse were arranged in a standard format and total fluorescence intensity was measured. Fluorescence intensity from each organ was quantified and averaged across each tissue by measuring total signal and subtracting the local background. High background signal was observed in the livers from all treated mice, so livers were excluded from the analysis. Without wishing to be bound by theory, it is believed that the liver may take up the fluorescent dye independent of antibody targeting. Similarly, background signal was observed in the stomach from all groups, including mice that were not treated with any antibody. Fluorescence was observed from the food fed to the mice, so the stomach was excluded from analysis.

Figs. 5A and 5B show fluorescent signal across tissues for PRO003 (Fig. 5A) and PRO004 (Fig. 5B). Distribution of both antibodies is strongly skewed to the skin. These data show that DSG1 antibodies can be used as an address for preferential skin targeting of an antibody.

EXAMPLE 8. EXEMPLARY ADDRESS-RESTRICTED BINDER FOR LUNG

This example demonstrates the restricted expression of an anti-RAGE antibody (address binder) in the lung.

8.1 Anti-RAGE monoclonal antibody expression and purification

Sequences encoding the variable heavy chain regions (SEQ ID NO: 32 and SEQ ID NO: 34, shown in Table 5) of two anti-RAGE mAbs named h11E6.8 and XT-M4 (Creative Biolabs) were fused to a hulgG1 backbone with the effector null mutations L234A, L235A, and P329G (LALA-PG) and cloned into a PCDNA3.4™ vector (ThermoFisher Scientific). Sequences encoding the variable light chain regions (SEQ ID NO: 33 and SEQ ID NO: 35) were fused to constant kappa light chains and cloned into PCDNA3.4™.

For expression and purification, a 1:1 ratio of heavy chain to light chain DNA was transfected into EXPI293F™ Cells (ThermoFisher Scientific) using the EXPIFECTAMINE™ 293 Transfection Kit (ThermoFisher Scientific) following the manufacturer's recommendations. Transiently expressed antibodies were purified from conditioned media 5 days post-transfection by filtering out the transfected cells. Conditioned media was incubated with protein A agarose beads for 1 hour. The bound beads were washed with Phosphate Buffered Saline (PBS) pH 7.4 followed by elution of the bound antibody with 0.1M Glycine pH 2.5 and neutralized with 1/10 volume of Tris pH8.5. The neutralized eluate was buffer exchanged into PBS. The resulting mAbs were designated PRO001 (h11E6.8) (heavy chain sequence: SEQ ID NO: 36; light chain sequence: SEQ ID NO: 37) and PRO002 (XT-M4) (heavy chain sequence: SEQ ID NO: 38; light chain sequence: SEQ ID NO: 39).

The purified mAbs were analyzed by analytical size exclusion chromatography for monodispersity and by SDS-PAGE for purity. PRO001 and PRO002 expressed highly monodispersed and resolved on SDS-PAGE at the expected molecular weight. Binding studies confirmed binding to the RAGE antigen (not shown).

Table 5. PRO001 and PRO002 sequences

Region	Sequence	SEQ ID number
h11E6.8 variable heavy chain sequence	EIQLVQSGSELKKPGASVKVSCASGYFTNFGMNWVRQAPGQGLEWMGYINTNTGESIYSEEFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYFCARSRMVTAYGMDYWGGGTTTVSS	SEQ ID NO: 32
h11E6.8 variable light chain sequence	EIVMTQSPATLSLSPGERATLSCASQNVGTAVAWYQQKPGQSPRLIFASNRYTGVPARFSGSGSDFTLTISLQSEDFAVYFCQQYSSYPLTFGGGKLEIK	SEQ ID NO: 33
XT-M4 variable heavy chain sequence	EVQLVESGGGLVQPGGSLRLSCAASGFTFNWMTWVRQAPGKGLEWVASIDNSGDNTYYPDSVKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCARGGDITGFDYWGGGTLTVSS	SEQ ID NO: 34
XT-M4 variable light chain sequence	DIQMTQSPSSLSASVGDRTITCRASQDVGIYVNWVFQQKPGKAPRRLIYRATNLADGVPSRFSGSRSGDFTLTISLQPEDFATYYCLEFDEHPLTFGGGKVEIK	SEQ ID NO: 35
PRO001 heavy chain	MGWSCIILFLVATATGVHSEIQLVQSGSELKKPGASVKVSCASGYFTNFGMNWVRQAPGQGLEWMGYINTNTGESIYSEEFKGRFVFSLDTSVSTAYLQICSLKAEDTAVYFCARSRMVTAYGMDYWGGGTTTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPGSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ	SEQ ID NO: 36

	DWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNN YTQKSLSLSPG	
PRO001 light chain	METDTLLLWVLLLVPGSTGEIVMTQSPATLSLSPGERATLS CKASQNVGTAVAWYQQKPGQSPRLIFASNRYTGVPARFS GSGSGTDFTLTISLQSEDFAVYFCQQYSSYPLTFGQGTKEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKH KVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 37
PRO002 heavy chain	MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCA ASGFTFNNYWMTWVRQAPGKGLEWVASIDNSGDNTYYPDS VKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCARGGDITG FDYWGGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVV TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPP CPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNN YTQKSLSLSPG	SEQ ID NO: 38
PRO002 light chain	METDTLLLWVLLLVPGSTGDIQMTQSPSSLSASVGDRVTIT CRASQDVGIIYNWFQQKPGKAPRRLIYRATNLADGVPSRFS GSRSGTDFTLTISLQPEDFATYYCLEFDEHPLTFGGGTKEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKH KVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 39

To test the binding of the anti-RAGE antibodies by ELISA, recombinant His-tagged murine RAGE protein (ab276858 from Abcam) was coated on NUNC-IMMUNO™ MAXISORP™ ELISA plates at 1 µg/mL concentration overnight. The next day, coated antigen was removed and the wells were

5 blocked with 1% IgG-free bovine serum albumin (BSA) followed by incubation with 11 four-fold serially diluted anti-RAGE antibodies (PRO001 and PRO002) with a starting concentration of 20nM. Bound antibodies were detected with peroxidase-conjugated anti-human IgG antibodies with tetramethylbenzidine (TMB) and acid stop reagents. Both PRO001 and PRO002 bound murine RAGE antigen at similar affinities by ELISA around 90pM apparent affinity, suggesting that both

10 antibodies are tight binders.

8.2 Anti-RAGE antibodies PRO001 and PRO002 bind to murine RAGE expressed on cells

PRO001 and PRO002 were tested for binding to mouse RAGE in cell culture. To confirm

15 binding activity and specificity of the two antibodies, mouse RAGE (NCBI accession NP_031451.2) with a c-Myc epitope tag at the protein C terminus was transiently expressed in EXPI293™ cells (ThermoFisher Scientific) using EXPIFECTAMINE™ (ThermoFisher Scientific) according to the manufacturer's protocol. Expression of RAGE was confirmed by fixing and permeabilizing the cells, followed by staining with anti-c-Myc antibody (Life Technologies A-21281) and analysis by flow

20 cytometry. Both antibodies bound specifically to murine RAGE expressed on cells, confirming that

they have the expected binding specificity and are suitable for studies in mice.

8.3 *Anti-RAGE antibodies injected into mice accumulate preferentially in lungs*

To demonstrate that binding to a lung address can cause accumulation of an antibody in the
5 lungs, the anti-RAGE antibodies PRO001 and PRO002 were chemically conjugated to the near-IR dye as described in Example 7.

The labeled antibodies were each administered to mice by tail vein injection and imaged as described in Example 7. Figs. 6A and 6B show fluorescent signal measured from tissues across mice treated with the two antibodies, each normalized so that the brightest signal is equal to 1. A group of
10 three untreated mice is included as a negative control for autofluorescence. Distribution of both antibodies is strongly skewed to the lung when compared to the other antibodies tested. These data show that two antibodies binding to RAGE accumulate preferentially in lung, demonstrating they can be used as an address for preferential lung targeting of an ANDbody.

15 8.4 *An anti-RAGE antibody accumulates specifically on alveolar cells*

Single-cell expression analysis indicated that RAGE is expressed specifically in type 1 alveolar cells, with lower expression in type 2 alveolar cells. To test the hypothesis that the antibodies can address a specific cell type, three Balb/C mice were treated by tail vein injection with 3 mg/kg of PRO002. Three untreated mice were used as negative control. Three days after dosing, the mice
20 were euthanized, lungs and other tissues were collected, and all tissues were fixed in formalin. Sections from each tissue were analyzed by immunohistochemistry (IHC) using an anti-human secondary antibody conjugated to horseradish peroxidase. Fig. 7 shows representative staining in treated and untreated mice. Strong staining was observed in the alveolar tissue of mice treated with PRO002, but not in adjacent airways or negative control conditions. This result shows that binders to
25 addresses specific to a particular cell type can be used to direct the distribution of antibodies to those cells within a larger tissue.

EXAMPLE 9. EXEMPLARY ADDRESS-RESTRICTED BINDER FOR KIDNEY

This example demonstrates the restricted expression of an anti-CDH16 antibody (address
30 binder) in the kidney.

9.1 *Anti-CDH16 monoclonal antibody expression and purification*

A sequence encoding the variable heavy chain region (SEQ ID NO: 40; shown in Table 6) of the anti-cadherin 16 (anti-CDH16) mAb Ab270263 (Abcam) was fused to a hulgG1 backbone with the effector null mutations L234A, L235A, and P329G (LALA-PG) and cloned into a PCDNA3.4™ vector
35 (ThermoFisher Scientific). A sequence encoding the variable light chain region (SEQ ID NO: 41) was fused to a constant kappa light chain and cloned into PCDNA3.4™.

For expression and purification, a 1:1 ratio of heavy chain to light chain DNA was transfected into EXPI293F™ Cells (ThermoFisher Scientific) using the EXPIFECTAMINE™ Transfection Kit

(ThermoFisher Scientific) following the manufacturer's recommendations. Transiently expressed antibodies were purified from conditioned media 5 days post-transfection by filtering out the transfected cells. Conditioned media was incubated with protein A agarose beads for 1 hour. The bound beads were washed with Phosphate Buffered Saline (PBS) pH 7.4 followed by elution of the bound antibody with 0.1M Glycine pH 2.5 and neutralized with 1/10 volume of Tris pH 8.5. The neutralized eluate was buffer exchanged into PBS. The resulting mAb was designated as PRO056 (heavy chain sequence: SEQ ID NO: 42; light chain sequence: SEQ ID NO: 43).

The purified mAb was analyzed by analytical size exclusion chromatography for monodispersity and by SDS-PAGE for purity. PRO056 expressed highly monodispersed and resolved on SDS-PAGE at the expected molecular weight.

Table 6. PRO056 sequences

Region	Sequence	SEQ ID number
Ab270263 variable heavy chain sequence	QVHLKESGPGVLVAPSQSL SITCTVSGFSLTSYAVHWVRQPPGKGLEWLGVIWAGGNTNYSVFM SRLTISKDNSKSQVFLKMNSLQTDDTAIYYCARLDDYDERFVYWGQGLTVTVSS	SEQ ID NO: 40
Ab270263 variable light chain sequence	DIVMSQSPSSLAVSVGEKVS MNCKSSQSLLYSSNHKNYLAWFQQKPGQSPKLLIYWASTRESGVPDRFTGSGSGTDFTLTIS VKAEDLAVYYCQQYYTYTWTFGGGTKLEIK	SEQ ID NO: 41
PRO056 heavy chain	MGWSCIIILFLVATATGVH SQVHLKESGPGVLVAPSQSL SITCTVSGFSLTSYAVHWVRQPPGKGLEWLGVIWAGGNTNYSVFM SRLTISKDNSKSQVFLKMNSLQTDDTAIYYCARLDDYDERFVYWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV PSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNKGKEYCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PVLDSGDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPG	SEQ ID NO: 42
PRO056 light chain	METDTLLLWVLLLWVPGSTGDIVMSQSPSSLAVSVGEKVS MNCKSSQSLLYSSNHKNYLAWFQQKPGQSPKLLIYWASTRESGVPDRFTGSGSGTDFTLTIS VKAEDLAVYYCQQYYTYTWTFGGGTKLEIKRTVAAPS VFIFPPSDEQLKSGTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTLS KADYEEKHKVYACEVTHQGLSSPVT KSFNRGEC	SEQ ID NO: 43

To test the binding of the anti-CDH16 antibodies by ELISA, recombinant His-tagged murine CDH16 protein, expressed and purified in house, was coated on NUNC-IMMUNO™ MAXISORP™ ELISA plates at 1 µg/mL concentration overnight. The next day, coated antigen was removed and the wells were blocked with 1% IgG-free BSA followed by incubation with 11 three-fold serially diluted anti-CDH16 antibody (PRO056) with a starting concentration of 533nM. Bound antibody was detected with peroxidase-conjugated anti-human IgG antibodies with TMB and acid stop reagents. PRO056 bound murine CDH16 antigen at an affinity of 200pM by ELISA.

9.2 *Anti-CDH16 antibody accumulates preferentially in the kidney*

The anti-CDH16 antibody PRO056 was chemically conjugated to near-IR fluorescent dye IRDYE® 800CW, as described in Example 7. The labeled antibody was administered to mice by tail vein injection at a dose level of 3 mg/kg. Two groups of 3 mice were used, which were euthanized at 3 days and 7 days after dosing. Following euthanization, organs were collected, and the near-IR fluorescence of each tissue was measured on a model IVIS® imager (PERKINELMER®), as above. Fluorescence intensity from each organ was quantified and averaged across each tissue by measuring total signal and subtracting the local background. Fig. 8 shows fluorescent signal measured from the tissues across mice treated with PRO056. Each is normalized so that the brightest signal is equal to 1. A group of three untreated mice is included as a negative control for autofluorescence.

The distribution is strongly skewed to the kidney when compared to the antibodies provided herein that target addresses in the skin, lung, or kidney. These data show that an antibody binding to CDH16 accumulates preferentially in kidney, demonstrating they can be used as an address bidding domain for preferential kidney targeting of an ANDbody.

EXAMPLE 10. EXEMPLARY ADDRESS-RESTRICTED BINDER FOR INTESTINE

This example demonstrates the restricted expression of an anti-CDH17 antibody (address binder) in the intestine.

10.1 *Anti-CDH17 monoclonal antibody expression and purification*

A sequence encoding the variable heavy chain region (SEQ ID NO: 44; shown in Table 7) of the anti-cadherin 17 (anti-CDH17) mAb MAB8524 (R&D Systems) was fused to a hulgG1 backbone with the effector null mutations L234A, L235A, P329G (LALA-PG) and cloned into a PCDNA3.4™ vector (ThermoFisher Scientific). A sequence encoding the variable light chain region (SEQ ID NO: 45) was fused to a constant kappa light chain and cloned into PCDNA3.4™.

For expression and purification, a 1:1 ratio of heavy chain to light chain DNA was transfected into EXPI293F™ cells (ThermoFisher Scientific) using the EXPIFECTAMINE™ 293 Transfection Kit (ThermoFisher Scientific) following the manufacturer's recommendations. Transiently expressed antibodies were purified from conditioned media 5 days post-transfection by filtering out the transfected cells. Conditioned media was incubated with protein A agarose beads for 1 hour. The bound beads were washed with Phosphate Buffered Saline (PBS) pH 7.4 followed by elution of the bound antibody with 0.1M Glycine pH 2.5 and neutralized with 1/10 volume of Tris pH 8.5. The neutralized eluate was buffer exchanged into PBS. The resulting mAb was designated as PRO061 (heavy chain sequence: SEQ ID NO: 46; light chain sequence: SEQ ID NO: 47).

The purified mAb was analyzed by analytical size exclusion chromatography for monodispersity and by SDS-PAGE for purity. PRO061 expressed highly monodispersed and resolved on SDS-PAGE at the expected molecular weight.

Table 7. PRO061 sequences

Region	Sequence	SEQ ID number
MAB8524 variable heavy chain sequence	QSLEESGGRLVTPGTPLTLTCTVSGFSLTSYDMNWVRQAPG KGLEWIGVVRGSGRTYYASWAKGRFTIARTSSTTVDLKMTSL TTGDTATYFCARGDANNYYEFDIWGPGLTVTVSS	SEQ ID NO: 44
MAB8524 variable light chain sequence	QDMTQTPSPVSAAVGGTVTINCQSSQSVYGDWLSWFQK PGQPPKLLIYSASTLASGVPSRFKGSQSGTQFTLTISDLESD AATYYCAGGYDGINDIRAFGGGTEVVVK	SEQ ID NO: 45
PRO061 heavy chain	MGWSCILFLVATATGVHQSLEESGGRLVTPGTPLTLTCTVS GFSLTSYDMNWVRQAPGKGLEWIGVVRGSGRTYYASWAKG RFTIARTSSTTVDLKMTSLTTGDTATYFCARGDANNYYEFDI WGPGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV P SSSLTGTQYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPA PEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNKKEYCKKVSNAKALGAPIEKTISKAKGQPREPQVYTLPPSR DELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPV L DSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYT QKSLSLSPG	SEQ ID NO: 46
PRO061 light chain	METDTLLLWVLLLVPGSTGQDMTQTPSPVSAAVGGTVTIN CQSSQSVYGDWLSWFQKPGQPPKLLIYSASTLASGVPSR FKGSGSGTQFTLTISDLESDAATYYCAGGYDGINDIRAFGG GTEVVVKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPR EAKVQWKVDNALQSGNSQESVTEQDSKSTYLSLSTLTLSK ADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 47

To confirm binding activity and specificity, mouse CDH17 (NCBI accession NP_062727.1) with a c-Myc epitope tag at the protein C terminus was transiently expressed in RAW 264.7 cells using LIPOFECTAMINE™ 3000 (ThermoFisher Scientific) according to the manufacturer's protocol. Expression of CDH17 was confirmed by fixing and permeabilizing the cells, followed by staining with an anti-c-Myc antibody (Life Technologies A-21281) and analysis by flow cytometry. PRO061 bound specifically to the cells transfected with mouse CDH17, confirming that it has the expected binding specificity and is suitable for studies in mice.

10.2 Anti-CDH17 antibody injected into mice accumulates preferentially in the intestine

PRO061 was chemically conjugated to near-IR fluorescent dye IRDYE® 800CW, as described in Example 7. The labeled antibody was administered to mice by tail vein injection at a dose level of 3 mg/kg. Two groups of 3 mice were used, which were euthanized at 3 days and 7 days after dosing. Following euthanization, organs were collected, and the near-IR fluorescence of each tissue was measured on a model IVIS® imager (PERKINELMER®), as above. Fluorescence intensity from each organ was quantified and averaged across each tissue by measuring total signal and subtracting the local background. Fig. 9 shows fluorescent signal measured from the tissues across mice treated with PRO061. Each is normalized so that the brightest signal is equal to 1. A group of three untreated mice is included as a negative control for autofluorescence. The distribution is strongly skewed to the intestine, showing that an antibody binding to CDH17 accumulates

preferentially in intestine and can be used as an address targeting domain for preferential intestine targeting of an ANDbody.

EXAMPLE 11. TISSUE RESTRICTION OF PREDICTED ADDRESSES

5 Immunohistochemistry (IHC) on fresh frozen (FF) healthy mouse tissue microarray (TMA) sections mounted onto glass slides was used for assaying whether predicted organ-specific or preferentially expressed addresses were actually of highest abundance in the predetermined organs, and for determining which monoclonal antibody clones (mAbs) bound with greatest preference to the desired organ.

10 Glass slides coated with FF TMA were generated by first assembling a fresh frozen tissue microarray block. To enable TMA block formation, individual organs from freshly sacrificed C57BL/6 mice were embedded in optimal cutting (OCT) medium in separate cryomolds and frozen. Cylindrical cores of tissue were then taken from each block and placed into a block to create the final FF TMA. Layers of the TMA were then cut off using a cryostat, mounted onto positively charged microscopy
15 glass slides, and stored at -80°C until stained.

Addresses were validated by direct binding of FF TMA-coated slides with either polyclonal antibodies or mAbs raised against the address in question. These address-specific antibodies were detected with horseradish peroxidase (HRP)-conjugated antibodies specific for the IgG of the host in which the primary address specific antibody was raised. Location and intensity of binding was
20 determined by the addition of the HRP substrate 3,3'Diaminobenzidine (DAB), which yields a brown color at the site of primary antibody binding, proportional to the abundance of deposited antibody. Nuclei were counterstained with hematoxylin to yield a blue color. For each of the respective addresses, a range of different mAb clones was assayed for tissue specificity, and their patterns of tissue binding were assessed by performing IHC on the same FF TMAs described above.

25 Table 8 summarizes observed binding of the antibodies tested. All the antibodies tested reacted primarily with the expected target tissue, with varying degrees of weaker reactivity on other tissues. Without wishing to be bound by theory, much of the off-tissue reactivity may reflect non-specific binding by the antibody. For example, four antibodies tested for binding to RAGE each show binding to the lung, but 3 show variable low-level binding to other tissues.

30

Table 8. Candidate addresses evaluated by IHC on mouse tissue microarrays

Ab #	Predicted Organ	Address	Clone/ Cat #	Source	Primary Ab reactivity matches prediction	Weaker reactivity
1	Lung	RAGE	NBP2-67095	Novus Bio	Yes	Spleen, pancreas, intestine
2	Lung	RAGE	PR002	in house	Yes	None detected
3	Lung	RAGE	MAB11795	R&D Systems	Yes	Spleen, intestine, heart, kidney, brain

4	Lung	RAGE	PR001	in house	Yes	Skin, Pancreas (low)
5	Kidney	CDH16	Ab270263	Abcam	Yes	None detected
6	Colon	CDH17	MAB8524	Novus Bio	Yes	Small intestine, spleen
7	Pancreas	GP2	D278-3	MBL Int. Corp.	Yes	None detected
8	Liver	ASGR1	MAB27552	R&D Systems	Yes	None detected
9	Small Intestine	HEPACAM2	LS-B888	LS Bio	Yes	None detected
10	Kidney	Nephrin	Ab227806	Abcam	Yes	None detected
11	Kidney	Aquaporin 2	PA5-78808	ThermoFisher	Yes	Colon (low)
12	Negative Control	n/a	PR0022	in house	Yes	None detected

EXAMPLE 12. ANDBODY PRODUCTION AND USE

This example demonstrates the production of an exemplary ANDbody that blocks Notch2 and binds RAGE as an address.

5

12.1 Anti-Notch2 monoclonal antibody expression and purification

Sequences encoding the variable heavy chain regions (SEQ ID NOs: 48, 50, 52 and 54; shown in Table 9) of four anti-Notch2 mAbs (Wu et al., *Nature*, 464: 1052–1057, 2010) were each individually fused to a hulgG1 backbone with the effector null mutations L234A, L235A, and P329G (LALA-PG) and cloned into a PCDNA3.4™ vector (ThermoFisher Scientific). Sequences encoding the corresponding variable light chain regions (SEQ ID NOs: 49, 51, 53, and 55) were fused to constant kappa light chains and cloned into PCDNA3.4™.

For expression and purification, a 1:1 ratio of heavy chain to light chain DNA was transfected into EXPI293F™ cells (ThermoFisher Scientific) using the EXPIFECTAMINE™ 293 Transfection Kit (ThermoFisher Scientific) following the manufacturer's recommendations. Transiently expressed antibodies were purified from conditioned media 5 days post-transfection by filtering out the transfected cells. Conditioned media was incubated with protein A agarose beads for 1 hour. The bound beads were washed with Phosphate Buffered Saline (PBS) pH 7.4 followed by elution of the bound antibody with 0.1M Glycine pH 2.5 and neutralized with 1/10 volume of Tris pH 8.5. The neutralized eluate was buffer exchanged into PBS. The resulting mAbs were designated as PRO034 (heavy chain sequence: SEQ ID NO: 56; light chain sequence: SEQ ID NO: 57), PRO035 (heavy chain sequence: SEQ ID NO: 58; light chain sequence: SEQ ID NO: 59), PRO036 (heavy chain sequence: SEQ ID NO: 60; light chain sequence: SEQ ID NO: 61), and PRO037 (heavy chain sequence: SEQ ID NO: 62; light chain sequence: SEQ ID NO: 63).

25

Table 9. PRO034, PRO035, PRO036, and PRO037 sequences

Region	Sequence	SEQ ID number
anti-Notch2 mAb 1 variable heavy chain sequence	EVQLVESGGGLVQPGGSLRLSCAASGYSTSYGMSWVRQA PGKGLEWVSYIYPYSGATYYADSVKGRFTISADTSKNTAYLQ MNSLRAEDTAVYYCARHSGYYRISSAMDVWGQGTTLTVSS	SEQ ID NO: 48
anti-Notch2 mAb 1 variable light chain sequence	DIQMTQSPSSLSASVGDRTITCRASQSISSYLAWYQQKPGK APKLLIYGASSRASGVPSRFSGSGSGTDFTLTISLQPEDFAT YYCQQYYSSPLTFGQGTKVEIK	SEQ ID NO: 49
anti-Notch2 mAb 2 variable heavy chain sequence	EVQLVESGGGLVQPGGSLRLSCAASGYTFSSYGMSWVRQA PGKGLEWVSYIYPYSGATYYADSVKGRFTISADTSKNTAYLQ MNSLRAEDTAVYYCARHSGYYRISSAMDVWGQGTTLTVSS	SEQ ID NO: 50
anti-Notch2 mAb 2 variable light chain sequence	DIQMTQSPSSLSASVGDRTITCRASQSNRRFLAWYQQKPG KAPKLLIYGASSRASGVPSRFSGSGSGTDFTLTISLQPEDFA TYYCQQYYISPLTFGQGTKVEIK	SEQ ID NO: 51
anti-Notch2 mAb 3 variable heavy chain sequence	EVQLVESGGGLVQPGGSLRLSCAASGYTFSSYGMSWVRQA PGKGLEWVSYIYPYSGATYYADSVKGRFTISADTSKNTAYLQ MNSLRAEDTAVYYCARHSGYYRISSAMDVWGQGTTLTVSS	SEQ ID NO: 52
anti-Notch2 mAb 3 variable light chain sequence	DIQMTQSPSSLSASVGDRTITCRASQSVRSFLAWYQQKPG KAPKLLIYRASIRASGVPSRFSGSGSGTDFTLTISLQPEDFA TYYCQQYYISPWTFGQGTKVEIK	SEQ ID NO: 53
anti-Notch2 mAb 4 variable heavy chain sequence	EVQLVESGGGLVQPGGSLRLSCAASGYTFSSYGMSWVRQA PGKGLEWVSYIYPYSGATYYADSVKGRFTISADTSKNTAYLQ MNSLRAEDTAVYYCARHSGYYRISSAMDVWGQGTTLTVSS	SEQ ID NO: 54
anti-Notch2 mAb 4 variable light chain sequence	DIQMTQSPSSLSASVGDRTITCRASQSNRRFLAWYQQKPG KAPKLLIYGASSRASGVPSRFSGSGSGTDFTLTISLQPEDFA TYYCQQYYISPLTFGQGTKVEIK	SEQ ID NO: 55
PRO034 heavy chain	MGWSCIIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCA ASGYSTSYGMSWVRQAPGKGLEWVSYIYPYSGATYYADS VKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARHSGYYRI SSAMDVWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAA LGCLVKDYFPEPVTWNSGALTSGVHTFPAVLQSSGLYSLS SVVTPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT CPPCPAPEAAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVS HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYT LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPG	SEQ ID NO: 56
PRO034 light chain	METDTLLLVLLLWVPGSTGDIQMTQSPSSLSASVGDRTIT CRASQSISSYLAWYQQKPGKAPKLLIYGASSRASGVPSRFSG SGSGTDFTLTISLQPEDFATYYCQQYYSSPLTFGQGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 57
PRO035 heavy chain	MGWSCIIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCA ASGYTFSSYGMSWVRQAPGKGLEWVSYIYPYSGATYYADS VKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARHSGYYRI SSAMDVWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAA LGCLVKDYFPEPVTWNSGALTSGVHTFPAVLQSSGLYSLS SVVTPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHT CPPCPAPEAAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVS HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYT LPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPG	SEQ ID NO: 58

PRO035 light chain	METDTLLLWVLLLWVPGSTGDIQMTQSPSSLSASVGDRTITCRASQSNRRFLAWYQQKPGKAPKLLIYGASSRASGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQYYISPLTFGGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 59
PRO036 heavy chain	MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCAASGYTFSSYGMSWVRQAPGKGLEWVSIIYPYSGATYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARHSGYYRISAMDVWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS SVVTPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPG	SEQ ID NO: 60
PRO036 light chain	METDTLLLWVLLLWVPGSTGDIQMTQSPSSLSASVGDRTITCRASQSVRSFLAWYQQKPGKAPKLLIYRASIRASGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQYYISPLTFGGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 61
PRO037 heavy chain	MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCAASGYTFSSYGMSWVRQAPGKGLEWVSIIYPYSGATYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARHSGYYRISAMDVWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS SVVTPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPG	SEQ ID NO: 62
PRO037 light chain	METDTLLLWVLLLWVPGSTGDIQMTQSPSSLSASVGDRTITCRASQSNRRFLAWYQQKPGKAPKLLIYGASSRASGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQYYISPLTFGGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 63

12.2 Anti Notch2 binding and affinity testing

- To test the binding of the anti-Notch2 antibodies by ELISA, recombinant His-tagged human and murine Notch2 NRR domains, expressed and purified in house, were coated on NUNC-
5 IMMUNO™ MAXISORP™ ELISA plates at 1 µg/mL concentration overnight. The next day, coated antigen was removed and the wells were blocked with 1% IgG-free BSA followed by incubation with 11 three-fold serially diluted anti-Notch2 antibodies (PRO034, PRO035, PRO036 and PRO037) with a starting concentration of 200nM for PRO035 and PRO037 and 666nM for PRO034 and PRO036. Bound antibody was detected with peroxidase-conjugated anti-human IgG antibodies with TMB and
10 acid stop reagents. Each of the antibodies bound human and murine NRR domain of Notch2 with affinities between 47 pM and 140 nM.

To test the binding affinity of the anti-Notch2 antibodies by biolayer interferometry (BLI), each of PRO034, PRO035, PRO036 and PRO037 were immobilized on anti-human IgG Fc biosensors and dipped into the recombinant His-tagged murine and human Notch2 NRR protein at various concentrations from 1000nM to 31nM to measure the rate of association with the antigen. The dissociation rate was then measured by dipping the biosensors into buffer. The binding affinity was calculated as a ratio of the dissociation rate to the association rate. The intrinsic affinities determined by BLI were all in the nM range, suggesting that avidity improves affinity in an ELISA format.

12.3 Design and production of Notch2/RAGE ANDbodies

ANDbodies containing a first fragment antigen-binding (Fab) arm of a anti-Notch2 antibody described above (PRO034, PRO035, and PRO036) and a second Fab arm of the anti-RAGE antibody PRO002 (Example 8) were generated using a controlled Fab arm exchange (cFAE) reaction (Labrijn et al., *Proc Natl Acad Sci U.S.A.*, 110(13): 5145-5150, 2013). Site-directed mutagenesis was performed to introduce a F405L amino acid substitution mutation in the Fc fragment of the anti-RAGE antibody (PRO002) and a K409R amino acid substitution mutation in the Fc fragment of each of the anti-Notch2 antibodies (PRO034, PRO035, and PRO036). These antibodies were expressed and purified as described previously for the parental antibodies. The individual monoclonal antibodies were then mixed in an equimolar ratio in a controlled reduction and reoxidation reaction that drives recombination of the bispecific antibody guided by the matching point mutations (F405L-K409R). The formation of the ANDbody was analyzed by analytical chromatography and SDS-PAGE. The resulting ANDbodies were designated as PRO051, PRO052 and PRO053 (comprising PRO034, PRO035, and PRO036, respectively).

SDS-PAGE and analytical size exclusion chromatography showed that the major product formed after cFAE reaction had a molecular weight of a typical IgG1 (150 kDa), suggesting complete reoxidation. Analytical hydrophobic interaction chromatography indicated the formation of a new product, the desired heterodimeric antibody.

12.4 Notch2/RAGE ANDbodies are shown to bind simultaneously to Notch2 and RAGE by BLI

To test simultaneous dual antigen binding of the Notch2/ RAGE ANDbodies by BLI, PRO051, PRO052 and PRO053, along with monovalent parental antibody controls were immobilized on anti-human IgG Fc biosensors and dipped into the recombinant His-tagged murine RAGE protein at 150nM, followed by a second association step into wells containing recombinant murine Notch2 NRR at 150nM to measure dual antigen binding. The dissociation rate was then measured by dipping the biosensors into buffer.

The sensorgrams showed that the ANDbodies PRO051, PRO052 and PRO053 were able to bind both RAGE and Notch2 antigens simultaneously, but the monovalent parental antibodies bound only one of RAGE and Notch2 NRR. This supports the conclusion that the ANDbodies were the correct composition and were functional in binding both antigens simultaneously.

12.5 Notch2/RAGE ANDbody are shown to bind preferentially to human lung tissue by immunohistochemistry

Immunohistochemistry (IHC) on fresh frozen healthy mouse tissue microarray (FF TMA) sections mounted onto glass slides was used to evaluate tissue binding by ANDbodies containing the Notch2 inhibitory antibodies described above. TMAs were constructed and stained as described in Example 11. Fig. 10 shows staining of mouse TMAs by the three anti-Notch2 antibodies PRO034, PRO035, and PRO036 alongside staining by the Notch2/RAGE ANDbodies PRO051, PRO052, and PRO053. In each case, there is a pronounced enhancement of binding to lung tissue in the RAGE-targeted ANDbody. These data show that combining a receptor-targeting binder with an addressing binder in antibody format can impart the tissue specificity of the addressing arm to the ANDbody.

12.6 A Notch2/RAGE ANDbody distributes preferentially to the lungs compared to a matched non-targeted anti-Notch2 antibody

To evaluate how an ANDbody targeting Notch2 and RAGE behaves in vivo, mice were treated by IV dosing with the PRO051, PRO052, and PRO053 antibodies at 3 mg/kg. All groups contained 3 mice. At 3, 7, 14, and 21 days after dosing, tissues were collected from each mouse. The accumulation of each antibody in the lungs was measured by homogenizing a fixed amount of lung tissue, normalizing each sample to a fixed amount of extracted protein, and then detecting the human antibody by sandwich ELISA.

Fig. 11 shows accumulation in the lungs of PRO052 compared with a matched antibody that binds to RAGE and the control target respiratory syncytial virus (RSV) glycoprotein F (RAGE XT-M4/Motavizumab) and one that binds to Notch2 and RSV glycoprotein F (Notch2-2/Motavizumab). The antibody targeting RSV glycoprotein F and Notch2 was not detectable in the lungs at any time point. In contrast, the Notch2/RAGE ANDbody was clearly detectable in the lung for at least two weeks. Overall accumulation of PRO052 was lower than that of the bispecific that binds to RAGE and RSV glycoprotein F, indicating that the overall specificity of PRO052 is intermediate between the two arms independently. These results show that an addressing arm in an ANDbody can significantly redirect the binding specificity of a target-binding arm.

EXAMPLE 13. ANDBODY PRODUCTION AND USE

This example describes the production of an exemplary ANDbody that (i) comprises a ligand effector that targets the IL-10 pathway and (ii) binds DSG1 as an address.

13.1 Description, design and production of IL-10/DSG1 ANDbodies

To test formats of IL-10/anti-DSG1 ANDbodies, three parameters were explored: valency of IL-10 (1 or 2 moieties of IL-10), valency of the anti-DSG1 arm (1 or 2 Fab arms) and two versions of IL-10 (dimeric or monomeric IL-10). Formats that represent different combinations of IL-10 molecules, IL-10 valency, and antibody valency were assessed. Wild-type (WT) IL-10 (accession number

P22301), a monomeric engineered IL-10 sequence (Josephson et al., *J Biol Chem.*, 275(18): 13552-7, 2000), and a dimeric engineered IL-10 sequence (Minshawi et al., *Front Immunol.*, 11: 1794, 2020) were fused to PRO003 sequences (Example 7) at the C-terminus of heavy chain for the bivalent formats. For monovalent formats, monomeric and dimeric IL-10 were fused at the N-terminus of the Fc and co-expressed with PRO003. The monovalent formats are asymmetric, and mutations in the Fc domain (chain A: S364K/K409S; chain B: K370S/F405K (WO 2017/106462 A1)) are used to enforce asymmetric pairing.

To express and purify the antibodies, a 1:1 ratio of heavy chain to light chain DNA or a 1:1:1 ratio of heavy chain to light chain to IL-10-Fc (listed below) was transfected into EXP1293FTM cells (ThermoFisher Scientific) using the EXPIFECTAMINETM 293 Transfection Kit (ThermoFisher Scientific) following the manufacturer's recommendations. Transiently expressed antibodies were purified from conditioned media 5 days post-transfection by filtering out the transfected cells. Conditioned media was incubated with protein A agarose beads for 1 hour. The bound beads were washed with Phosphate Buffered Saline (PBS) pH 7.4 followed by elution of the bound antibody with 0.1M Glycine pH 2.5 and neutralized with 1/10 volume of Tris pH 8.5. The neutralized eluate was buffer exchanged into PBS.

The resulting mAbs were designated as PRO023, PRO024, PRO025, PRO026 and PRO027 (Fig. 12).

PRO023 comprises (a) a heavy chain sequence (SEQ ID NO: 67) comprising the heavy chain sequence of PRO003 (SEQ ID NO: 28) and the wild-type human IL-10 sequence (SEQ ID NO: 64) and (b) the light chain sequence of PRO003 (SEQ ID NO: 29).

PRO024 comprises (a) a heavy chain sequence (SEQ ID NO: 68) comprising the heavy chain sequence of PRO003 (SEQ ID NO: 28) and the monomeric human IL-10 sequence (SEQ ID NO: 64) and (b) the light chain sequence of PRO003 (SEQ ID NO: 29).

PRO025 comprises (a) a heavy chain sequence (SEQ ID NO: 69) comprising the heavy chain sequence of PRO003 (SEQ ID NO: 28) and the dimeric human IL-10 sequence (SEQ ID NO: 66) and (b) the light chain sequence of PRO003 (SEQ ID NO: 29).

PRO026 comprises (a) the heavy chain sequence of PRO003, further comprising mutations in the Fc domain to enforce asymmetric pairing (SEQ ID NO: 70), (b) the light chain sequence of PRO003 (SEQ ID NO: 29), and (c) an IL-10-Fc fusion protein (SEQ ID NO: 72) comprising an Fc region including mutations to enforce asymmetric pairing (SEQ ID NO: 71) and a monomeric human IL-10 sequence (SEQ ID NO: 64).

PRO027 comprises (a) the heavy chain sequence of PRO003, further comprising mutations in the Fc domain to enforce asymmetric pairing (SEQ ID NO: 70), (b) the light chain sequence of PRO003 (SEQ ID NO: 29), and (c) an IL-10-Fc fusion protein (SEQ ID NO: 73) comprising an Fc region including mutations to enforce asymmetric pairing (SEQ ID NO: 71) and the dimeric human IL-10 sequence (SEQ ID NO: 66).

The purified ANDbodies were analyzed by analytical size exclusion chromatography for

monodispersity and by SDS-PAGE for purity. PRO024 and PRO026 had the highest yields and monodispersity after single-step purification. PRO023 and PRO027 had moderate yields and were ~70% monodispersed. PRO025 had lower yields with ~89% monodispersity.

5 **Table 10. PRO023, PRO024, PRO025, PRO026, PRO058, and PRO027 sequences**

Region	Sequence	SEQ ID number
Wild-type (WT) IL-10 (accession number P22301)	SPGQGTQSENSCTHFGNLPNMLRDLRDAFSRVKTFQMK DQLDNLLLKESLLEDFKGYLGCCQALSEMIQFYLEEVMQAEN QDPDIKAHVNSLGENLKTLLRLRRCHRFLPCENKSKAVEQV KNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRN	SEQ ID NO: 64
Monomeric engineered IL-10 sequence (Josephson et al., <i>J Biol Chem.</i> , 275(18): 13552-7, 2000)	SPGQGTQSENSCTHFGNLPNMLRDLRDAFSRVKTFQMK DQLDNLLLKESLLEDFKGYLGCCQALSEMIQFYLEEVMQAEN QDPDIKAHVNSLGENLKTLLRLRRCHRFLPCENGGGSGGK SKAVEQVKNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRN	SEQ ID NO: 65
Dimeric engineered IL-10 sequence (Minshawi et al., <i>Front Immunol.</i> , 11: 1794, 2020)	SPGQGTQSENSCTHFGNLPNMLRDLRDAFSRVKTFQMK DQLDNLLLKESLLEDFKGYLGCCQALSEMIQFYLEEVMQAEN QDPDIKAHVNSLGENLKTLLRLRRCHRFLPCENKSKAVEQV KNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRN	SEQ ID NO: 66
PRO023 heavy chain	MGWSCILFLVATATGVHSEVQLVESGGGLVQPGRSLRLSCA ASGFTFDDYAMHWVRQAPGKGLEWVSGISWNSGSDYADS VKGRFTISRDNKNSLYLQMNSLRVEDTALYYCAKDGSRVF GVGGGDFDFWGQGTMTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPGSGGGGSGGGGSGGGGSSPGQGT QSENSCTHFGNLPNMLRDLRDAFSRVKTFQMKDQLDNLL LKESSLLEDFKGYLGCCQALSEMIQFYLEEVMQAENQDPDIKA HVNSLGENLKTLLRLRRCHRFLPCENKSKAVEQVKNAFNKL QEKGIYKAMSEFDIFINYIEAYMTMKIRN	SEQ ID NO: 67
PRO024 heavy chain	MGWSCILFLVATATGVHSEVQLVESGGGLVQPGRSLRLSCA ASGFTFDDYAMHWVRQAPGKGLEWVSGISWNSGSDYADS VKGRFTISRDNKNSLYLQMNSLRVEDTALYYCAKDGSRVF GVGGGDFDFWGQGTMTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFCFSVM HEALHNHYTQKSLSLSPGSGGGGSGGGGSGGGGSSPGQGT QSENSCTHFGNLPNMLRDLRDAFSRVKTFQMKDQLDNLL	SEQ ID NO: 68

	LKESLLEDFKGYLGCGQALSEMIQFYLEEVMPPQAENQDQDIKA HVNSLGENLKTLLRLRLRRCHRFPCENGSGSGGKSKAVEQV KNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRN	
PRO025 heavy chain	MGWSCILFLVATATGVHSEVQLVESGGGLVQPGRSLRLSCA ASGFTFDDYAMHWVRQAPGKGLEWVSGISWNSGSDIYADS VKGRFTISRDNAKNSLYLQMNSLRVEDTALYYCAKDGSRVF GVGGGFDVWGQGTMTVTSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVM HEALHNHYTQKSLSLSPG QSENSCTHFPGNLPNMLRDLRDAFSRVKTFQMKDQLDNLL LKESLLEDFKGYLGCGQALSEMIQFYLEEVMPPQAENQDQDIKA HVNSLGENLKTLLRLRLRRCHRFPCENKSKAVEQVKNAFNKL QEKGIYKAMSEFDIFINYIEAYMTMKIRNNGGSGGGSPGQGT QSENSCTHFPGNLPNMLRDLRDAFSRVKTFQMKDQLDNLL LKESLLEDFKGYLGCGQALSEMIQFYLEEVMPPQAENQDQDIKA HVNSLGENLKTLLRLRLRRCHRFPCENKSKAVEQVKNAFNKL QEKGIYKAMSEFDIFINYIEAYMTMKIRN	SEQ ID NO: 69
PRO026, PRO058, and PRO027 heavy chain	MGWSCILFLVATATGVHSEVQLVESGGGLVQPGRSLRLSCA ASGFTFDDYAMHWVRQAPGKGLEWVSGISWNSGSDIYADS VKGRFTISRDNAKNSLYLQMNSLRVEDTALYYCAKDGSRVF GVGGGFDVWGQGTMTVTSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLYSSLTVDKSRWQQGNVFCSSVM HEALHNHYTQKSLSLSPG	SEQ ID NO: 70
Fc domain of IL-10 Fc fusion	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPR EPQVYTLPPSRDELTKNQVSLTCLVSGFYPSDIAVEWESNGQ PENNYKTTTPVLDSDGSFKLYSKLTVDKSRWQQGNVFCSSV MHEALHNHYTQKSLSLSPG	SEQ ID NO: 71
PRO026 IL-10-Fc	SPGQGTQSENSCTHFPGNLPNMLRDLRDAFSRVKTFQMK DQLDNLLLKESLLEDFKGYLGCGQALSEMIQFYLEEVMPPQAEN QDQDIKAHVNSLGENLKTLLRLRLRRCHRFPCENGSGSGGK SKAVEQVKNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRN GGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVSGFY PSDIAVEWESNGQPENNYKTTTPVLDSDGSFKLYSKLTVDKSR WQQGNVFCSSVMHEALHNHYTQKSLSLSPG	SEQ ID NO: 72
PRO027 IL-10-Fc	SPGQGTQSENSCTHFPGNLPNMLRDLRDAFSRVKTFQMK DQLDNLLLKESLLEDFKGYLGCGQALSEMIQFYLEEVMPPQAEN QDQDIKAHVNSLGENLKTLLRLRLRRCHRFPCENKSKAVEQV KNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRNNGGSGGG SPGQGTQSENSCTHFPGNLPNMLRDLRDAFSRVKTFQMK DQLDNLLLKESLLEDFKGYLGCGQALSEMIQFYLEEVMPPQAEN QDQDIKAHVNSLGENLKTLLRLRLRRCHRFPCENKSKAVEQV KNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRN	SEQ ID NO: 73

	KNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRNGGGGSGG GGSDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKG QPREPQVYTLPPSRDELTKNQVSLTCLVSGFYPSDIAVEWES NGQPENNYKTTTPVLDSDGSFKLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPG	
Fc domain of IL-10 Fc fusion (with substitutions)	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKTISKAKGQPR EPQVYTLPPSRDELTKNQVSLTCLVSGFYPSDIAVEWESNGQ PENNYKTTTPVLDSDGSFKLYSKLTVDKSRWQQGNVFS MHEALHNHYTQKSLSLSPG	SEQ ID NO: 74
PRO058 IL-10-Fc	SPGQGTQSENSCTHFPGNLPLNMLRDLRDAFSRVKTFQMK DQLDNLKESLLEDFKGYLGCAQALSEMIQFYLEEVMQAEN QDPDIKAHVNSLGENLKLRLRLRRCHRFLPCENGSGSGGK SKAVEQVKNAFNKLQEKGIYKAMSEFDIFINYIEAYMTMKIRN GGGGSGGGGSDKTHTCPPCPAPEAAGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPI EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVSGFY SDIAVEWESNGQPENNYKTTTPVLDSDGSFKLYSKLTVDKSR WQQGNVFSVMHEALHNHYTQKSLSLSPG	SEQ ID NO: 75

13.2 IL-10/DSG1 ANDbodies bind to both IL-10 receptors

- To test the binding of the IL-10/anti-DSG1 ANDbodies to IL-10 receptor alpha (IL-10Ra) by ELISA, recombinant His-tagged human IL-10Ra (Creative Biomart) was coated on NUNC-IMMUNO™
- 5 MAXISORP™ ELISA plates at 1 µg/mL concentration overnight. The next day, coated antigen was removed and the wells were blocked with 1% IgG-free BSA followed by incubation with 11 three-fold serially diluted anti-IL-10/anti-DSG1 ANDbodies (as provided above) with a starting concentration of 30µg/mL. Bound antibody was detected with peroxidase-conjugated anti-human IgG antibodies with TMB and acid stop reagents.
- 10 Of the molecules tested, only those containing an IL-10 moiety (PRO023, PRO024, PRO025, PRO026, PRO027, and the positive control IL-10 Fc) (Creative Biomart IL10-326H) bound IL-10Ra, demonstrating that the binding was driven by IL-10 and not the negative control anti-DSG1 antibody (PRO003) and that the IL-10 moiety was functional in binding its receptor.

15 13.3 IL-10/DSG1 ANDbodies activate the IL-10 signaling pathway

- To show that IL-10 retains its biological activity as a part of the various ANDbodies described above, the ability to each IL-10/DSG1 ANDbody to activate the IL-10 signaling pathway was tested. HEK-BLUE™ IL-10 cells (InvivoGen) were used to evaluate the signaling activity and relative potency of each molecule. These cells express all the components of the IL-10 signaling pathway, including
- 20 an IL-10-inducible gene encoding secreted embryonic alkaline phosphatase (SEAP). When IL-10 signaling is activated in these cells, they express and secrete SEAP in to the cell culture media. The degree of IL-10 signal is measured by adding QUANTI-BLUE™ solution colorimetric reagent (InvivoGen) to the cell culture media, followed by reading absorbance at 630 nm.

In this experiment, each of PRO023, PRO024, PRO025, PRO026, and PRO027 was titrated from 1 pM to >1 nM with overnight incubation in cell culture. Figs. 18A and 18B show representative activity data for each IL-10/DSG1 ANDbody, along with positive and negative controls as described in Table 11. Table 11 shows the EC50 for response of HEK-BLUE™ cells to three control molecules ((1) recombinant human IL-10 (BioLegend #573204) (rhIL-10), (2) recombinant human IL-10 fused to a human Fc domain (hIL-10 Fc fusion), and (3) the parental anti-DSG1 antibody (PRO003)) and to each IL-10/DSG1 ANDbody described above. These data confirm that all five IL-10/DSG1 ANDbodies retain the signaling activity of human IL-10. They show a range of potency, indicating that the relative biological potency of ANDbodies can be adjusted by variations in the format of the molecule, structure of the biologically active moiety, and valency of the active moiety.

Table 11. Potency of IL-10/DSG1 ANDbodies in the HEK-BLUE™ IL-10 signaling assay

Molecule	Description	Address valency	IL-10 valency	EC50 (pM)
rhIL-10	Human IL-10 (positive control)	0	2	21
hIL-10 Fc fusion	Human IL-10 fused (positive control)	0	2	50
Anti-DSG1 mAb PRO003	Negative control (targeting moiety alone)	2	0	NA
PRO023	Native IL-10 fused to mAb C-termini	2	1	54
PRO024	Monomeric IL-10 fused to mAb C-termini	2	2	293
PRO025	IL-10 dimer fused to each mAb C-terminus	2	2	46
PRO026	Monomeric IL-10 replacing one Fab of the anti-DSG1 mAb	1	1	750
PRO027	IL-10 dimer replacing one Fab of the anti-DSG1 mAb	1	1	19

13.4 IL-10/DSG1 ANDbodies suppress the inflammatory response in primary mouse macrophages

To show that IL-10/DSG1 ANDbodies are able to inhibit inflammatory immune responses, the effects of IL-10/DSG1 ANDbodies on mouse peripheral blood mononucleocytes (PBMCs) and macrophages treated with lipid polysaccharide (LPS) as an inflammatory stimulus were evaluated. In these experiments, PBMCs were isolated from blood and macrophages were isolated from the spleens of Balb/C mice by negative enrichment on magnetic beads (Miltenyi Biotec #130-110-434). Macrophage activation was assayed by measuring the level of TNF α cytokine present in the media after 3 hours and 5-6 hours of stimulation with LPS.

Figs. 13A-13G show the level of tumor necrosis factor alpha (TNF α) in PBMC cell culture after pre-stimulation with the indicated IL-10/DSG1 ANDbodies or control molecules followed by treatment with LPS for the indicated lengths of time. Figs. 14A-14G show the level of TNF α in primary macrophage cell culture after pre-stimulation with the indicated IL-10/DSG1 ANDbodies or control molecules followed by treatment with LPS for the indicated lengths of time. Because the panels represent experiments run across multiple days, data are not comparable between panels. These data show that all five IL-10/DSG1 ANDbodies are able to suppress inflammatory stimuli in primary macrophages.

13.5 *Engagement of an address target enhances the activity/potency of the effector function of an ANDbody*

The combination of addressing (e.g., using an address targeting domain) with a biologically active molecule has the potential to enhance a biological activity in a variety of ways. One exemplary enhancement is by increasing the potency of the effector moiety on specific cells where the address target is also present.

To test whether signaling potency of the effector targeting domain can be enhanced by the presence of an address targeting domain, human DSG1 was expressed on the HEK-BLUE™ IL-10 cells using stable expression with a lentivirus (the stable expressing cells are denoted HEKBLUE™ IL-10/DSG1). The DSG1 gene (NP_034209.2) was cloned into a suitable lentiviral plasmid backbone, packaged into viral particles using the VIRAPOWERTM Lentiviral Packing Mix (ThermoFisher Scientific) and transduced according to the manufacturer's instructions. Expression of DSG1 was confirmed by qPCR.

The potency of recombinant human IL-10, an ANDbody in which monomeric IL-10 replaces one Fab of the anti-DSG1 mAb (PRO058, functionally equivalent to PRO026), and a matched control in which the antibody sequence contains Motavizumab as a negative control were evaluated. Activity was tested on HEK-BLUE™ IL-10 cells and on HEK-BLUE™ IL-10 cells stably expressing DSG1. Fig. 15 shows the representative signaling response of each molecule in the parental HEK-BLUE™ IL-10 cells and the HEK-BLUE™ IL-10/DSG1 cells. The two cell lines responded similarly to recombinant IL-10, confirming that DSG1 expression did not have a large impact on their sensitivity to IL-10. The DSG1/IL-10 ANDbody showed approximately a 15-fold increase in potency when DSG1 was expressed on the target cells. No effect was seen on the potency of a matched IL-10/Motavizumab protein, confirming that the effect is mediated by binding to DSG1. This shows that the ANDbody designs provided herein are capable of address-mediated enhancement in their biological potency, allowing the use of less potent target binder moieties in ANDbodies to further decrease unwanted off-target effects.

13.6 *IL-10/DSG1 ANDbodies retain the pharmacokinetic and tissue distribution properties of the parental anti-DSG1 antibody*

In some ANDbodies the targeting moiety is intended to impart the tissue or cellular targeting of a parental mAb or other targeting molecule onto a biologically active moiety that would otherwise have undesirable pharmacokinetics or tissue distribution.

The IL-10/DSG1 ANDbodies are intended to direct IL-10 activity to the skin. In Example 7, it was shown that this anti-DSG1 antibody distributes preferentially into the skin of mice. In contrast, IL-10 is reported to clear from circulation in humans with a half-life of approximately 2 hours (Radwanski et al, Pharm Res. 1998 Dec;15(12):1895-901. We therefore evaluated whether IL-10/DSG1 ANDbodies retain the skin targeting capability of the parental antibody.

BALB/c mice were dosed by tail vein injection with 3 mg/kg of PRO003, PRO024, or PRO058.

PRO058 is functionally equivalent to PRO026, with a substitution in the Fc domain to improve purification of the recombinant protein. PRO058 comprises (a) the heavy chain sequence of PRO0026 (SEQ ID NO: 70), (b) the light chain sequence of PRO003 (SEQ ID NO: 29), and (c) an IL-10-Fc fusion protein (SEQ ID NO: 75) comprising an Fc region (SEQ ID NO: 74) and a monomeric human IL-10 sequence (SEQ ID NO: 64).

Serum samples were collected at time points from 1 hour to 48 hours. Tissue samples were collected at 1, 2, 4 and 7 days after dosing. The amount of anti-DSG1 or ANDbody in each serum or tissue sample was measured by ELISA. Figs. 16A and 16B show that the IL-10/anti-DSG1 ANDbodies PRO024 and PRO058 have PK properties in skin and serum that are similar to the parental anti-DSG1 antibody PRO003. These data demonstrate that antibody-cytokine fusions comprising a recombinant IL-10 can retain the pharmacokinetic properties of the parental antibody.

EXAMPLE 14. TNF α -BLOCKING MOLECULES COUPLED TO DSG1-TARGETING MOIETIES

This example describes the production of exemplary ANDbodies that block TNF α and bind DSG1 as an address.

14.1 Anti TNF α monoclonal antibody expression and purification

Anti TNF α antibodies having VH and VL sequences from a commercial antibody fused to a hulgG1 backbone with effector null mutations L234A, L235A, P329G (LALA-PG) were produced and their binding and affinity to TNF α was characterized as described above. The resulting mAbs were designated as PRO076 and PRO078.

14.2 Anti TNF α – DSG1 ANDbody design, expression and purification

ANDbodies were designed by combining PRO004 (Example 7) with a previously reported dominant-negative TNF α (Steed et al. Science. 2003 Sep 26;301(5641) or clinically validated anti-TNF α antibodies listed below with the aim of locally downmodulating TNF α in the extracellular milieu of the inflamed skin. The TNF α -blocking anti-DSG1 ANDbody designs explored various formats and valencies, including cytokine/antibody and TNF receptor 2 (TNFR2)/antibody fusions.

To express and purify the antibodies, a 1:1 ratio of heavy chain to light chain DNA was transfected into EXPI293F™ Cells (ThermoFisher Scientific) using the EXPIFECTAMINE™ 293 Transfection Kit (ThermoFisher Scientific) following the manufacturer's recommendations. Transiently expressed antibodies were purified from conditioned media 5 days post-transfection by filtering out the transfected cells. Conditioned media was incubated with protein A agarose beads for 1 hour. The bound beads were washed with Phosphate Buffered Saline (PBS) pH 7.4 followed by elution of the bound antibody with 0.1M Glycine pH 2.5 and neutralized with 1/10 volume of Tris pH 8.5. The neutralized eluate was buffer exchanged into PBS. The resulting mAbs were designated as PRO070, PRO074, PRO075 and PRO077 (Fig. 17).

The purified ANDbodies were analyzed by analytical size exclusion chromatography for monodispersity and by SDS-PAGE for purity. Standard additional purification steps were performed

to remove aggregation. PRO077 had the highest final yield, followed by PRO074 and PRO075, while PRO070 had the lowest final yield. The polished ANDbodies were pure and of the correct composition as seen by SDS-PAGE.

5 14.3 *Anti TNF α – DSG1 ANDbody binding and affinity testing*

ELISA binding assays demonstrated that all constructs were active in binding human and murine TNF α with varying affinities. PRO074 and PRO075 had similar affinities to both human and murine TNF α , which was within two/three-fold difference to the parent antibody. PRO077 had a 5-fold and a 12-fold decrease in binding affinity to human and murine TNF α , respectively, when compared to
10 the parent antibody. This reduction in affinity is probably due to the change of format from Fab to single-chain variable fragment (scFv).

14.4 *Anti TNF α – DSG1 ANDbody in vitro activity assays*

The ability of each anti-TNF α /anti-DSG1 ANDbody to inhibit TNF α signaling was evaluated
15 using HEK-BLUE™ TNF α cells (InvivoGen). These cells are engineered to express secreted embryonic alkaline phosphatase (SEAP) in response to signaling to TNF α signaling. TNF α was measured according to the manufacturer's instructions. To evaluate inhibitory activity, the concentration of TNF α was fixed at 225 pm (approximately the EC₈₀ of a recombinant human TNF α in this assay), and cells were pre-incubated with concentrations of TNF α blocking molecules from 10 nM
20 to approximately 10 pM. Table 12 shows the IC₅₀ of each anti-TNF α /DSG1 ANDbody alongside matched parent antibodies as positive controls. These data show that the ANDbodies retain TNF α blocking activity comparable to the original anti-TNF α parent antibodies.

Table 12. IC₅₀ of anti-TNF α /anti-DSG1 ANDbodies compared to matched controls

Protein	IC ₅₀ (nM, replicate 1)	IC ₅₀ (nM, replicate 2)
Adalimumab (PRO076)	0.05	0.03
Etanercept (PRO078)	0.06	0.07
PRO070	No inhibition	No inhibition
PRO074	0.3	0.2
PRO075	0.2	0.1
PRO077	0.04	0.04

25

VII. OTHER EMBODIMENTS

Some embodiments of the technology described herein can be defined according to any of
30 the following numbered embodiments:

1. A macromolecule comprising a first binding site and a second binding site, wherein:

(a) the first binding site is specific for an effector target in a subject, and
(b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein:

- 5 (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;
(ii) the second binding site does not substantially influence signaling upon binding the address target; and
(iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site.

10

2. A macromolecule comprising a first binding site and a second binding site, wherein:

(a) the first binding site is specific for an effector target in a subject, and
(b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein:

- 15 (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;
(ii) the second binding site does not substantially influence signaling upon binding the address target; and
(iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site;

20

and wherein localization of the macromolecule to a non-target tissue or cell is substantially reduced relative to localization of a reference macromolecule lacking the second binding site.

3. A macromolecule comprising a first binding site and a second binding site, wherein:

- 25 (a) the first binding site is specific for an effector target in a subject, and
(b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein:

(i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;

- 30 (ii) the second binding site does not substantially influence signaling upon binding the address target; and

(iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site;

- 35 and wherein localization of the macromolecule to a target tissue or cell is substantially increased relative to localization of a reference macromolecule lacking the second binding site.

4. A macromolecule comprising a first binding site and a second binding site, wherein:

- (a) the first binding site is specific for an effector target in a subject, and
(b) the second binding site is specific for an address target expressed in a target tissue or cell in

the subject; wherein:

(i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;

(ii) the second binding site does not substantially influence signaling upon binding the address target; and

(iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site;

and wherein at least **25%** of the macromolecule administered to a subject is detected at the target tissue or cell at a time point between 1 and 7 days following administration.

10

5. A macromolecule comprising a first binding site and a second binding site, wherein:

(a) the first binding site is specific for an effector target in a subject, and

(b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein:

(i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;

(ii) the second binding site does not substantially influence signaling upon binding the address target; and

(iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site;

and wherein the affinity of the first binding site for the effector target is lower than the affinity of the second binding site for the address target.

6. A macromolecule comprising a first binding site and a second binding site, wherein:

(a) the first binding site is specific for an effector target in a subject, and

(b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein:

(i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;

(ii) the second binding site does not substantially influence signaling upon binding the address target; and

(iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site;

and wherein the avidity of the first binding site for the effector target is lower than the avidity of the second binding site for the address target.

7. A macromolecule comprising a first binding site and a second binding site, wherein:

(a) the first binding site is specific for an effector target in a subject, and

(b) the second binding site is specific for an address target expressed in a target tissue or cell in

the subject; wherein:

(i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;

(ii) the second binding site does not substantially influence signaling upon binding the address target; and

(iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site;

and wherein the potency of the first binding site at the target tissue or cell is substantially increased relative to a reference macromolecule lacking the second binding site.

8. The macromolecule of any one of embodiments 1-7, wherein the first binding site has a low affinity for the effector target.

9. The macromolecule of any one of embodiments 1-7, wherein the first binding site has a low avidity for the effector target.

10. The macromolecule of any one of embodiments 1-4 and 6-9, wherein the affinity of the first binding site for the effector target is lower than the affinity of the second binding site for the address target.

11. The macromolecule of any one of embodiments 1-10, wherein the avidity of the first binding site for the effector target is lower than the avidity of the second binding site for the address target.

12. The macromolecule of any one of embodiments 1-11, wherein:

(a) the K_d of the first binding site for the effector target is higher than the K_d of the second binding site for the address target;

(b) the EC_{50} of the first binding site for the effector target is higher than the EC_{50} of the second binding site for the address target; or

(c) the IC_{50} of the first binding site for the effector target is higher than the IC_{50} of the second binding site for the address target.

13. The macromolecule of any one of embodiments 1-12, wherein the first binding site has an affinity to the effector target of at least about 2 times, at least about 5 times, or at least about 10 times less than the affinity of the second binding site to the address target.

14. The macromolecule of any one of embodiments 1-13, wherein the affinity of the second binding site to the address target has a K_d of greater than about 1 nM, greater than about 2 nM, or greater than about 50 nM.

15. The macromolecule of any one of embodiments 1-14, wherein the effector target is a protein, lipid, or sugar.

5 16. The macromolecule of any one of embodiments 1-15, wherein the effector target is a cell membrane-associated target.

17. The macromolecule of embodiment 15 or 16, wherein the effector target is a protein.

10 18. The macromolecule of embodiment 17, wherein the effector target is a secreted protein.

19. The macromolecule of embodiment 17 or 18, wherein the effector target is encoded by a gene selected from the group consisting of the genes recited in Table 1.

15 20. The macromolecule of any one of embodiments 1-19, wherein the macromolecule agonizes the effector target.

21. The macromolecule of any one of embodiments 1-19, wherein the macromolecule antagonizes the effector target.

20 22. The macromolecule of any one of embodiments 1-21, wherein the address target is a protein, lipid, or sugar.

23. The macromolecule of embodiment 22, wherein the address target is a protein.

25 24. The macromolecule of any one of embodiments 17-23, wherein expression of the effector target or the address target is expression of an RNA sequence encoding the effector target or the address target.

30 25. The macromolecule of embodiment 24, wherein the expression level of the effector target or the address target is assessed by using a RNA sequence dataset.

26. The macromolecule of embodiment 25, wherein the RNA sequence dataset is a Genotype-Tissue Expression (GTEx) dataset or a Human Protein Atlas (HPA) dataset.

35 27. The macromolecule of embodiment 23, wherein expression of the effector target or the address target is protein expression.

40 28. The macromolecule of any one of embodiments 1-27, wherein the effector target is systemically expressed in the subject.

29. The macromolecule of any one of embodiments 1-27, wherein the effector target is regionally expressed in the subject.

5 30. The macromolecule of any one of embodiments 1-27, wherein the effector target is locally expressed in the subject.

31. The macromolecule of any one of embodiments 1-30, wherein the address target is regionally expressed in the subject.

10 32. The macromolecule of any one of embodiments 1-30, wherein the address target is locally expressed in the subject.

33. The macromolecule of any one of embodiments 1-30, wherein the expression of the address target is restricted to a cell type in the subject.

15 34. The macromolecule of any one of embodiments 1-33, wherein the address target is a soluble protein or an extracellular matrix (ECM)-associated protein and is not present in detectable amounts on the cell surface.

20 35. The macromolecule of embodiment 34, wherein the address target is expressed in the ECM and is not present in detectable amounts elsewhere in the subject.

36. The macromolecule of any one of embodiments 1-35, wherein the address target is expressed only by a cell in the subject when in a specific cell state.

25 37. The macromolecule of any one of embodiments 1-36, wherein the address target is expressed only by a cell in the subject when in a disease state.

38. The macromolecule of any one of embodiments 1-37, wherein the address target is not expressed in a tissue in which binding of the second binding site to the effector target is deleterious to the subject.

39. The macromolecule of any one of embodiments 1-38, wherein the binding site for the address target does not bind in detectable amounts to the binding site of a natural ligand of the address target.

35 40. The macromolecule of any one of embodiments 1-39, wherein expression of the effector target or address target includes expression in one or more of minor salivary gland, thyroid, lung, breast, mammary tissue, pancreas, adrenal gland, liver, kidney, kidney cortex, kidney medulla, adipose-visceral tissue, omentum, small intestine, terminal ileum, fallopian tube, ovary, uterus, skin, skin not sun exposed, suprapubic skin, cervix, endocervix, ectocervix, vagina, skin sun exposed,

lower leg skin, eneanterior cingulate cortex, Brodmann area 24 (BA24), basal ganglia, caudate nucleus, putamen, nucleus acumbens, hypothalamus, amygdala, hippocampus, cerebellum, cerebellar hemisphere, substantia nigra, pituitary gland, spinal cord, cervical spinal cord, artery, aorta, heart, atrial appendage, coronary artery, left ventricle, esophagus, esophagus mucosa, esophagus
 5 muscularis, gastroesophageal junction, spleen, stomach, colon, transverse colon, sigmoid colon, testis, whole blood cells, EBV-transformed lymphocytes, artery-tibial, or nerve-tibial tissues.

41. The macromolecule of embodiment 40, wherein expression of the effector target or address target includes expression in skin tissue, lung tissue, kidney tissue, or intestine tissue.
 10

42. The macromolecule of embodiment 41, wherein expression of the address target is substantially higher in skin tissue, lung tissue, kidney tissue, or intestine tissue than in any other tissue.

15 43. The macromolecule of any one of embodiments 1-42, wherein the effector target and/or the address target is expressed on a structural tissue in the subject.

44. The macromolecule of any one of embodiments 1-43, wherein the effector target and address target are on the same cell.
 20

45. The macromolecule of any one of embodiments 1-43, wherein the effector target and address target are on different cells.

46. The macromolecule of embodiment 45, wherein the effector target and address target are on
 25 different cells of the same cell type.

47. The macromolecule of embodiment 45, wherein the effector target and address target are on different cells of different cell types.

30 48. The macromolecule of embodiment 45, wherein the effector target and address target are on different cells in the same tissue.

49. The macromolecule of any one of embodiments 45, 47, and 48, wherein:
 (a) the effector target is on a circulating cell and the address target is on a tissue-restricted cell; or
 35 (b) the effector target is on a tissue-restricted cell and the address target is on a circulating cell.

50. The macromolecule of any one of embodiments 45-49, wherein the effector target and address target are on different cells located within 100 nm of each other in the subject.

51. The macromolecule of any one of embodiments 45-49, wherein either the effector target or the address target is present on a cell surface.

52. The macromolecule of any one of embodiments 1-51, wherein the macromolecule is a DNA polynucleotide.

53. The macromolecule of any one of embodiments 1-51, wherein the macromolecule comprises an RNA or RNA-polypeptide conjugate.

54. The macromolecule of any one of embodiments 1-51 and 53, wherein the macromolecule comprises a polypeptide.

55. The macromolecule of any one of embodiments 1-51, wherein the macromolecule is a polypeptide.

56. The macromolecule of embodiment 54 or 55, wherein the polypeptide is an antibody or antigen-binding fragment thereof.

57. The macromolecule of embodiment 56, wherein the first binding site and the second binding site each comprise a VH and/or a VL.

58. The macromolecule of embodiment 57, wherein the macromolecule is an antibody comprising a first binding site that is specific for the effector target in the subject and a second binding site that is specific for the address target.

59. The macromolecule of embodiment 57 or 58, wherein the macromolecule is an asymmetric antibody or a symmetric antibody.

60. The macromolecule of any one of embodiments 56-59, wherein the antibody or antigen-binding fragment thereof comprises an scFv, BslgG, a BsAb fragment, a BiTE, a dual-affinity re-targeting protein (DART), a tandem diabody (TandAb), a diabody, an Fab2, a di-scFv, chemically linked F(ab')₂, an Ig molecule with 2, 3 or 4 different antigen binding sites, a DVI-IgG four-in-one, an ImmTac, an HSAbody, an IgG-IgG, a Cov-X-Body, an scFv1-PEG-scFv₂, an appended IgG, an DVD-IgG, an affibody, an affilin, an affimer, an affitin, an alphabody, an anticalin, an avimer, a DARPin, a Fynomer, a monobody, a nanoCLAMP, a bis-Fab, an Fv, a Fab, a Fab'-SH, a linear antibody, an scFv, an antibody with only a heavy chain (Humabody), an ScFab, an IgG antibody fragment, a single-chain variable region antibody, a single-domain heavy chain antibody, a bispecific triplebody, a BiKE, a CrossMAb, a dsDb, an scDb, tandem a dAb / VHH, a triple dAb VHH, a tetravalent dAb / VHH, a Fab-scFv, a Fab-Fv, or a DART-Fc, an adnectin, a Kunitz-type inhibitor, or a receptor decoy.

61. The macromolecule of embodiment 54, wherein the polypeptide is a ligand of the effector target or a ligand of the address target.

5 62. The macromolecule of embodiment 61, wherein the ligand is a natural ligand, a modified ligand, or a synthetic ligand.

63. The macromolecule of embodiment 61 or 62, wherein the effector target or address target is a receptor and the polypeptide is a ligand thereof.

10 64. The macromolecule of any one of embodiments 61-63, wherein the first binding site comprises an antibody or antigen-binding fragment thereof and the second binding site comprises a ligand of the address target.

15 65. The macromolecule of any one of embodiments 61-63, wherein the first binding site comprises a ligand of the effector target and the second binding site comprises an antibody or antigen-binding fragment thereof.

20 66. The macromolecule of any one of embodiments 1-51 and 54-65, wherein the amino acid sequences of the first and second binding sites are at least about 10% identical, at least about 20% identical, at least about 30% identical, at least about 40% identical, at least about 50% identical, at least about 60% identical, or at least about 70% identical.

25 67. The macromolecule of any one of embodiments 1-66, wherein the address target has a Gini coefficient higher than about 0.4, about 0.5, about 0.57, about 0.65, about 0.7, about 0.85, about 0.90, or about 0.95.

68. The macromolecule of any one of embodiments 1-67, wherein the address target has a Tau coefficient higher than about 0.67, about 0.75, about 0.8, about 0.85, about 0.90, or about 0.95.

30 69. The macromolecule of any one of embodiments 1-68, wherein the effector target has a Gini coefficient lower than about 0.25, about 0.20, or about 0.15.

70. The macromolecule of any one of embodiments 1-69, wherein the effector target has a Tau coefficient lower than about 0.25, about 0.20, or about 0.15.

35 71. The macromolecule of any one of embodiments 1-70, further comprising a third binding site.

72. The macromolecule of embodiment 71, wherein the third binding site is the same as the first binding site.

40

73. The macromolecule of embodiment 71, wherein the third binding site is the same as the second binding site.

5 74. The macromolecule of any one of embodiments 1-73, wherein the first binding site and second binding site are directly joined to each other in the macromolecule.

75. The macromolecule of any one of embodiments 1-73, wherein the first binding site and the second binding site in the macromolecule are joined by a stable domain.

10 76. The macromolecule of any one of embodiments 1-75, wherein the effector target is Notch2 and the address target is RAGE.

77. The macromolecule of embodiment 76, wherein RAGE signaling is not influenced by the second site binding the RAGE address target.

15 78. The macromolecule of any one of embodiments 1-75, wherein the effector target is Notch2 and the address target is uromodulin (UMOD).

79. The macromolecule of embodiment 78, wherein UMOD signaling is not influenced by the second site binding the UMOD address target.

80. The macromolecule of any one of embodiments 1-75, wherein the effector target is Notch2 and the address target is meprin A subunit beta (MEP1B).

25 81. The macromolecule of embodiment 80, wherein MEP1B signaling is not influenced by the second site binding the MEP1B address target.

82. The macromolecule of any one of embodiments 1-75, wherein the effector target is IL11Ra and the address target is RAGE.

30 83. The macromolecule of embodiment 82, wherein RAGE signaling is not influenced by the second site binding the RAGE address target.

84. The macromolecule of any one of embodiments 1-75, wherein the effector target is IL 11Ra and the address target is UMOD.

85. The macromolecule of embodiment 84, wherein UMOD signaling is not influenced by the second site binding the UMOD address target.

40 86. The macromolecule of any one of embodiments 1-85, wherein the subject is a human.

87. A method of delivering a moiety to a target tissue or cell in a subject, comprising administering to the subject a macromolecule of any one of embodiments 1-86, wherein the target tissue comprises the address target.

5 88. The method of embodiment 87, wherein the moiety is a molecule.

89. The method of embodiment 87 or 88, wherein the moiety is not a toxin.

90. The method of embodiment 87, wherein the moiety is a cell.

10

91. The method of embodiment 90, wherein the moiety is not a T cell or an NK cell.

92. The method of any one of embodiments 87-91, wherein the target tissue is not a tumor.

15 93. A method of modulating an effector target in a target tissue, comprising administering to the tissue a macromolecule of any one of embodiments 1-86, wherein the target tissue comprises the address target and the effector target.

20 94. A method of biasing a binding agent away from binding an effector target when the effector target is found in the heart or lungs, comprising administering the macromolecule of any one of embodiments 1-86, wherein the address target is not substantially expressed in the heart or lungs.

25 95. A method of modulating a target tissue in a subject, comprising administering to the subject a macromolecule of any one of embodiments 1-86, wherein the target tissue comprises the address target and the effector target.

30 96. A method of treating a subject having a disease or condition associated with an effector target, comprising administering to the subject a macromolecule of any one of embodiments 1-86, wherein the first binding site of the macromolecule binds the effector target.

30

97. A macromolecule comprising a first binding site and a second binding site, wherein:

(a) the first binding site is specific for an effector target in a subject, and

(b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject;

35 wherein the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell,

wherein the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site, and

wherein the second binding site does not bind to the binding site of the natural ligand of the

address target.

98. A macromolecule comprising a first binding site and a second binding site, wherein:

- (a) the first binding site is specific for an effector target in a subject, and
5 (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject;

wherein the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell,

- wherein the first binding site does not substantially influence effector target signaling in the
10 absence of localization by the second binding site, and

wherein the first binding site and second binding site are directly joined to each other in the macromolecule.

99. A macromolecule comprising a first binding site and a second binding site, wherein:

- 15 (a) the first binding site is specific for an effector target in a subject, and
(b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject;

wherein the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell,

- 20 wherein the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site, and

wherein the first binding site and second binding are joined to each other by a stable domain.

100. A macromolecule comprising a first binding site and a second binding site, wherein:

- 25 (a) the first binding site is specific for an effector target in a subject, and
(b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject;

wherein the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell,

- 30 wherein the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site, and

wherein the effector target and/or the address target is expressed on a structural tissue in a host.

101. A pharmaceutical composition comprising the macromolecule of any one of embodiments 1-

35 86.

102. A pharmaceutical composition comprising a macromolecule and one or more pharmaceutically acceptable excipients,

wherein the macromolecule comprises a first binding site and a second binding site, wherein:

(a) the first binding site is specific for an effector target in a subject, and
(b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject;

wherein the second binding site localizes the first binding site to the address target such that the
5 first binding site influences effector target signaling in the target tissue or cell, and
wherein the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site.

103. The pharmaceutical composition of embodiment 101 or 102, wherein the pharmaceutical
10 composition is an RNA pharmaceutical composition.

104. The pharmaceutical composition of any one of embodiments 101-103, further comprising a carrier.

15 105. The pharmaceutical composition of embodiment 104, wherein the carrier is a lipid nanoparticle.

106. The pharmaceutical composition of embodiment 104, wherein the carrier is a viral vector.

20 107. The pharmaceutical composition of embodiment 104, wherein the carrier is a membrane-based carrier.

108. The pharmaceutical composition of embodiment 107, wherein the membrane-based carrier is a cell.
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109. The pharmaceutical composition of embodiment 107, wherein the membrane-based carrier is a vesicle.

110. A method for modulating activity of an effector target in the skin of a subject, the method
30 comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein:

- (a) the first binding site is specific for an effector target in the subject, and
- (b) the second binding site is specific for desmoglein-1 (DSG-1).

35 111. A method for modulating activity of an effector target in the lung of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein:

- (a) the first binding site is specific for an effector target in the subject, and
- (b) the second binding site is specific for RAGE.

112. A method for modulating activity of an effector target in the kidney of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein:

- 5 (a) the first binding site is specific for an effector target in the subject, and
 (b) the second binding site is specific for cadherin 16 (CDH16).

113. A method for modulating activity of an effector target in the intestine of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein:

- 10 (a) the first binding site is specific for an effector target in the subject, and
 (b) the second binding site is specific for cadherin 17 (CDH17).

114. A method of localizing a macromolecule at a target tissue or cell of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein:

- (a) the first binding site is specific for an effector target in the subject, and
 (b) the second binding site is specific for an address target expressed in the target tissue or cell in the subject; wherein:
20 (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;
 (ii) the second binding site does not substantially influence signaling upon binding the address target; and
 (iii) the first binding site does not substantially influence effector target signaling in the absence of
25 localization by the second binding site; and
 allowing the macromolecule to localize at the target tissue or cell of the subject.

115. A method of concentrating a macromolecule in a target tissue or cell in a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein:

- (a) the first binding site is specific for an effector target in a subject, and
 (b) the second binding site is specific for an address target expressed in a target tissue or cell in the subject; wherein:
 (i) the second binding site localizes the first binding site to the address target such that the first
35 binding site influences effector target signaling in the target tissue or cell;
 (ii) the second binding site does not substantially influence signaling upon binding the address target; and

(iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site;

and allowing the macromolecule to concentrate at the target tissue or cell of the subject, wherein at least 25% of the macromolecule detectable in the subject is detected at the target tissue or cell at a
5 time point between 1 and 7 days following administration of the macromolecule to the subject.

116. The method of embodiment 114 or 115, wherein the potency of the first binding site at the target tissue or cell is substantially increased relative to a reference macromolecule lacking the second binding site.
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117. The method of embodiment 114 or 115, wherein effector target signaling by the macromolecule in a non-target tissue or cell of the subject is substantially decreased relative to a reference macromolecule lacking the second binding site.

118. The method of embodiments 110-117, wherein the macromolecule is a macromolecule of any one of embodiments 1-86.
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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
20 construed as limiting the scope of the invention.

WHAT IS CLAIMED IS:

1. A method of localizing a macromolecule at a target tissue or cell of a subject, the method comprising administering to the subject a macromolecule comprising a first binding site and a second binding site, wherein:
 - (a) the first binding site is specific for an effector target in the subject, and
 - (b) the second binding site is specific for an address target expressed in the target tissue or cell in the subject;wherein:
 - (i) the second binding site localizes the first binding site to the address target such that the first binding site influences effector target signaling in the target tissue or cell;
 - (ii) the second binding site does not substantially influence signaling upon binding the address target; and
 - (iii) the first binding site does not substantially influence effector target signaling in the absence of localization by the second binding site; andallowing the macromolecule to localize at the target tissue or cell of the subject.
2. The method of claim 1, wherein at least 25% of the macromolecule detectable in the subject is detected at the target tissue or cell at a time point between 1 and 7 days following administration of the macromolecule to the subject.
3. The method of claim 1, wherein the potency of the first binding site at the target tissue or cell is substantially increased relative to a reference macromolecule lacking the second binding site.
4. The method of claim 3, wherein the first binding site has a low affinity for the effector target.
5. The method of claim 3, wherein the first binding site has a low avidity for the effector target.
6. The method of claim 1, wherein the affinity of the first binding site for the effector target is lower than the affinity of the second binding site for the address target.
7. The method of claim 1, wherein the avidity of the first binding site for the effector target is lower than the avidity of the second binding site for the address target.
8. The method of claim 1, wherein effector target signaling by the macromolecule in a non-target tissue or cell of the subject is substantially decreased relative to a reference macromolecule lacking the second binding site.
9. The method of claim 1, wherein the address target is regionally expressed in the subject

10. The method of claim 1, wherein the address target is locally expressed in the subject.
11. The method of claim 1, wherein the expression of the address target is restricted to a cell type in the subject.
12. The method of claim 1, wherein the address target is expressed only by a cell in the subject when in a specific cell state.
13. The method of claim 1, wherein the address target is expressed only by a cell in the subject in a disease state.
14. The method of claim 1, wherein the first binding site or the second binding site comprises a polypeptide.
15. The method of claim 14, wherein the polypeptide is an antibody or antigen-binding fragment thereof.
16. The method of claim 15, wherein the macromolecule is an antibody comprising a first binding site that is specific for the effector target in the subject and a second binding site that is specific for the address target.
17. The method of claim 14, wherein the polypeptide is a ligand of the effector target or a ligand of the address target.
18. The method of claim 17, wherein:
 - (a) the first binding site comprises an antibody or antigen-binding fragment thereof and the second binding site comprises a ligand of the address target; or
 - (b) the first binding site comprises a ligand of the effector target and the second binding site comprises an antibody or antigen-binding fragment thereof.
19. The method of claim 1, wherein the target tissue is skin and the second binding site is specific for desmoglein-1 (DSG-1).
20. The method of claim 1, wherein the target tissue is lung tissue and the second binding site is specific for RAGE.
21. The method of claim 1, wherein the target tissue is kidney tissue and the second binding site is specific for cadherin 16 (CDH16).

22. The method of claim 1, wherein the target tissue is intestine tissue and the second binding site is specific for cadherin 17 (CDH17).