

ENGINEERING CELL LINES CAPABLE OF PROLIFERATION IN GROWTH FACTOR FREE MEDIA FORMULATIONS

1. CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] [1] This application claims the benefit of U.S. Provisional Application No. 63/349,865 filed June 7, 2022; which is hereby incorporated in its entirety by reference.

2. SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing with 131 sequences, which has been submitted via Patent Center and is hereby incorporated by reference in its entirety. Said XML copy, created on June 7, 2023, is named 55926WO-SequenceListing.xml, and is 252,422 bytes in size.

3. BACKGROUND

[0003] The mass production of cells remains limited by several factors, thus limiting final yields. Mass production of cells finds several downstream applications. For example, foods formulated from metazoan cells, cultured in vitro, have prospective advantages over their corporal-derived animal counterparts, including improved nutrition and safety. Production of these products have been projected to require fewer resources, convert biomass at a higher caloric efficiency and result in reduced environmental impacts relative to conventional in vivo methods. Together, metazoan cells, and their extracellular products, constitute a biomass that can potentially be harvested from a cultivation infrastructure for formulation of cell-based food products, such as cultured meat.

[0004] However, mass production of cells originating from cultured metazoan cells remains limited by several factors, for example, by the maximum culture density that can be conventionally achieved and the requirement for supplemented proteins, such as growth factors, which support the productivity of the cultivation process, thus limiting final yields. Provided herein are compositions and methods that address this and other related needs.

4. SUMMARY

[0005] This disclosure is based in part on the finding that introducing a polynucleotide comprising a coding sequence of a growth factor ligand and/or a coding sequence of a growth factor receptor into a cell line results in the cell line's reduced reliance on exogenous growth factors. For example, the Applicant found that introducing a polynucleotide comprising a coding sequence of a growth factor ligand and/or a coding sequence of a growth factor receptor into a cell line results in maintenance of cell proliferation rates similar to controls

and an increase in the number of non-adherent cells (i.e., cells from anchorage-dependent growth) all while cells are grown in the absence of one or more exogenous growth factors (see FIG. 1).

[0006] Overall, this work demonstrated the ability to engineer cells to have reduced dependence on exogenous growth factors without compromising the cell's ability to proliferate or differentiate into myogenic cells. These findings are important because manufacturing cells suitable for consumption requires vast amounts of exogenous growth factors, which is both cost and time prohibitive (when factoring in supply chain). The engineered cells provided herein supply their own source of growth factor signaling—thereby bypassing or at least reducing the need to supplement the cultures with exogenous growth factors. Moreover, by promoting anchorage independent growth, which is currently essential for manufacturing cell based meats suitable for consumption, the engineered cell lines provided herein increase the efficiency by which cell based meats suitable for consumption can be produced.

[0007] In one aspect, this disclosure features method of engineering a cell line for reduced dependence on exogenous growth factors, comprising: (a) introducing into the cell line one or more of: (i) a polynucleotide comprising a coding sequence of a growth factor ligand; (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or (iii) a polynucleotide comprising a coding sequence of an activated downstream growth factor target; and (b) culturing the cell line in a cultivation infrastructure.

[0008] In one aspect, this disclosure features method of increasing the concentration of a growth factor ligand in culture medium of cells in culture, comprising: (a) introducing into a cell line one or more of: (i) a polynucleotide comprising a coding sequence of a growth factor ligand; and (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or (iii) a polynucleotide comprising a coding sequence of an activated downstream growth factor target; and (b) culturing the cell line in a cultivation infrastructure.

[0009] In one aspect, this disclosure features method for improving anchorage independent growth in a cell line, comprising: (a) introducing into the cell line one or more of: (i) a polynucleotide comprising a coding sequence of a growth factor ligand; and (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or (iii) a polynucleotide comprising a coding sequence of an activated downstream growth factor target; and (b) culturing the cell line in a cultivation infrastructure.

[0010] In one aspect, this disclosure features method for increasing the cell density of a culture comprising a cell line, comprising: (a) introducing into the cell line one or more of: (i) a polynucleotide comprising a coding sequence of a growth factor ligand; and (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or (iii) a polynucleotide comprising a coding sequence of an activated growth factor receptor; and (b) culturing the cell line in a cultivation infrastructure.

[0011] In some embodiments, the growth factor ligand is selected from basic fibroblast growth factor (FGF2), insulin-like growth factor 1 (IGF1), and platelet-derived growth factor subunit B (PDGFb).

[0012] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand further comprises an additional two or more growth factor ligands, wherein each of the additional growth factor ligands is selected from FGF2, IGF1, and PDGFb.

[0013] In some embodiments, the growth factor ligand is FGF2. In some embodiments, the FGF2 comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 1-15.

[0014] In some embodiments, the growth factor ligand is IGF1. In some embodiments, the IGF1 comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 16-17.

[0015] In some embodiments, the growth factor ligand is PDGFb. In some embodiments, the PDGFb comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 18-21.

[0016] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of a signal peptide located 5' to the coding sequence of the growth factor ligand, and wherein the signal sequence and the growth factor ligand are a fusion protein. In some embodiments, the signal sequence comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 22-31.

[0017] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a regulatory sequence operably linked to the coding sequence of the growth factor ligand and/or additional growth factor ligands.

[0018] In some embodiments, the regulatory sequence comprises a promoter selected from: an inducible promoter, a tissue specific promoter, and a constitutively active promoter.

[0019] In some embodiments, the promoter is selected from EF1alpha, PGK, CMV, RSV, and β -actin.

[0020] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand comprises a sequence encoding a polycistronic mRNA, wherein the polycistronic mRNA comprises the coding sequence of the growth factor ligand and the coding sequence one or more additional growth factor ligands.

[0021] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand comprises one or more sequences encoding a self-cleaving peptide, one or more internal ribosome entry sites (IRES), or a combination thereof.

[0022] In some embodiments, activity and/or expression of the growth factor ligand is controllable.

[0023] In some embodiments, activity and/or expression of the growth factor ligand is controlled using an inducible promoter, an inducible tag, or a degradation tag.

[0024] In some embodiments, expression of the growth factor ligands is controlled using an inducible promoter. In some embodiments, the coding sequence of the growth factor ligand is operably linked to the inducible promoter. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible promoter, thereby enabling expression of the growth factor ligand.

[0025] In some embodiments, activity of the growth factor ligand is controlled using an inducible tag. In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of an inducible tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the inducible tag and the growth factor ligand are a fusion protein. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible tag, thereby inducing activity of the growth factor ligand/fusion protein.

[0026] In some embodiments, activity of the one or more growth factor ligands is controlled using a degradation tag. In some embodiments, the polynucleotide comprising a

coding sequence of a growth factor ligand further comprises a coding sequence of a degradation tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the degradation tag and the growth factor ligand are a fusion protein. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the degradation tag, thereby targeting the growth factor ligand/fusion protein for degradation.

[0027] In some embodiments, (a) the concentration of FGF2 in the culture medium is increased by at least 0.001 ng/mL as compared to cell lines not engineered to include a polynucleotide encoding FGF2; (b) the concentration of IGF-1 in the culture medium is increased by at least 0.001 ng/mL as compared to cell lines not engineered to include a polynucleotide encoding IGF1; and/or (c) the concentration of PDGFb in the culture medium is increased by at least 0.001 ng/mL as compared to cell lines not engineered to include a polynucleotide encoding PDGFb.

[0028] In some embodiments, (a) the concentration of FGF2 in the culture medium is increased by at least 2.5% as compared to cell lines not engineered to include a polynucleotide encoding FGF2; (b) the concentration of IGF-1 in the culture medium is increased by at least 2.5% as compared to cell lines not engineered to include a polynucleotide encoding IGF1; and/or (c) the concentration of PDGFb in the culture medium is increased by at least 2.5% as compared to cell lines not engineered to include a polynucleotide encoding PDGFb.

[0029] In some embodiments, the growth factor receptor is selected from fibroblast growth factor receptor (FGFR), insulin growth factor 1 receptor (IGF1R), and platelet-derived growth factor receptor (PDGFR).

[0030] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor further comprises an additional two or more growth factor receptors, wherein each additional growth factor receptor is selected from FGFR, IGFR, and PDGFR.

[0031] In some embodiments, the growth factor receptor is an FGFR selected from FGFR1, FGFR2, FGFR3, and FGFR4. In some embodiments, the FGFR comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 32-49.

[0032] In some embodiments, the growth factor receptor is IGF1R. In some embodiments, the IGF1R comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 50-51.

[0033] In some embodiments, the growth factor receptor is PDGFR. In some embodiments, the PDGFR comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 52-58.

[0034] In some embodiments, the polynucleotide comprising a coding sequence of an activated downstream growth factor target comprises a growth factor receptor comprising one or more amino acid insertions, deletions, or substitutions that result in the receptor being constitutively activated.

[0035] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor comprises a regulatory sequence operably linked to the coding sequence of the growth factor receptor and/or the coding sequence of the additional growth factor receptors.

[0036] In some embodiments, the regulatory sequence comprises a promoter selected from: an inducible promoter, a tissue specific promoter, and a constitutively active promoter.

[0037] In some embodiments, the promoter is selected from EF1alpha, PGK, CMV, RSV, and β -actin.

[0038] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor comprises a sequence encoding a polycistronic mRNA, wherein the polycistronic mRNA comprises the coding sequence of the growth factor receptor and the coding sequence of the two or more additional growth factor receptors.

[0039] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor comprises one or more sequences encoding a self-cleaving peptide, one or more internal ribosome entry sites (IRES), or a combination thereof.

[0040] In some embodiments, activity and/or expression of the growth factor receptors is controllable.

[0041] In some embodiments, expression of the growth factor receptor is controlled using an inducible promoter, an inducible tag, and a degradation tag.

[0042] In some embodiments, expression of the growth factor receptor is controlled using an inducible promoter. In some embodiments, the coding sequence of the growth factor

receptor is operably linked to the inducible promoter. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible promoter, thereby enabling expression of the growth factor receptor.

[0043] In some embodiments, activity of the growth factor receptor is controlled using an inducible tag. In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor further comprises a coding sequence of an inducible tag located 5' or 3' to the coding sequence of the growth factor receptor, and wherein the inducible tag and the growth factor receptor are a fusion protein.

[0044] In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible tag, thereby inducing activity of the growth factor receptor/fusion protein.

[0045] In some embodiments, activity of the one or more growth factor ligands is controlled using a degradation tag. In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor further comprises a coding sequence of a degradation tag located 5' or 3' to the coding sequence of the growth factor receptor, and wherein the degradation tag and the growth factor receptor are a fusion protein.

[0046] In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the degradation tag, thereby targeting the growth factor receptor/fusion protein for degradation.

[0047] In some embodiments, the method also includes introducing a polynucleotide sequence encoding an accessory protein.

[0048] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand and/or the polynucleotide comprising a coding sequence of a growth factor receptor further comprises a coding sequence of an accessory protein.

[0049] In some embodiments, the accessory protein is fibroblast growth factor binding protein (FGFBP). In some embodiments, the FGFBP comprises an amino acid sequence having at least 80% sequence identity to a sequence of SEQ ID NO: 59.

[0050] In some embodiments, the accessory protein is RASV12. In some embodiments, the RASV12 comprises an amino acid sequence having at least 80% sequence identity to a sequence of SEQ ID NO: 60.

[0051] In some embodiments, the method comprises introducing into the cell: (i) a polynucleotide comprising a coding sequence of FGF2, and a polynucleotide comprising a FGFR; (ii) a polynucleotide comprising a coding sequence of IGF1, and a polynucleotide comprising an IGF1R; (iii) a polynucleotide comprising a coding sequence of PDGF, and a polynucleotide comprising a PDGFR, or (iv) a combination selected from: (i) and (ii), (ii) and (iii), (ii) and iii), and (i), (ii), and (iii).

[0052] In some embodiments, the cell line is from a livestock, poultry, game or aquatic animal species. In some embodiments, the cell line is from a chicken, duck, or turkey. In some embodiments, the cell line is from a fish. In some embodiments, the cell line is from a livestock species. In some embodiments, the livestock species is porcine or bovine. In some embodiments, the cells are from any animal species intended for human or non-human dietary consumption.

[0053] In some embodiments, the cells are myogenic cells. In some embodiments, the myogenic cells are myoblasts, myocytes, satellite cells, side population cells, muscle derived stem cells, mesenchymal stem cells, myogenic pericytes, or mesoangioblasts.

[0054] In some embodiments, the cells are non-myogenic cells.

[0055] In some embodiments, the cells are fibroblasts, stem cells, or are cells otherwise having myogenic or fibroblastic capacity.

[0056] In another aspect, this disclosure features in vitro methods for producing cell-based meat suitable for consumption, comprising: (a) introducing into a cell one or more of: (i) a polynucleotide comprising a coding sequence of a growth factor; (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or (iii) a polynucleotide comprising a coding sequence of an activated downstream growth factor target; and (b) inducing myogenic specific differentiation, wherein the differentiated cells form myocytes and multinucleated myotubes; (c) culturing the myocytes and myotubes to generate skeletal muscle fibers, thereby producing a cell-based meat suitable for consumption.

[0057] In some embodiments, the cell line is avian or mammalian. In all embodiments, the cell line is non-human. In some embodiments, the cell line is from a livestock, poultry, game or aquatic animal species. In some embodiments, the cell line is from a chicken, duck, or turkey. In some embodiments, the cell line is from a fish. In some embodiments, the cell line is from a livestock species. In some embodiments, the livestock species is porcine or bovine.

[0058] In some embodiments, the cells are from any animal species intended for human or non-human dietary consumption.

[0059] In some embodiments, the cells are myogenic cells. In some embodiments, the myogenic cells are myoblasts, myocytes, satellite cells, side population cells, muscle derived stem cells, mesenchymal stem cells, myogenic pericytes, or mesoangioblasts.

[0060] In some embodiments, the cells are non-myogenic cells.

[0061] In some embodiments, the growth factor ligand is selected from basic fibroblast growth factor (FGF2), insulin-like growth factor 1 (IGF1), and platelet-derived growth factor subunit B (PDGFb).

[0062] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand further comprises an additional two or more growth factor ligands, wherein each of the additional growth factor ligands is selected from FGF2, IGF1, and PDGFb.

[0063] In some embodiments, the growth factor ligands is FGF2. In some embodiments, the FGF2 comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 1-15.

[0064] In some embodiments, the growth factor ligands is IGF1. In some embodiments, the IGF1 comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 16-17.

[0065] In some embodiments, the growth factor ligands is PDGFb. In some embodiments, the PDGFb comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 18-21.

[0066] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of a signal peptide located 5' to the coding sequence of the growth factor ligand, and wherein the signal sequence and the growth factor ligand are a fusion protein.

[0067] In some embodiments, the signal sequence comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 22-31.

[0068] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand comprises a regulatory sequence operably linked to the coding sequence of the growth factor ligand and/or additional growth factor ligands.

[0069] In some embodiments, the regulatory sequence comprises a promoter selected from: an inducible promoter, a tissue specific promoter, and a constitutively active promoter.

[0070] In some embodiments, the promoter is selected from EF1alpha, PGK, CMV, RSV, and β -actin.

[0071] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand comprises a sequence encoding a polycistronic mRNA, wherein the polycistronic mRNA comprises the coding sequence of the growth factor ligand and the coding sequence one or more additional growth factor ligands.

[0072] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand further comprises one or more sequences encoding a self-cleaving peptide, one or more internal ribosome entry sites (IRES), or a combination thereof.

[0073] In some embodiments, activity and/or expression of the growth factor ligand is controllable.

[0074] In some embodiments, activity and/or expression of the growth factor ligand is controlled using an inducible promoter, an inducible tag, or a degradation tag.

[0075] In some embodiments, expression of the growth factor ligands is controlled using an inducible promoter. In some embodiments, the coding sequence of the growth factor ligand is operably linked to the inducible promoter. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible promoter, thereby enabling expression of the growth factor ligand.

[0076] In some embodiments, activity of the growth factor ligand is controlled using an inducible tag. In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of an inducible tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the inducible tag and the growth factor ligand are a fusion protein. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible tag, thereby inducing activity of the growth factor ligand/fusion protein.

[0077] In some embodiments, activity of the one or more growth factor ligands is controlled using a degradation tag. In some embodiments, the polynucleotide comprising a

coding sequence of a growth factor ligand further comprises a coding sequence of a degradation tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the degradation tag and the growth factor ligand are a fusion protein. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the degradation tag, thereby targeting the growth factor ligand/fusion protein for degradation.

[0078] In some embodiments, the growth factor receptor is selected from fibroblast growth factor receptor (FGFR), insulin growth factor 1 receptor (IGF1R), and platelet-derived growth factor receptor (PDGFR).

[0079] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor further comprises an additional two or more growth factor receptors, wherein each additional growth factor receptor is selected from FGFR, IGF1R, and PDGFR.

[0080] In some embodiments, the growth factor receptor is an FGFR selected from FGFR1, FGFR2, FGFR3, and FGFR4. In some embodiments, the FGFR comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 32-49.

[0081] In some embodiments, the growth factor receptor is IGF1R. In some embodiments, the IGF1R comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 50-51.

[0082] In some embodiments, the growth factor receptor is PDGFR. In some embodiments, the PDGFR comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 52-58.

[0083] In some embodiments, the polynucleotide comprising a coding sequence of an activated downstream growth factor target comprises a growth factor receptor comprising one or more amino acid insertions, deletions, or substitutions that result in the receptor being constitutively activated.

[0084] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor comprises a regulatory sequence operably linked to the coding sequence of the growth factor receptor and/or the coding sequence of the additional growth factor receptors.

[0085] In some embodiments, the regulatory sequence comprises a promoter selected from: an inducible promoter, a tissue specific promoter, and a constitutively active promoter.

[0086] In some embodiments, the promoter is selected from EF1alpha, PGK, CMV, RSV, and β -actin.

[0087] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor comprises a sequence encoding a polycistronic mRNA, wherein the polycistronic mRNA comprises the coding sequence of the growth factor receptor and the coding sequence of the two or more additional growth factor receptors.

[0088] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor comprises one or more sequences encoding a self-cleaving peptide, one or more internal ribosome entry sites (IRES), or both.

[0089] In some embodiments, activity and/or expression of the growth factor receptors is controllable.

[0090] In some embodiments, expression of the growth factor receptor is controlled using an inducible promoter, an inducible tag, and a degradation tag.

[0091] In some embodiments, expression of the growth factor receptor is controlled using an inducible promoter. In some embodiments, the coding sequence of the growth factor receptor is operably linked to the inducible promoter. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible promoter, thereby enabling expression of the growth factor receptor.

[0092] In some embodiments, activity of the growth factor receptor is controlled using an inducible tag. In some embodiments, the polynucleotide comprising a coding sequence of a growth factor receptor further comprises a coding sequence of an inducible tag located 5' or 3' to the coding sequence of the growth factor receptor, and wherein the inducible tag and the growth factor receptor are a fusion protein. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible tag, thereby inducing activity of the growth factor receptor/fusion protein.

[0093] In some embodiments, activity of the one or more growth factor ligands is controlled using a degradation tag. In some embodiments, the polynucleotide comprising a

coding sequence of a growth factor receptor further comprises a coding sequence of a degradation tag located 5' or 3' to the coding sequence of the growth factor receptor, and wherein the degradation tag and the growth factor receptor are a fusion protein. In some embodiments, the method also includes: maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the degradation tag, thereby targeting the growth factor receptor/fusion protein for degradation.

[0094] In some embodiments, the method also includes introducing a polynucleotide sequence encoding an accessory protein.

[0095] In some embodiments, the polynucleotide comprising a coding sequence of a growth factor ligand, the polynucleotide comprising a coding sequence of a growth factor receptor, or both, further comprises a coding sequence of an accessory protein.

[0096] In some embodiments, the accessory protein is fibroblast growth factor binding protein (FGFBP). In some embodiments, the FGFBP comprises an amino acid sequence having at least 80% sequence identity to a sequence of SEQ ID NO: 59.

[0097] In some embodiments, the accessory protein is RASV12. In some embodiments, the RASV12 comprises an amino acid sequence having at least 80% sequence identity to a sequence of SEQ ID NO: 60.

[0098] In some embodiments, the method comprises introducing into the cell: (i) a polynucleotide comprising a coding sequence of FGF2, and a polynucleotide comprising a coding sequence of FGFR; (ii) a polynucleotide comprising a coding sequence of IGF1, and a polynucleotide comprising a coding sequence of IGF1R; (iii) a polynucleotide comprising a coding sequence of PDGF, and a polynucleotide comprising a coding sequence of PDGFR, or (iv) a combination selected from: (i) and (ii), (ii) and (iii), (ii) and iii), and (i), (ii), and (iii).

[0099] In another aspect, this disclosure features a myogenic cell suitable for consumption comprising cells having increased expression of FGF2, IGF1, PDGFb, FGFR, IGF1R, or PDGFR, or a combination thereof.

[0100] In another aspect, this disclosure features a population of cells suitable for consumption comprising cells having increased expression of FGF2, IGF1, PDGFb, FGFR, IGF1R, or PDGFR, or a combination thereof.

[0101] In another aspect, this disclosure features a vector comprising a polynucleotide encoding a fusion protein comprising a coding sequence of a signaling sequence and a coding

sequence of a growth factor ligand, and optionally a coding sequence of an inducible tag or a degradation tag.

[0102] In another aspect, this disclosure features a cell comprising a polynucleotide encoding a fusion protein comprising a coding sequence of a signaling sequence and a coding sequence of a growth factor ligand, and optionally a coding sequence of an inducible tag or a degradation tag.

[0103] In another aspect, this disclosure features a vector comprising a polynucleotide comprising a first coding sequence of a growth factor ligand, and a second coding sequence of growth factor receptor.

[0104] In another aspect, this disclosure features a cell comprising a polynucleotide comprising a coding sequence of a growth factor ligand or a fragment thereof, and a polynucleotide comprising a coding sequence of a growth factor receptor or a fragment thereof.

[0105] In another aspect, this disclosure features cell-based meat suitable for consumption produced using the any of the methods described herein.

5. BRIEF DESCRIPTION OF THE DRAWINGS

[0106] These and other features, aspects, and advantages of the present invention will become better understood with regard to the following description, and accompanying drawings, where:

[0107] **FIG. 1** shows illustration of three approaches to generate growth factor independent cell lines. Specific growth factors required for cell proliferation and/or tissue formation phenotypes are identified by conducting a growth factor screen and/or analysis for upregulated growth factor receptors. Growth factor-independent cell lines are generated with the following approaches: 1. Genetically engineer cells to overexpress native growth factor or growth factor variants with higher thermostability (heat stable), increased half-life, and/or enhanced secretions. 2. Genetically engineer cells to overexpress native downstream growth factor targets such as growth factor receptors or growth factor receptor variants with constitutively active signaling. 3. Genetically engineer cells to overexpression both growth factor and activated downstream target.

[0108] **FIG. 2A** shows sequence alignment of amino acid sequences for FGF2 from human, chicken, bovine, and salmon. Chicken FGF2 amino acid sequence has 91.6%, 92.9%, and 76.1% identity with human, bovine, and salmon FGF2 sequences, respectively.

[0109] **FIG. 2B** shows a sequence alignment of amino acid sequences for IGF1 (truncated) from chicken, bovine (cow), pig, and human.

[0110] **FIG. 2C** shows a sequence alignment of amino acid sequences for PDGFb from chicken, bovine, and human. Chicken PDGFb sequence has 53.5% and 53.1% identity with bovine and human sequences, respectively. Bovine and human PDGFb sequences share 90.5% identity.

[0111] **FIG. 3A** shows a schematic of a vector used for promoter selection experiments. Gene of interest is expressed from a mouse PGK promoter.

[0112] **FIG. 3B** shows a schematic of a vector used for promoter selection experiments. Gene of interest is expressed from a human EF1alpha promoter.

[0113] **FIG. 4** is a bar graph showing the fold change (RLU) in expression for the promoter analysis performed in Example 1. Chicken cells were transiently transfected (n=3) with vectors expressing nano luciferase (NLucP) under control of a mouse PGK promoter or human EF1a promoter. After 24hrs, luciferase expression was measured and depicted as relative light units (RLU). $p < 0.001(**)$.

[0114] **FIG. 5** is a bar graph showing FGF2 concentration in the supernatant after 72 hours in culture (serum-free) for cell lines expressing: mPGK-BM40-FGF2-WT and hEF1a-BM40-FGF2-WT. Abbreviations: PGK – PKG promoter, BM40 – signal peptide; FGF2 – growth factor ligand; and WT – wild type FGF2.

[0115] **FIG. 6** is bar graph showing the FGF2 concentration in the supernatant in culture medium for the various transduction conditions. X-axis nomenclature: “signal peptide-growth factor ligand” (e.g., for “GLuc-FGF2” GLuc is signal peptide fused to FGF2).

[0116] **FIG. 7** is a bar graph showing cell proliferation as fold change for each of the various transduction conditions noted on the x-axis. Top dotted line indicates fold change for a serum containing positive control (i.e., cells transduced with empty vector (EV) and cultured in serum). Bottom dotted line indicates fold change for a serum containing positive control (i.e., cells transduced with empty vector) and grown in media include 100 ng/mL FGF2. X-axis nomenclature: “signal peptide-growth factor ligand” (e.g., for “GLuc-FGF2” GLuc is signal peptide fused to FGF2).

[0117] **FIG. 8** shows representative images of control (FC550A) and FGF2-WT cells plated in serum free media not supplemented with FGF2. Images were taken 12 hours after initial seed at 4x magnification.

[0118] **FIG. 9** shows representative images of control (FC550A) and FGF2-WT cells plated in serum free media not supplemented with FGF2. Images were taken 48 hours after initial seed at 4x magnification. Arrow indicates a secondary cell population that was not attached to the plate.

[0119] **FIG. 10** is a bar graph showing Viable Cell Densities (VCD) for each of the various transduction conditions indicated on the x-axis. Top dotted line indices the VCD for a positive control (i.e., cells transduced with empty vector (EV) and cultured in media supplemented with 100 ng/mL FGF2). Bottom dotted line indicates the VCD for a negative control (i.e., cells transduced with empty vector (EV) and cultured in media not supplemented with FGF2). X-axis nomenclature: “signal peptide-growth factor ligand” (e.g., for “GLuc-FGF2” GLuc is signal peptide fused to FGF2).

[0120] **FIG. 11** is a bar graph showing Viable Cell Densities (VCD) for each of the various transduction conditions indicated on the x-axis. Dotted line indicates the seeding density of 0.4×10^6 cells/mL. X-axis nomenclature: “signal peptide-growth factor ligand” (e.g., for “GLuc-FGF2” GLuc is signal peptide fused to FGF2).

[0121] **FIG. 12** is a bar graph showing Viable Cell Densities (VCD) for each of the cell lines indicated on the x-axis: chicken FGF2, bovine FGF2, salmon FGF2, heat stable variants of FGF2 (e.g., FGF2-Q68I-N114G and FGF2-Q68I-C99S-N114G), FGF2 having a secretion tags (e.g., ggIL2-FGF2 and hIL2-co1-ggFGF2(xMet)), FGF2 variants that preserve amino acid for non-canonical secretion (FGF2-C77-Y81), and FGF2-STAB variants (STAB-C77Y81, c96-STAB-Gen2-ggFGF2, STAB-Gen3-ggFGF2, and c96-STAB-Gen3-ggFGF2). VCD data was collected on day 2 of passage 4.

[0122] **FIG. 13** is a bar graph showing percent (%) Packed Cell Volumes for each of the cell lines indicated on the x-axis: chicken FGF2, bovine FGF2, salmon FGF2, heat stable variants of FGF2 (e.g., FGF2-Q68I-N114G and FGF2-Q68I-C99S-N114G), FGF2 having a secretion tags (e.g., ggIL2-FGF2 and hIL2-co1-ggFGF2(xMet)), and FGF2 variants that preserve amino acid for non-canonical secretion (FGF2-C77-Y81). Percent packed cell volumes were assessed on day 2 of passage 5.

[0123] FIG. 14 is a bar graph of an ELISA showing FGF2 concentration in (pg/mL) in supernatants taken from the cultures indicated on the x-axis: chicken FGF2, bovine FGF2, salmon FGF2, heat stable variants of FGF2 (e.g., FGF2-Q68I-N114G and FGF2-Q68I-C99S-N114G), FGF2 having a secretion tags (e.g., ggIL2-FGF2 and hIL2-co1-ggFGF2(xMet)), and FGF2 variants that preserve amino acid for non-canonical secretion (FGF2-C77-Y81).

[0124] FIG. 15 is a bar graph of an ELISA showing Viable Cell Density (VCD) for each of the cell lines indicated on the x-axis. FGF1 receptors included: FGFR1C, FGFR1C-N546K, FGFR1C-V561M, and myrist-FGFR1C-K656E. FGF2 receptors included: FGFR2, FGFR2-N550K, FGFR2-K660E, and FGFR2-3xMuts. FGF3 receptors included: FGFR3, FGFR3-N540K, FGFR3-K560E, FGFR3-N540K-K560E, and myrist-FGF3R-K560E. FGF4 receptors included: FGF4R, FGF4R-Y367C, and FGF4R-Y367C-K654E.

[0125] FIG. 16 is a bar graph showing percent (%) Packed Cell Volumes for each of the cell lines indicated on the x-axis. FGF1 receptors included: FGFR1C, FGFR1C-N546K, FGFR1C-V561M, and myrist-FGFR1C-K656E. FGF2 receptors included: FGFR2, FGFR2-N550K, FGFR2-K660E, and FGFR2-3xMuts. FGF3 receptors included: FGFR3, FGFR3-N540K, FGFR3-K560E, FGFR3-N540K-K560E, and myrist-FGF3R-K560E. FGF4 receptors included: FGF4R, FGF4R-Y367C, and FGF4R-Y367C-K654E.

[0126] FIG. 17 is a bar graph of an ELISA showing FGF2 concentration in (pg/mL) in supernatants taken from the cultures indicated on the x-axis. FGF1 receptors included: FGFR1C, FGFR1C-N546K, FGFR1C-V561M, and myrist-FGFR1C-K656E. FGF2 receptors included: FGFR2, FGFR2-N550K, FGFR2-K660E, and FGFR2-3xMuts. FGF3 receptors included: FGFR3, FGFR3-N540K, FGFR3-K560E, FGFR3-N540K-K560E, and myrist-FGF3R-K560E. FGF4 receptors included: FGF4R, FGF4R-Y367C, and FGF4R-Y367C-K654E.

[0127] FIG. 18 is a bar graph showing viable cell density data for chicken cells engineered to express IGF1 (or variant) or IGF1 receptor (or variant).

[0128] FIG. 19 is a bar graph showing packed cell volume data for chicken cells engineered to express IGF1 (or variant) or IGF1 receptor (or variant).

[0129] FIGs. 20A-20B are line graphs showing growth curves (Viable Cell Densities (VCD)) for controls (Naïve and empty vector (EV)) and IGF1 engineered cells. Cells are grown in media supplemented with either 0µg/L IGF1 or 10µg/L IGF1. FIG. 20A shows VCD data for cells engineered to express low levels of IGF1 (IGF1^{Low}) and controls with

measurements taken every 24 hours and cells passaged on a 2-day cadence (e.g., about every 48 hours). **FIG. 20B** shows VCD data for cells engineered to express high levels of IGF1 (IGF1^{High}) and controls with measurements taken every 24 hours and cells passaged on a 2-day cadence (e.g., about every 48 hours).

[0130] **FIGs. 21A-21B** are bar graphs showing data from an IGF1 ELISA for cells engineered to express IGF1^{low} or IGF1^{high}. **FIG. 21A** shows IGF1 ELISA data for cells engineered to express IGF1^{low}. **FIG. 21B** shows IGF1 ELISA data for cells engineered to express IGF1^{high}.

[0131] **FIG. 22** are bar graphs showing doubling time (hours) data for cells engineered to express IGF1^{low}.

[0132] **FIGs. 23A-23B** are bar graphs showing Viable Cell Densities (VCD) for controls (Naïve and empty vector (EV)) and IGF1 engineered cells. Cells are grown in media supplemented with either 0µg/L IGF1 or 10µg/L IGF1. Cultures are analyzed at day 2 after the third passage. **FIG. 23A** shows VCD data for cells engineered to express low levels of IGF1 (IGF1^{Low}) and controls. **FIG. 23B** shows VCD data for cells engineered to express high levels of IGF1 (IGF1^{High}) and controls.

[0133] **FIGs. 23C-23D** are bar graphs showing Packed Cell Volumes (PCV) for controls (Naïve and empty vector (EV)) and IGF1 engineered cells. Cells are grown in media supplement with either 0µg/L IGF1 or 10µg/L IGF1. Cultures are analyzed at day 2 after the third passage. **FIG. 23C** shows PCV data for cells engineered to express low levels of IGF1 (IGF1^{Low}) and controls. **FIG. 23D** shows PCV data for cells engineered to express high levels of IGF1 (IGF1^{High}) and controls.

[0134] **FIG. 24** shows doubling time (hours) for chicken cells engineered to express IGF1 (IGF1^{low}) grown in media supplement without ("−") and with ("+") IGF1.

[0135] **FIG. 25** shows packed cell volume estimated yield (g/L) for chicken cells engineered to express IGF1 (IGF1^{low}) grown in media supplement without ("−") and with ("+") IGF1.

[0136] **FIG. 26** shows viable cell density data for chicken cells engineered to express IGF1 and a FGF2 variant (chicken (Chicken FGF2), bovine (Bovine FGF2), salmon (Salmon FGF2), heat stable variants (FGF2-Q68I-N114G, FGF2-Q68I-C99S-N114G), secretion tagged variants (ggIL2-FGF2, hIL2-co1-ggFGF2(xMet)) or variant to preserve amino acid

for non-canonical secretion (FGF2-C77Y81)). Controls grown with or without growth factors IGF1 (10ug/L) and FGF2 (100ug/L) consisted of dual empty vector (EVmRuby and EVeBFP2) that were used to construct IGF1 and FGF2 variants, respectively.

[0137] **FIG. 27** shows that viable cell density data for chicken cells engineered to express IGF1 and a FGF receptor (FGFR1c-N546K, FGFR1c-V561M, myrist-FGFR1c-K656E, FGFR3-N540K, FGFR3-K650E, FGFR3-N540K-K650E, or myrist-FGFR3-K650E). Controls grown with or without growth factors IGF1 (10ug/L) and FGF2 (100ug/L) consisted of dual empty vector (EVmRuby and EVeBFP2) that were used to construct IGF1 and FGF receptor variants, respectively.

[0138] **FIG. 28** shows that viable cell density data for chicken cells engineered to expressed FGFR2. Naïve chicken cells were used a controls.

[0139] **FIGs. 29A-29C** show viable cell density (VCD) data over 200 hours in culture. **FIG. 29A** shows VCD data for chicken cells engineered to express FGF2 from different species (chicken, bovine, and salmon). **FIG. 29B** shows VCD data for chicken cells engineered to express FGF2 variants that have amino acid substitutions that increase heat stability. **FIG. 29C** shows VCD data for chicken cells engineered to express FGF2 designed with secretion signals or variants to preserve non-canonical secretion.

[0140] **FIG. 30** show viable cell density (VCD) data summarizing **FIGs. 29A-29C**.

[0141] **FIGs. 31A-31C** show viable cell density (VCD) data over 200 hours in culture for chicken cells engineered to express the indicated FGF receptor variants. **FIG. 31A** shows VCD data for chicken cells engineered to express variants of FGFR1. **FIG. 31B** shows VCD data for chicken cells engineered to express FGFR2 variants. **FIG. 31C** shows VCD data for chicken cells engineered to express FGFR3 variants.

[0142] **FIG. 32** shows viable cell density (VCD) data) for chicken cells engineered to express the indicated FGF receptor variants. One way ANOVA performed compared to empty vector control in growth factor containing media, Not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***) $p < 0.0001$ (****).

[0143] **FIG. 33** shows Wet Mass per Area ($\mu\text{g}/\text{cm}^2$) for engineered cells and controls cultured in roller bottles over 14 day period in serum free media. Controls include Naive and empty vector (EV) cells grown with/without 50ug/L PDGF (N=4). Chicken cells were engineered to express PDGFRa-D842V, PDGF(WT) or PDGF-211*.

[0144] **FIGs. 34A-34D** show an overview diagram of growing and processing different types of cells in accordance with one or more embodiments of the present disclosure. **FIG. 34A** shows tissue collection, processing, culturing, and cryopreserving. **FIG. 34B** shows immortalizing, culturing until confluency, suspension culturing, cryopreserving, and expanding in larger culture vessels. **FIG. 34C** shows a bioreactor system. **FIG. 34D** shows a pressure apparatus that compresses cell masses.

6. DETAILED DESCRIPTION

6.1. Definitions

[0145] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art to which this disclosure belongs. In the event that there is a plurality of definitions for terms cited herein, those in this section prevail unless otherwise stated.

[0146] Throughout this disclosure, the term “a” or “an” entity refers to one or more of that entity. As such, the terms “a” (or “an”), “one or more,” and “at least one” can be used interchangeably herein. Furthermore, “and/or” as used in a phrase such as “A and/or B” herein is intended to include “A and B,” “A” (alone), and “B” (alone). Likewise, the term “and/or” as used in a phrase such as “A, B, and/or C” is intended to encompass each of the following aspects: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

[0147] As used herein, the term “accessory protein” refers to a protein that modulates the actions or downstream signaling of a growth factor ligand or a growth factor receptor. Accessory proteins can modulate the actions of growth factor ligand and/or a growth factor receptor either directly (e.g., binding/interacting directly) or indirectly.

[0148] As used herein, the terms “comprising” and “including” or grammatical variants thereof are to be taken as specifying the stated features, integers, steps, or components but do not preclude the addition of one or more additional features, integers, steps, components, or groups thereof. This term encompasses the terms “consisting of” and “consisting essentially of”.

[0149] As used herein, the terms “cell” and “cell line” are sometimes used interchangeably. As used herein, the term “cell” can refer to one or more cells originating from a cell line. As used herein, the term “cell line” can refer to a population of cells.

[0150] As used herein, the terms “cell surface” or “surface of the cell” when referring to a receptor refers to the presence of the receptor on the surface of the cell.

[0151] As used herein, the term “cultivation infrastructure” refers to the environment in which the cells, cell lines, myocytes, multinucleated myotubes, or skeletal muscle fibers are cultured.

[0152] As used herein, the term “differentiation capacity” refers to a cell’s ability to differentiate to a particular cell lineage, stem cell, progenitor cell, or terminally differentiated cell.

[0153] As used herein, the term “exogenous,” when referring to growth factors, refers to a growth factor derived from a source external to the culture and added (supplemented) to the culture medium.

[0154] As used herein, the term “fragment” or “portion” when referring to a protein or a polynucleotide refers to a protein that comprises a domain, portion, or fragment of a parent or reference protein or polypeptide. The term “portion” can be used interchangeably with the term “functional portion.” The term “fragment” can be used interchangeably with the term “functional fragment.” The terms “functional portion” or “functional fragment” refers to components that retain at least 50% activity associated with the domain, portion or fragment of the parent or reference compound, preferably at least 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, 99.9%, or 100% level of activity of the parent protein or polypeptide, or provides a biological benefit. A “functional portion” or “functional fragment” of a protein or polypeptide has “similar binding” or “similar activity” when the functional portion or fragment displays no more than a 50% reduction in performance in a selected assay as compared to the parent or reference protein or polypeptide (preferably no more than 20% or 10%, or no more than a log difference as compared to the parent or reference with regard to affinity).

[0155] As used herein, the terms “growth factor ligand” refers to a secreted biologically active molecule that can affect the growth of cells, promote or inhibit mitosis, or affect cellular differentiation.

[0156] As used herein, the term “immortalized cell” refers to cells that are passaged or modified to proliferate indefinitely and evade normal cellular senescence.

[0157] As used herein, the term “myoblast” refers to mononucleated muscle cells. They are embryonic precursors of myocytes, also called muscle cells. Although myoblasts may be classified as skeletal muscle myoblasts, smooth muscle myoblasts, and cardiac muscle myoblasts depending on the type of muscle cell that they will differentiate into, in this specification the term myoblasts refer to skeletal muscle myoblasts.

[0158] As used herein, the term “myotube” refers to elongated structures, the result of differentiated myoblast. Upon differentiation, myoblasts fuse into one or more nucleated myotubes and express skeletal muscle markers.

[0159] As used herein the term “passaged cell” refers to the number of times the cells in the culture have been subcultured. This may occur without consideration of the inoculation densities or recoveries involved.

[0160] As used herein, the term “population doubling level (PDL)” refers to the total number of times the cells in the population have doubled since their primary isolation in vitro. Mathematically this is described as $n = 3.32 (\log UCY - \log I) + X$, where n = the final PDL number at end of a given subculture, UCY = the cell yield at that point, I = the cell number used as inoculum to begin that subculture, and X = the doubling level of the inoculum used to initiate the subculture being quantitated.

[0161] As used herein, the term “substantially free of” or “substantially free from” means the amount (e.g., absolute number within a population or concentration/percentage within a population) of a cell or cell type is below a value where the cell or cell type, or any cell derived therefrom, could contribute to the population. For example, a population substantially free of a cell means that upon differentiation of the population the cell does not sustain progeny in the differentiated population. When referring to culture reagents, “substantially free of” or “substantially free from” refer to the amount (e.g., concentration) of the reagent that is below a value where the cell culture reagent does not have a biological effect on the culture (i.e., the reagent is not capable of producing a biological effect at such low concentrations).

[0162] As used herein, the term “transdifferentiation” refers to the conversion of a cell type present in one tissue or organ into a cell type from another tissue or organ without going through a pluripotent cell state. Transdifferentiation between some cell types can occur naturally. In other cases, transdifferentiation can be induced using exogenous factors including small molecules, growth factors, and/or genetic engineering.

[0163] As used herein, the terms “transformed,” “transduced,” and “transfected” are used interchangeably unless otherwise noted. Each term refers to introduction of a nucleic acid sequence or polypeptide into a cell (e.g., an immortalized cell).

[0164] Before the present invention is further described, it is to be understood that this invention is not limited to particular embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

[0165] Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit, unless the context clearly dictates otherwise, between the upper and lower limit of that range and any other stated or intervening value in that stated range, is encompassed within the invention. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges, and are also encompassed within the invention, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the invention.

[0166] It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination. All combinations of the embodiments pertaining to the invention are specifically embraced by the present invention and are disclosed herein just as if each and every combination was individually and explicitly disclosed. In addition, all sub-combinations of the various embodiments and elements thereof are also specifically embraced by the present invention and are disclosed herein just as if each and every such sub-combination was individually and explicitly disclosed herein.

6.2. Growth Factor Ligands

[0167] Provided herein are methods for introducing into a cell a polynucleotide comprising a coding sequence of a growth factor ligand (see **FIG. 1**). In some embodiments, introducing the polynucleotide comprising the coding sequence of the growth factor ligand into the cells results in the cells having reduced reliance on exogenous growth factors. In such cases, the cells are engineered to overexpress the coding sequence of the growth factor ligand. In some

embodiments, the cells are genetically engineered to have stable integration of the one or more copies of a coding sequence for a growth factor ligand. In some embodiments, the cells overexpress the coding sequence of the growth factor ligand at levels sufficient to increase production and/or secretion of the growth factor ligands into the cell culture medium. In some embodiments, the growth factor ligand is selected from basic fibroblast growth factor (FGF2), insulin-like growth factor 1 (IGF1), insulin-like growth factor 2 (IGF2), and platelet-derived growth factor (PDGF). The FGF2, IGF1, IGF2, PDGF is selected from any metazoan species.

[0168] In some embodiments, the methods provided herein include introducing a polynucleotide comprising a coding sequence of FGF2, IGF1, IGF2, PDGF, or a combination thereof. For example, the polynucleotide comprises a coding sequence of FGF2, FGF2 and IGF1, FGF2 and PDGF, IGF1 and PDGF, or FGF2, IGF1 and PDGF.

6.2.1. Fibroblast Growth Factor 2

[0169] In some embodiments, the methods provided herein include introducing into a cell a polynucleotide comprising a coding sequence of fibroblast growth factor 2 (FGF2) or a fragment thereof. As used herein, “FGF2” refers to the fibroblast growth factor 2 (Fgf2) gene or FGF2 protein, which is a member of the fibroblast growth factor (FGF) family. FGF family members bind heparin and possess broad mitogenic and angiogenic activities. FGF2: acts as a ligand for FGFR1, FGFR2, FGFR3 and FGFR4; acts as an integrin ligand which is required for FGF2 signaling; binds to integrin ITGAV:ITGB3; plays an important role in the regulation of cell survival, cell division, cell differentiation and cell migration; functions as a potent mitogen in vitro; induces angiogenesis; and mediates phosphorylation of ERK1/2.

[0170] In some embodiments, the cells are modified to overexpress the coding sequence of an FGF2 protein. In some embodiments, the cells are genetically modified and carry stable integrations of one or more copies of an FGF2 coding sequence. In some embodiments, the cells overexpress the coding sequence of FGF2 protein at levels sufficient to increase production and/or secretion of FGF2 into the cell culture medium.

[0171] In some embodiments, the FGF2 coding sequence is selected from any metazoan species. In some embodiments, the FGF2 coding sequence is from any animal, such as vertebrate and invertebrate animal species. In some embodiments, the FGF2 coding sequence is from any vertebrate animal species such as mammals, reptiles, birds, amphibians, and the like. In some embodiments, the FGF2 coding sequence is from any mammalian species such

as a human, murine, bovine, porcine, poultry, and the like. In some embodiments, the coding sequence of the FGF2 protein is derived from a species selected from any metazoan species, including without limitation, *Gallus gallus*, *Bos taurus*, *Sus scrofa*, *Meleagris gallopavo*, *Anas platyrhynchos*, *Salmo salar*, *Thunnus thynnus*, *Ovis aries*, *Coturnix*, *Copra aegagrus hircus*, or *Homarus americanus*.

[0172] In some embodiments, increasing expression of FGF2 may be achieved using different approaches. In some embodiments, the expression is inducible. In some embodiments, the method comprises expressing polynucleotides comprising the coding sequence of FGF2. In some embodiments, the polynucleotides are ectopically expressed from constructs that are introduced into the cells, for example expressed from a plasmid, or other expression vector. In some embodiments, the constructs are integrated into the cell's genome, and the expression is driven in that manner (e.g., PhiC31 Integration Systems). In some embodiments, the expression of the FGF2 gene involves electroporating a DNA, delivering a DNA complexed with a transfection vehicle, using a viral vector (e.g. retrovirus, lentivirus, adenovirus, adeno-associated virus), and the like, or combinations thereof. In some embodiments, the expression is constitutive. In some embodiments, the expression is conditional (e.g. inducible).

[0173] In the methods described herein, a polynucleotide comprising a coding sequence of FGF2 may encode any homolog of FGF2, including FGF2 paralogs, such as FGF1, FGF3, FGF5, FGF9, and FGF16, or any other FGF2 paralogs, or an FGF2 protein translated from any splice variants of an FGF2 gene, or may comprise any mutations in the FGF2 gene sequence including, but not limited to nucleotide deletions, truncations, fusions, or substitutions. Mutations may be synthetic or naturally occurring.

[0174] In some embodiments, FGF2 refers to the *Fgf2* gene or FGF2 protein, or fragment or variant thereof (e.g., a FGF2 protein having one or more (e.g., one, two, three, four, five, six, seven, eight, nine, ten, or more amino acid substitutions, deletions or insertions as compared to a wild type FGF2 protein)). FIG. 2A shows a sequence alignment for FGF2 from chicken, bovine and human. In some embodiments, FGF2 refers to a sequence listed in FIG. 2A.

[0175] In some embodiments, a FGF2 protein comprises an amino acid sequence having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence identity to a

sequence selected from SEQ ID NOs: 1-15. In some embodiments, the FGF protein sequence comprises an amino acid sequence selected from SEQ ID NOs: 1-15.

[0176] In some embodiments, the FGF2 protein is a wild type (WT) chicken FGF2 (SEQ ID NO: 1). In some embodiments, the FGF2 is a stabilized version of wild type chicken FGF2 (SEQ ID NO: 2). In such embodiments, the FGF2 comprises one or more amino acid substitutions engineered to impart increased thermostability on the FGF2 protein (i.e., increase half-life in the culture medium). In some embodiments, a thermostable FGF2 is referred to as a STAB FGF2. In some embodiments, the one or more amino acid substitutions are selected from R31L, V52T, E54D, H59F, L92Y, S94I, C96N, S109E, T121P as compared to SEQ ID NO: 1.

[0177] In some embodiments, introducing the polynucleotide comprising the coding sequence of the FGF2 protein alone is not sufficient to confer reduced reliance on exogenous growth factors. In such embodiments, one or more additional growth factor ligands can be introduced into the cell line. For example, a polynucleotide comprising the coding sequence of a IGF1 protein or a PDGF protein can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In other embodiments, a polynucleotide comprising a coding sequence of a growth factor receptor can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In such embodiments, the growth factor receptor can be selected from a FGF2R, an IGF-1R, and a PDGFR. For example, in order to confer reduced reliance on exogenous growth factors on the cell line, a polynucleotide comprising a coding sequence of a growth factor ligand (e.g., FGF2) or a fragment thereof; and a polynucleotide comprising a coding sequence of a growth factor receptor (e.g., FGFR) are introduced into the cell line.

6.2.2. Insulin Growth Factor 1

[0178] In some embodiments, the methods provided herein include introducing into a cell a polynucleotide comprising a coding sequence of Insulin-like growth factor 1 (IGF1) or a fragment thereof. As used herein, "IGF1" refers to the insulin-like growth factor 1 (Igf1) gene or IGF1 protein that is gene similar to insulin in function and is a member of a family of proteins involved in mediating growth and development. Without wishing to be bound by theory, IGF1 acts as a ligand for insulin-like growth factor 1 receptor (IGF1R). IGF-1 binds to the alpha subunit of IGF1R, leading to the activation of the intrinsic tyrosine kinase activity which autophosphorylates tyrosine residues in the beta subunit thus initiating a

cascade of down-stream signaling events leading to activation of the PI3K-AKT/PKB and the Ras-MAPK pathways. IGF1 can bind to integrins ITGA5:ITGB3 and ITGA6:ITGB4. Its binding to integrins and subsequent ternary complex formation with integrins and IGFR1 are important for IGF1 signaling. IGF1 induces the phosphorylation and activation of IGFR1, MAPK3/ERK1, MAPK1/ERK2 and AKT1.

[0179] In some embodiments, the cells are modified to overexpress the coding sequence of an IGF1 protein. In some embodiments, the cells are genetically modified and carry stable integrations of one or more copies of an IGF1 coding sequence. In some embodiments, the cells overexpress the coding sequence of IGF1 protein at levels sufficient to increase production and/or secretion of IGF1 into the cell culture medium.

[0180] In some embodiments, the IGF1 coding sequence is selected from any metazoan species. In some embodiments, the IGF1 coding sequence is from any animal, such as vertebrate and invertebrate animal species. In some embodiments, the IGF1 coding sequence is from any vertebrate animal species such as mammals, reptiles, birds, amphibians, and the like. In some embodiments, the IGF1 coding sequence is from any mammalian species such as a human, murine, bovine, porcine, poultry, and the like. In some embodiments, the coding sequence of the IGF1 protein is derived from a species selected from any metazoan species, including without limitation, *Gallus gallus*, *Bos taurus*, *Sus scrofa*, *Meleagris gallopavo*, *Anas platyrhynchos*, *Salmo salar*, *Thunnus thynnus*, *Ovis aries*, *Coturnix coturnix*, *Copra aegagrus hircus*, or *Homarus americanus*.

[0181] In some embodiments, increasing expression of IGF1 may be achieved using different approaches. In some embodiments, the expression is inducible. In some embodiments, the method comprises expressing polynucleotides comprising the coding sequence of IGF1. In some embodiments, the polynucleotides are ectopically expressed from constructs that are introduced into the cells, for example expressed from a plasmid, or other expression vector. In some embodiments, the constructs are integrated into the cell's genome, and the expression is driven in that manner (e.g., PhiC31 Integration Systems). In some embodiments, the expression of the IGF1 gene involves electroporating a DNA, delivering a DNA complexed with a transfection vehicle, using a viral vector (e.g. retrovirus, lentivirus, adenovirus, adeno-associated virus), and the like, or combinations thereof. In some embodiments, the expression is constitutive. In some embodiments, the expression is conditional (e.g. inducible).

[0182] In the methods described herein, a polynucleotide comprising a coding sequence of IGF1 may encode any homolog of IGF1, including IGF1 paralogs, such as IGF2, INS, and INS-IGF2, or any other IGF1 paralogs, or an IGF1 protein translated from any splice variants of an IGF1 gene, or may comprise any mutations in the IGF1 gene sequence including, but not limited to nucleotide deletions, truncations, fusions, or substitutions. Mutations may be synthetic or naturally occurring.

[0183] In some embodiments, IGF1 refers to the Igf1 gene or IGF1 protein, or fragment or variant thereof (e.g., a IGF1 protein having one or more (e.g., one, two, three, four, five, six, seven, eight, nine, ten, or more amino acid substitutions, deletions or insertions as compared to a wild type IGF1 protein)). FIG. 2B shows a sequence alignment for IGF1 from chicken, bovine, pig and human. In some embodiments, IGF1 refers to a sequence listed in FIG. 2B.

[0184] In some embodiments, an IGF1 protein comprises an amino acid sequence having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence identity to a sequence selected from SEQ ID NO: 16 or 17. In some embodiments, the FGF protein sequence comprises an amino acid sequence selected from SEQ ID NO: 16 or 17.

[0185] In some embodiments, introducing the polynucleotide comprising the coding sequence of the IGF-1 protein alone is not sufficient to confer reduced reliance on exogenous growth factors. In such embodiments, one or more additional growth factor ligands can be introduced into the cell line. For example, a polynucleotide comprising the coding sequence of a FGF2 protein or a PDGF protein can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In other embodiments, a polynucleotide (e.g., a second polynucleotide) comprising a coding sequence of a growth factor receptor can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In such embodiments, the growth factor receptor can be selected from a FGF2R, a IGF1R, and a PDGFR. For example, in order to confer reduced reliance on exogenous growth factors on the cell line, a polynucleotide comprising a coding sequence of a growth factor ligand (e.g., IGF1) or a fragment thereof; and a polynucleotide comprising a coding sequence of a growth factor receptor (e.g., IGF-1R) are introduced into the cell line.

6.2.3. Platelet Derived Growth Factor

[0186] In some embodiments, the methods provided herein include introducing into a cell a polynucleotide comprising a coding sequence of platelet derived growth factor (PDGF) or a fragment thereof. The PDGF family consists of PDGF-A, -B, -C and -D, which form either

homo- or heterodimers (PDGF-AA, -AB, -BB, -CC, -DD). In some embodiments, the PDGF is PDGFA. In some embodiments, the PDGF is a PDGFB. In some embodiments, the PDGF is a PDGFC. In some embodiments, the PDGF is a PDGFD. As used herein, “PDGFb” refers to the platelet derived growth factor subunit b (Pdgfb) gene or PDGFb protein of the family comprised of both platelet-derived growth factors (PDGF) and vascular endothelial growth factors (VEGF). The encoded preproprotein is proteolytically processed to generate platelet-derived growth factor subunit B, which can homodimerize, or alternatively, heterodimerize with the related platelet-derived growth factor subunit A. PDGFb can bind and activate PDGF receptor tyrosine kinases, which play a role in a wide range of developmental processes, angiogenesis, cell proliferation, and differentiation. PDGFb plays an essential role in the regulation of embryonic development, cell proliferation, cell migration, survival and chemotaxis. PDGFb is also a potent mitogen for cells of mesenchymal origin; required for normal proliferation and recruitment of pericytes and vascular smooth muscle cells in the central nervous system, skin, lung, heart and placenta; is required for normal blood vessel development, and for normal development of kidney glomeruli; plays an important role in wound healing.

[0187] In some embodiments, the cells are modified to overexpress the coding sequence of an PDGFb protein. In some embodiments, the cells are genetically modified and carry stable integrations of one or more copies of an PDGFb coding sequence. In some embodiments, the cells overexpress the coding sequence of PDGFb protein at levels sufficient to increase production and/or secretion of PDGFb into the cell culture medium.

[0188] In some embodiments, the PDGFb coding sequence is selected from any metazoan species. In some embodiments, the PDGFb coding sequence is from any animal, such as vertebrate and invertebrate animal species. In some embodiments, the PDGFb coding sequence is from any vertebrate animal species such as mammals, reptiles, birds, amphibians, and the like. In some embodiments, the PDGFb coding sequence is from any mammalian species such as a human, murine, bovine, porcine, poultry, and the like. In some embodiments, the coding sequence of the PDGFb protein is derived from a species selected from any metazoan species, including without limitation, *Gallus gallus*, *Bos taurus*, *Sus scrofa*, *Meleagris gallopavo*, *Anas platyrhynchos*, *Salmo salar*, *Thunnus thynnus*, *Ovis aries*, *Coturnix coturnix*, *Copra aegagrus hircus*, or *Homarus americanus*.

[0189] In some embodiments, increasing expression of PDGFb may be achieved using different approaches. In some embodiments, the expression is inducible. In some

embodiments, the method comprises expressing polynucleotides comprising the coding sequence of PDGFb. In some embodiments, the polynucleotides are ectopically expressed from constructs that are introduced into the cells, for example expressed from a plasmid, or other expression vector. In some embodiments, the constructs are integrated into the cell's genome, and the expression is driven in that manner (e.g., PhiC31 Integration Systems). In some embodiments, the expression of the PDGFb gene involves electroporating a DNA, delivering a DNA complexed with a transfection vehicle, using a viral vector (e.g. retrovirus, lentivirus, adenovirus, adeno-associated virus, and the like, or combinations thereof. In some embodiments, the expression is constitutive. In some embodiments, the expression is conditional (e.g. inducible).

[0190] In the methods described herein, a polynucleotide comprising a coding sequence of PDGFb may encode any homolog of PDGFb, including PDGFb paralogs, such as PDGFa, or any other PDGFb paralogs, or an PDGFb protein translated from any splice variants of an PDGFb gene, or may comprise any mutations in the PDGFb gene sequence including, but not limited to nucleotide deletions, truncations, fusions, or substitutions. Mutations may be synthetic or naturally occurring.

[0191] In some embodiments, PDGFB refers to the Pdgfb gene or PDGFB protein, or fragment or variant thereof (e.g., a PDGFB protein having one or more (e.g., one, two, three, four, five, six, seven, eight, nine, ten, or more amino acid substitutions, deletions or insertions as compared to a wild type PDGFB polypeptide)). FIG. 2C shows a sequence alignment for PDGFb from chicken, bovine, and human. In some embodiments, PDGFb refers to a sequence listed in FIG. 2C.

[0192] In some embodiments, a PDGFb protein comprises an amino acid sequence having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence identity to a sequence selected from SEQ ID NOs: 18-21. In some embodiments, the PDGFb protein sequence comprises an amino acid sequence selected from SEQ ID NOs: 18-21.

[0193] In some embodiments, introducing the polynucleotide comprising the coding sequence of the PDGFb protein alone is not sufficient to confer reduced reliance on exogenous growth factors on the cell line. In such embodiments, one or more additional growth factor ligands can be introduced into the cell line. For example, a polynucleotide comprising the coding sequence of a FGF2 protein or an IGF-1 protein can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In other

embodiments, a polynucleotide comprising a coding sequence of a growth factor receptor can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In such embodiments, the growth factor receptor can be selected from a FGF2R, an IGF1R, and a PDGFR. For example, in order to confer reduced reliance on exogenous growth factors on the cell line, a polynucleotide comprising a coding sequence of a growth factor ligand (e.g., PDGFb) or a fragment thereof; and a polynucleotide comprising a coding sequence of a growth factor receptor (e.g., PDGFR) are introduced into the cell line.

6.3. Growth Factor Receptors and Activated Downstream Targets

[0194] Provided herein are methods for introducing into a cell a polynucleotide comprising a coding sequence of a growth factor receptor and/or an activated downstream growth factor target. In some embodiments, introducing the polynucleotide comprising the coding sequence of the growth factor receptor (and/or an activated downstream growth factor target) into the cells results in the cells having reduced reliance on exogenous growth factors.

[0195] In some embodiments, the growth factor receptor is selected from fibroblast growth factor receptor (FGFR), insulin growth factor 1 receptor (IGF1R), and platelet-derived growth factor receptor (PDGFR). In some embodiments, the method include introducing an additional two or more growth factor receptors into the cell, wherein each additional growth factor receptor is selected from FGFR, IGF1R, and PDGFR.

[0196] In some embodiments, the methods provided herein include introducing into a cell a polynucleotide comprising a coding sequence of a growth factor ligand and a polynucleotide comprising a coding sequence of a growth factor receptor. In such cases, the cells are engineered to overexpress the coding sequence of the growth factor ligand, the growth factor receptor, or both. In some embodiments, the growth factor ligand and the growth factor receptor are components of the same signaling axis, for example, FGF2 and FGF1/2/3/4; IGF1 and IGF1R; or PDGFb and PDGFR. In such cases, the overexpressing the growth factor ligand and growth factor receptor results in a synergistic effect on the results described herein. Without wishing to be bound by theory, overexpressing both a growth factor ligand and a growth factor receptor enables a cell (or population of cells) to circumvent feedback mechanisms used by the cell to regulate signaling, thereby driving continued signaling within a cell. For example, the cell (or population of cells) can circumvent the feedback loop by expressing and secreting more growth factor ligands, expressing more receptors at the surface of the cell, or by expressing constitutively active receptors.

[0197] In some embodiments, the cells are engineered to overexpress the coding sequence of the growth factor receptor. In some embodiments, the cells are genetically engineered to have stable integration of the one or more copies of a coding sequence for a growth factor receptor. In some embodiments, the cells overexpress the coding sequence of the growth factor receptor at levels sufficient to reduce reliance on exogenous growth factors.

[0198] In some embodiments, introducing the polynucleotide comprising the coding sequence of the activated downstream growth factor target into the cells results in the cells having reduced reliance on exogenous growth factors. In some embodiments, the activated downstream growth factor target comprises a growth factor receptor comprising one or more amino acid insertions, deletions, or substitutions that result in the receptor being constitutively activated. In some embodiments, the activated downstream growth factor target includes a mutation in the intracellular portion or the growth factor receptor that triggers a signaling cascade (e.g., a phosphorylation cascade). In some embodiments, the activated downstream growth factor target comprises a gene and/or target associated with FGF signaling, IGF1 signaling, or PDGF signaling.

6.3.1. Fibroblast Growth Factor Receptor

[0199] In some embodiments, the methods provided herein include introducing into a cell a polynucleotide comprising a coding sequence of fibroblast growth factor receptor (FGFR). As used herein, the term “FGFR” refers to fibroblast growth factor receptor (Fgfr) gene or FGFR protein that is a family where amino acid sequence is highly conserved between members and throughout evolution. FGFR family members differ from one another in their ligand affinities and tissue distribution. The extracellular portion of the protein interacts with fibroblast growth factors, setting in motion a cascade of downstream signals, ultimately influencing mitogenesis and differentiation. The FGFR family include from FGFR1, FGFR2, FGFR3, and FGFR4.

[0200] In some embodiments, the cells are modified to overexpress the coding sequence of an FGFR. In some embodiments, the cells are genetically modified and carry stable integrations of one or more copies of an FGFR coding sequence. In some embodiments, the cells overexpress the coding sequence of FGFR protein at levels sufficient to increase expression of FGFR at the surface of the cell.

[0201] In some embodiments, the FGFR coding sequence is selected from any metazoan species. In some embodiments, the FGFR coding sequence is from any animal, such as

vertebrate and invertebrate animal species. In some embodiments, the FGFR coding sequence is from any vertebrate animal species such as mammals, reptiles, birds, amphibians, and the like. In some embodiments, the FGFR coding sequence is from any mammalian species such as a human, murine, bovine, porcine, poultry, and the like. In some embodiments, the coding sequence of the FGFR is derived from a species selected from any metazoan species, including without limitation, *Gallus gallus*, *Bos taurus*, *Sus scrofa*, *Meleagris gallopavo*, *Anas platyrhynchos*, *Salmo salar*, *Thunnus thynnus*, *Ovis aries*, *Coturnix coturnix*, *Copra aegagrus hircus*, or *Homarus americanus*.

[0202] In some embodiments, increasing expression of FGFR may be achieved using different approaches. In some embodiments, the expression is inducible. In some embodiments, the method comprises expressing polynucleotides comprising the coding sequence of FGFR. In some embodiments, the polynucleotides are ectopically expressed from constructs that are introduced into the cells, for example expressed from a plasmid, or other expression vector. In some embodiments, the constructs are integrated into the cell's genome, and the expression is driven in that manner (e.g., PhiC31 Integration Systems). In some embodiments, the expression of the FGFR gene involves electroporating a DNA, delivering a DNA complexed with a transfection vehicle, using a viral vector (e.g. retrovirus, lentivirus, adenovirus, adeno-associated virus), and the like, or combinations thereof. In some embodiments, the expression is constitutive. In some embodiments, the expression is conditional (e.g. inducible).

[0203] In some embodiments, a polynucleotide comprising a coding sequence of FGFR may encode any homolog of FGFR, including FGFR paralogs, such as FGFR1, FGFR2, FGFR3, and FGFR4, or any other FGFR paralogs, or an FGFR protein translated from any splice variants of an FGFR gene, or may comprise any mutations in the FGFR gene sequence including, but not limited to nucleotide deletions, truncations, fusions, or substitutions. Mutations may be synthetic or naturally occurring.

[0204] In some embodiments, FGFR refers to the FGFR protein, or fragment or variant thereof (e.g., a FGFR protein having one or more (e.g., one, two, three, four, five, six, seven, eight, nine, ten, or more amino acid substitutions, deletions or insertions as compared to a wild type FGFR protein)).

[0205] In some embodiments, a FGFR protein comprises an amino acid sequence having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence identity to a

sequence selected from SEQ ID NOs: 32-49. In some embodiments, the FGFR protein sequence comprises an amino acid sequence selected from SEQ ID NOs: 32-49.

[0206] In some embodiments, introducing the polynucleotide comprising the coding sequence of the FGFR protein alone is not sufficient to confer reduced reliance on exogenous growth factors on the cell line. In such embodiments, one or more additional growth factor receptors can be introduced into the cell line. For example, a polynucleotide comprising the coding sequence of a PDGFR protein or an IGF-1R protein can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In other embodiments, a polynucleotide comprising a coding sequence of a growth factor ligand can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In such embodiments, the growth factor ligand can be selected from FGF2, IGF-1, and PDGF. For example, in order to confer reduced reliance on exogenous growth factors on the cell line, a polynucleotide sequence comprising a coding sequence of a growth factor receptor (e.g., FGFR) or a fragment thereof, and a polynucleotide comprising a coding sequence of a growth factor ligand (e.g., FGF2) are introduced into the cell line.

6.3.2. Insulin Growth Factor Receptor

[0207] In some embodiments, the methods provide herein include introducing into a cell a polynucleotide comprising a coding sequence of insulin-like growth factor receptor (IGFR). In some embodiments, the IGFR is an insulin like growth factor -1 receptor (IGF1R). As used herein, “IGFR1” refers to the insulin-like growth factor receptor (Igfr1) gene or IGF1R belonging to the class of tyrosine kinase receptors. IGF1R mediates the effects of IGF1, which is a polypeptide protein hormone similar in molecular structure to insulin.

[0208] In some embodiments, the cells are modified to overexpress the coding sequence of an IGF1R protein. In some embodiments, the cells are genetically modified and carry stable integrations of one or more copies of an IGF1R coding sequence. In some embodiments, the cells overexpress the coding sequence of IGF1R protein at levels sufficient to increase expression of IGF1R at the surface of the cell.

[0209] In some embodiments, the IGF1R coding sequence is selected from any metazoan species. In some embodiments, the IGF1R coding sequence is from any animal, such as vertebrate and invertebrate animal species. In some embodiments, the IGF1R coding sequence is from any vertebrate animal species such as mammals, reptiles, birds, amphibians, and the like. In some embodiments, the IGF1R coding sequence is from any mammalian

species such as a human, murine, bovine, porcine, poultry, and the like. In some embodiments, the coding sequence of the IGF1R protein is derived from a species selected from any metazoan species, including without limitation, *Gallus gallus*, *Bos taurus*, *Sus scrofa*, *Meleagris gallopavo*, *Anas platyrhynchos*, *Salmo salar*, *Thunnus thynnus*, *Ovis aries*, *Coturnix coturnix*, *Copra aegagrus hircus*, or *Homarus americanus*.

[0210] In some embodiments, increasing expression of IGF1R may be achieved using different approaches. In some embodiments, the expression is inducible. In some embodiments, the method comprises expressing polynucleotides comprising the coding sequence of IGF1R. In some embodiments, the polynucleotides are ectopically expressed from constructs that are introduced into the cells, for example expressed from a plasmid, or other expression vector. In some embodiments, the constructs are integrated into the cell's genome, and the expression is driven in that manner (e.g., PhiC31 Integration Systems). In some embodiments, the expression of the IGF1R gene involves electroporating a DNA, delivering a DNA complexed with a transfection vehicle, using a viral vector (e.g. retrovirus, lentivirus, adenovirus, adeno-associated virus), and the like, or combinations thereof. In some embodiments, the expression is constitutive. In some embodiments, the expression is conditional (e.g. inducible).

[0211] In the methods described herein, a polynucleotide comprising a coding sequence of IGFR may encode any homolog of IGF1R, including IGF1R paralogs, such as IGF1R, INSR, INSR, ROS1, ERBB4, EPHA, or any other IGF1R paralogs, or an IGF1R protein translated from any splice variants of an IGF1 gene, or may comprise any mutations in the IGF1R gene sequence including, but not limited to nucleotide deletions, truncations, fusions, or substitutions. Mutations may be synthetic or naturally occurring.

[0212] In some embodiments, IGF1R refers to the IGF1R protein, or fragment or variant thereof (e.g., a IGF1R protein having one or more (e.g., one, two, three, four, five, six, seven, eight, nine, ten, or more amino acid substitutions, deletions or insertions as compared to a wild type IGF1R protein)).

[0213] In some embodiments, a IGF1R protein comprises an amino acid sequence having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence identity to a sequence selected from SEQ ID NOs: 50-51. In some embodiments, the IGF1R protein sequence comprises an amino acid sequence selected from SEQ ID NOs: 50-51.

[0214] In some embodiments, introducing the polynucleotide comprising the coding sequence of the IGF1R protein alone is not sufficient to confer reduced reliance on exogenous growth factors on the cell line. In such embodiments, one or more additional growth factor receptors can be introduced into the cell line. For example, a polynucleotide comprising the coding sequence of a FGFR protein or an PDGFR protein can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In other embodiments, a polynucleotide comprising a coding sequence of a growth factor ligand can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In such embodiments, the growth factor ligand can be selected from FGF2, IGF1, and PDGF. For example, in order to confer reduced reliance on exogenous growth factors on the cell line, a polynucleotide sequence comprising a coding sequence of a growth factor receptor (e.g., IGF1R) or a fragment thereof; and a polynucleotide comprising a coding sequence of a growth factor ligand (e.g., IGF1) are introduced into the cell line.

6.3.3. Platelet Derived Growth Factor Receptor

[0215] In some embodiments, the methods provide herein include introducing into a cell a polynucleotide comprising a coding sequence of platelet derived growth factor receptor (PDGFR). As used herein, "PDGFR" refers to the platelet derived growth factor receptor (Pdgfr) gene or PDGFR protein of the protein family comprised of both platelet-derived growth factors (PDGF) and vascular endothelial growth factors (VEGF). PDGFRs are catalytic receptors that have intracellular tyrosine kinase activity. PDGFR have roles in the regulation of many biological processes including embryonic development, angiogenesis, cell proliferation and differentiation.

[0216] In some embodiments, the cells are modified to overexpress the coding sequence of an PDGFR protein. In some embodiments, the cells are genetically modified and carry stable integrations of one or more copies of an PDGFR coding sequence. In some embodiments, the cells overexpress the coding sequence of PDGFR protein at levels sufficient to increase expression of FGFR at the surface of the cell.

[0217] In some embodiments, the PDGFR coding sequence is selected from any metazoan species. In some embodiments, the PDGFR coding sequence is from any animal, such as vertebrate and invertebrate animal species. In some embodiments, the PDGFR coding sequence is from any vertebrate animal species such as mammals, reptiles, birds, amphibians, and the like. In some embodiments, the PDGFR coding sequence is from any mammalian

species such as a human, murine, bovine, porcine, poultry, and the like. In some embodiments, the coding sequence of the PDGFR protein is derived from a species selected from any metazoan species, including without limitation, *Gallus gallus*, *Bos taurus*, *Sus scrofa*, *Meleagris gallopavo*, *Anas platyrhynchos*, *Salmo salar*, *Thunnus thynnus*, *Ovis aries*, *Coturnix coturnix*, *Copra aegagrus hircus*, or *Homarus americanus*.

[0218] In some embodiments, increasing expression of PDGFR may be achieved using different approaches. In some embodiments, the expression is inducible. In some embodiments, the method comprises expressing polynucleotides comprising the coding sequence of PDGFR. In some embodiments, the polynucleotides are ectopically expressed from constructs that are introduced into the cells, for example expressed from a plasmid, or other expression vector. In some embodiments, the constructs are integrated into the cell's genome, and the expression is driven in that manner (e.g., PhiC31 Integration Systems). In some embodiments, the expression of the PDGFR gene involves electroporating a DNA, delivering a DNA complexed with a transfection vehicle, using a viral vector (e.g. retrovirus, lentivirus, adenovirus, adeno-associated virus), and the like, or combinations thereof. In some embodiments, the expression is constitutive. In some embodiments, the expression is conditional (e.g. inducible).

[0219] In the methods described herein, a polynucleotide comprising a coding sequence of PDGFR may encode any homolog of PDGFR, including PDGFR paralogs, such as PDGFRA and PDGFRB, or any other PDGFR paralogs, or an PDGFR protein translated from any splice variants of an PDGFR gene, or may comprise any mutations in the PDGFR gene sequence including, but not limited to nucleotide deletions, truncations, fusions, or substitutions. Mutations may be synthetic or naturally occurring.

[0220] In some embodiments, PDGFR refers to the PDGFR protein, or fragment or variant thereof (e.g., a PDGFR protein having one or more (e.g., one, two, three, four, five, six, seven, eight, nine, ten, or more amino acid substitutions, deletions or insertions as compared to a wild type PDGFR protein)).

[0221] In some embodiments, a PDGFR protein comprises an amino acid sequence having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence identity to a sequence selected from SEQ ID NOs: 52-58. In some embodiments, the PDGFR protein sequence comprises an amino acid sequence selected from SEQ ID NOs: 52-58.

[0222] In some embodiments, introducing the polynucleotide comprising the coding sequence of the PDGFRB protein alone is not sufficient to confer reduced reliance on exogenous growth factors on the cell line. In such embodiments, one or more additional growth factor receptors can be introduced into the cell line. For example, a polynucleotide comprising the coding sequence of a FGFR protein or an IGF1R protein can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In other embodiments, a polynucleotide comprising a coding sequence of a growth factor ligand can be introduced into the cell line to help confer reduced reliance on exogenous growth factors. In such embodiments, the growth factor ligand can be selected from FGF2, IGF1, and PDGF. For example, in order to confer reduced reliance on exogenous growth factors on the cell line, a polynucleotide sequence comprising a coding sequence of a growth factor receptor (e.g., PDGFRB) or a fragment thereof; and a polynucleotide comprising a coding sequence of a growth factor ligand (e.g., PDGF) are introduced into the cell line.

6.4. Accessory Proteins

[0223] In some embodiments, the methods provided herein include introducing into a cell a polynucleotide comprising a coding sequence of an accessory protein.

6.4.1. Fibroblast Growth Factor Binding Protein

[0224] In some embodiments, accessory protein refers to a fibroblast growth factor binding protein (FGFBP). As used herein, “FGFBP” refers to the fibroblast growth factor binding protein (Fgfbp) gene or FGFBP protein, which belongs to a family of fibroblast growth factor carrier proteins. Family members include, without limitation, FGFBP1, FGFBP2, and FGFBP3. FGFBPs play a role in cell proliferation, differentiation and migration by binding to fibroblast growth factors and potentiating their biological effects on target cells.

[0225] In some embodiments, the FGFBP is FGFBP1 or a fragment thereof. In some embodiments, FGFBP1 enhances FGF2 signaling.

[0226] In some embodiments, FGFBP1 refers to the Fgfbp1 gene or FGFBP1 protein, or fragment or variant thereof (e.g., a FGFBP1 protein having one or more (e.g., one, two, three, four, five, six, seven, eight, nine, ten, or more amino acid substitutions, deletions or insertions as compared to a wild type FGFBP1 polypeptide)).

[0227] In some embodiments, a FGFBP1 protein comprises an amino acid sequence having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence

identity to a sequence selected from SEQ ID NOs: 59. In some embodiments, the FGFBP1 protein sequence comprises an amino acid sequence selected from SEQ ID NOs: 59.

6.4.2. RASV12

[0228] In some embodiments, accessory protein refers to a H-RasV12 or RASV12. As used herein, “RASV12” refers to the H-RasV12 protein or RASV12 protein. RASV12 is involved in the activation of Ras protein signal transduction and binds GDP/GTP and possess intrinsic GTPase activity.

[0229] In some embodiments, RASV12 refers to the RASV12 protein, or fragment or variant thereof (e.g., a RASV12 protein having one or more (e.g., one, two, three, four, five, six, seven, eight, nine, ten, or more amino acid substitutions, deletions or insertions as compared to a wild type RASH or RASV12 polypeptide)).

[0230] In some embodiments, a RASV12 protein comprises an amino acid sequence having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence identity to a sequence selected from SEQ ID NOs: 60. In some embodiments, the RASV12 protein sequence comprises an amino acid sequence selected from SEQ ID NOs: 60.

6.5. Signal Peptides

[0231] In some embodiments, the methods provided herein include introducing into a cell a polynucleotide comprising a coding sequence of a growth factor ligand, where the growth factor ligand is fused to a signal peptide. In some embodiments, the polynucleotide includes a sequence encoding a signal peptide located 5' to the coding sequence of the growth factor ligand, and wherein the signal sequence and the growth factor ligand are a fusion protein. In some embodiments, the polynucleotide includes a sequence encoding a signal peptide located 3' to the coding sequence of the growth factor ligand, and wherein the signal sequence and the growth factor ligand are a fusion protein. Non-limiting examples of signal peptides having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence identity to a sequence selected from SEQ ID NOs: 22-31.

6.6. Method for Increasing Concentration of a Growth Factor in Culture Medium

[0232] Provided herein are methods of increasing the concentration of a growth factor ligand in culture medium of cells in culture where the method includes introducing one or more of a coding sequence of any of the growth factor ligands described herein, a coding sequence of any of the growth factor receptors described herein, a coding sequence of any of

the activated downstream growth factors described herein, a coding sequence of any of the accessory proteins described herein, or a combination thereof, into the cell line; and culturing the cell line in a cultivation infrastructure.

[0233] In some embodiments, introducing a polynucleotide comprising a coding sequence of FGF2 into a cell line and culturing the cells in a cultivating infrastructure results in an increase of FGF2 in the medium of the cells in culture.

[0234] In some embodiments, the concentration of FGF2 in the culture medium is increased by at least 0.00001 ng/mL, (e.g., at least 0.000025 ng/mL, at least 0.000075 ng/mL, by at least 0.0005 ng/mL, at least 0.001 ng/mL, at least 0.005 ng/mL, at least 0.01 ng/mL, at least 0.05 ng/mL, at least 0.1 ng/mL, at least 0.5 ng/mL, at least 1.0 ng/mL, at least 2.5 ng/mL, at least 5.0 ng/mL, at least 7.5 ng/mL, at least 10 ng/mL, at least 15 ng/mL, at least 20 ng/mL, at least 25 ng/mL, at least 30 ng/mL, at least 40 ng/mL, at least 50 ng/mL, at least 60 ng/mL, at least 70 ng/mL, at least 80 ng/mL, at least 90 ng/mL, at least 100 ng/mL, at least 150 ng/mL, at least 200 ng/mL, at least 200 ng/mL, at least 250 ng/mL, at least 300 ng/mL, at least 350 ng/mL, at least 400 ng/mL, at least 450 ng/mL, at least 500 ng/mL, at least 550 ng/mL, at least 600 ng/mL, at least 650 ng/mL, at least 700 ng/mL, at least 750 ng/mL, at least 800 ng/mL, at least 850 ng/mL, at least 900 ng/mL, at least 950 ng/mL, or at least 1000 ng/mL) as compared to a cell line not engineered to include a polynucleotide comprising a coding sequence of FGF2.

[0235] In some embodiments, the concentration of FGF2 in the culture medium is increased by at least 0.01% (e.g., at least 0.05%, at least 0.1%, at least 0.5%, at least 1.0%, at least 1.5%, at least 2.0%, at least 2.5%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, 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 100%, at least 150%, at least 200%, at least 250%, at least 300%, at least 350%, at least 400%, at least 450%, at least 500%, at least 550%, at least 600%, at least 650%, at least 700%, at least 750%, at least 800%, at least 850%, at least 900%, at least 950%, at least 1000%, at least 1,100%, at least 1,200%, at least 1,300%, at least 1,400%, at least 1,500%, at least 1,600%, at least 1,700%, at least 1,800%, at least 1,900%, at least 2,000%, at least 2,250%, at least 2,500%, at least 2,750%, at least 3,000%, at least 3,500%, at least 4,000%, at least 4,500%, at least 5,000%, at least 6,000%, at least 7,000%, at least 8,000%, at least 9,000%, or at least 10,000%) as compared to a cell line not engineered to include a polynucleotide encoding FGF2.

[0236] In some embodiments, introducing a polynucleotide comprising a coding sequence of IGF1 into a cell line and culturing the cells in a cultivating infrastructure results in an increase of IGF1 in the medium of the cells in culture.

[0237] In some embodiments, the concentration of IGF1 in the culture medium is increased by at least 0.00001 ng/mL, (e.g., at least 0.000025 ng/mL, at least 0.000075 ng/mL, at least 0.0005 ng/mL, at least 0.001 ng/mL, at least 0.005 ng/mL, at least 0.01 ng/mL, at least 0.05 ng/mL, at least 0.1 ng/mL, at least 0.5 ng/mL, at least 1.0 ng/mL, at least 2.5 ng/mL, at least 5.0 ng/mL, at least 7.5 ng/mL, at least 10 ng/mL, at least 15 ng/mL, at least 20 ng/mL, at least 25 ng/mL, at least 30 ng/mL, at least 40 ng/mL, at least 50 ng/mL, at least 60 ng/mL, at least 70 ng/mL, at least 80 ng/mL, at least 90 ng/mL, at least 100 ng/mL, at least 150 ng/mL, at least 200 ng/mL, at least 200 ng/mL, at least 250 ng/mL, at least 300 ng/mL, at least 350 ng/mL, at least 400 ng/mL, at least 450 ng/mL, at least 500 ng/mL, at least 550 ng/mL, at least 600 ng/mL, at least 650 ng/mL, at least 700 ng/mL, at least 750 ng/mL, at least 800 ng/mL, at least 850 ng/mL, at least 900 ng/mL, at least 950 ng/mL, or at least 1000 ng/mL) as compared to a cell line not engineered to include a polynucleotide encoding IGF-1.

[0238] In some embodiments, the concentration of IGF1 in the culture medium is increased by at least 0.01% (e.g., at least 0.05%, at least 0.1%, at least 0.5%, at least 1.0%, at least 1.5%, at least 2.0%, at least 2.5%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, 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 100%, at least 150%, at least 200%, at least 250%, at least 300%, at least 350%, at least 400%, at least 450%, at least 500%, at least 550%, at least 600%, at least 650%, at least 700%, at least 750%, at least 800%, at least 850%, at least 900%, at least 950%, at least 1000%, at least 1,100%, at least 1,200%, at least 1,300%, at least 1,400%, at least 1,500%, at least 1,600%, at least 1,700%, at least 1,800%, at least 1,900%, at least 2,000%, at least 2,250%, at least 2,500%, at least 2,750%, at least 3,000%, at least 3,500%, at least 4,000%, at least 4,500%, at least 5,000%, at least 6,000%, at least 7,000%, at least 8,000%, at least 9,000%, or by at least 10,000%) as compared to a cell line not engineered to include a polynucleotide encoding IGF1.

[0239] In some embodiments, introducing a polynucleotide comprising a coding sequence of PDGFb into a cell line and culturing the cells in a cultivating infrastructure results in an increase of PDGFb in the medium of the cells in culture.

[0240] In some embodiments, the concentration of PDGFb in the culture medium is increased by at least 0.00001 ng/mL, (e.g., at least 0.000025 ng/mL, at least 0.000075 ng/mL, at least 0.0005 ng/mL, at least 0.001 ng/mL, at least 0.005 ng/mL, at least 0.01 ng/mL, at least 0.05 ng/mL, at least 0.1 ng/mL, at least 0.5 ng/mL, at least 1.0 ng/mL, at least 2.5 ng/mL, at least 5.0 ng/mL, at least 7.5 ng/mL, at least 10 ng/mL, at least 15 ng/mL, at least 20 ng/mL, at least 25 ng/mL, at least 30 ng/mL, at least 40 ng/mL, at least 50 ng/mL, at least 60 ng/mL, at least 70 ng/mL, at least 80 ng/mL, at least 90 ng/mL, at least 100 ng/mL, at least 150 ng/mL, at least 200 ng/mL, at least 200 ng/mL, at least 250 ng/mL, at least 300 ng/mL, at least 350 ng/mL, at least 400 ng/mL, at least 450 ng/mL, at least 500 ng/mL, at least 550 ng/mL, at least 600 ng/mL, at least 650 ng/mL, at least 700 ng/mL, at least 750 ng/mL, at least 800 ng/mL, at least 850 ng/mL, at least 900 ng/mL, at least 950 ng/mL, or at least 1000 ng/mL) as compared to a cell line not engineered to include a polynucleotide encoding PDGFb.

[0241]) In some embodiments, the concentration of PDGFb in the culture medium is increased by at least 0.01% (e.g., at least 0.05%, at least 0.1%, at least 0.5%, at least 1.0%, at least 1.5%, at least 2.0%, at least 2.5%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, 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 100%, at least 150%, at least 200%, at least 250%, at least 300%, at least 350%, at least 400%, at least 450%, at least 500%, at least 550%, at least 600%, at least 650%, at least 700%, at least 750%, at least 800%, at least 850%, at least 900%, at least 950%, at least 1000%, at least 1,100%, at least 1,200%, at least 1,300%, at least 1,400%, at least 1,500%, at least 1,600%, at least 1,700%, at least 1,800%, at least 1,900%, at least 2,000%, at least 2,250%, at least 2,500%, at least 2,750%, at least 3,000%, at least 3,500%, at least 4,000%, at least 4,500%, at least 5,000%, at least 6,000%, at least 7,000%, at least 8,000%, at least 9,000%, or at least 10,000%) as compared to a cell line not engineered to include a polynucleotide encoding PDGFb.

[0242] The methods of the present disclosure advantageously enable selection of transfected cells using only the absence of growth factors, thereby obviating the need for antibiotic and cre-lox selection protocols, which are less desirable when creating a food product since they are not recognized as generally acceptable for consumption.

6.7. Method of Increasing Cell Density

[0243] Provided herein are methods of increasing the cell density of a culture where the method includes introducing one or more of a coding sequence of any of the growth factor ligands described herein, a coding sequence of any of the growth factor receptors described herein, a coding sequence of any of the activated downstream growth factor targets described herein, a coding sequence of any of the accessory proteins described herein, or a combination thereof, into the cell line; and culturing the cell line in a cultivation infrastructure.

[0244] In some embodiments, an increase in the cell density of a culture (e.g., suspension culture) using the methods described herein is about 1.025 fold, 1.05 fold, 1.10-fold, 1.15-fold, 1.20-fold, 1.25-fold, 1.30 fold, 1.35-fold, 1.40-fold, 1.45-fold, 1.5-fold, 2-fold, 2.5-fold, 3-fold, 3.5-fold, 4-fold, 4.5-fold, 5-fold, 7.5-fold, 10-fold, 15-fold, 20-fold, 25-fold, 30-fold, 40-fold, or even about 50-fold, 75-fold, 100-fold, 150-fold, or about 200-fold, compared to the density of a culture comprising cells that do not include a coding sequence of any of the growth factor ligands described herein, a coding sequence of any of the growth factor receptors described herein, a coding sequence of any of the accessory proteins described herein, or a combination thereof.

[0245] In some embodiments, an increase in the density of cells in a culture (e.g., suspension culture) using the methods described herein is at least 10%, at least 15%, at least 20%, at least 25%, 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 100%, at least 150%, at least 200%, at least 250%, at least 300%, at least 350%, at least 400%, at least 450%, at least 500%, at least 550%, at least 600%, at least 650%, at least 700%, at least 750%, at least 800%, at least 850%, at least 900%, at least 950%, at least 1000%, compared to the density of a culture comprising cells that do not include a coding sequence of any of the growth factor ligands described herein, a coding sequence of any of the growth factor receptors described herein, a coding sequence of any of the accessory proteins described herein, or a combination thereof.

[0246] In some embodiments, methods described herein increase the density of cells in a culture (e.g., suspension culture) by increasing the rate of proliferation of cells in the culture. In some embodiments, the increase in the rate of cell proliferation is at least 2.5%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, 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 100%, at least 150%, at least 200%, at least 250%, at least 300%, at least 350%, at least 400%, at least 450%, at least 500%, at least 550%, at least 600%, at least 650%, at least 700%, at least 750%, at least 800%, at least 850%, at least 900%, at least 950%, or at least 1000%), including values and ranges therebetween, compared to the density of a culture comprising cells that do not include a coding sequence of any of the growth factor ligands described herein, a coding sequence of any of the growth factor receptors described herein, a coding sequence of any of the accessory proteins described herein, or a combination thereof. In some embodiments, the increase in the rate of cell proliferation is about 25-1000%, about 25-750%, about 25-500%, about 50-1000%, about 50-750%, about 50-500%, about 100-1000%, about 100-750%, or about 100-500%, including values and ranges therebetween, compared to the density of a culture comprising cells that do not include a coding sequence of any of the growth factor ligands described herein, a coding sequence of any of the growth factor receptors described herein, a coding sequence of any of the accessory proteins described herein, or a combination thereof.

[0247] In some embodiments, methods described herein increase the cell density of a culture (e.g., suspension culture) by decreasing cell death within the cellular biomass. In some embodiments, the decrease in cell death is at least 2.5%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, 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 100%), including values and ranges therebetween, compared to the density of a culture comprising cells that do not include a coding sequence of any of the growth factor ligands described herein, a coding sequence of any of the growth factor receptors described herein, a coding sequence of any of the accessory proteins described herein, or a combination thereof. In some embodiments, a decrease in the rate of cell death within the cellular biomass is about 2.5-10%, about 2.5-75%, about 2.5-50%, about 5.0-100%, about 5.0-75%, about 5.0-50%, about 10-100%, about 10-75%, or about 10-50%, including values and ranges therebetween, compared to the density of a culture comprising cells that do not include a coding sequence of any of the growth factor ligands described herein, a coding sequence of any of the growth factor receptors described herein, a coding sequence of any of the accessory proteins described herein, or a combination thereof.

[0248] In some embodiments, using the methods described herein, the density of cells in a culture may reach about 1E4 cells/mL, about 1E5 cells/mL, about 1E6 cells/mL, about 1E7 cells/mL, about 1E8 cells/mL, about 1E9 cells/mL, about 1E10 cells/mL, about 1E11 cells/mL, about 1E12 cells/mL, or about 1E13 cells/mL (cells in suspension culture or cells in the cellular biomass/mL of cultivation infrastructure), including values and ranges therebetween.

[0249] In some embodiments, using the methods described herein, the density of cells in a culture (e.g., suspension culture) may reach about 1 g/L, 5 g/L, 10 g/L, 25 g/L, 50 g/L, 75 g/L, 100 g/L, 150 g/L, 200 g/L, 250 g/L, 300 g/L, 350 g/L, 400 g/L, 450 g/L, 500 g/L, 550 g/L, 600 g/L, 650 g/L, 700 g/L, 750 g/L, 800 g/L, 850 g/L, 900 g/L, or 1000 g/L (g of cellular biomass/L of cultivation infrastructure), including values and ranges therebetween. In some embodiments, the density of cells in a culture (e.g., suspension culture) may range from about 1 g/L to about 5 g/L, about 1 g/L to about 750 g/L, about 1 g/L to about 500 g/L, about 1 g/L to about 250 g/L, about 1 g/L to about 100 g/L, about 1 g/L to about 50 g/L, about 5 g/L to about 1000 g/L, about 5 g/L to about 750 g/L, about 5 g/L to about 500 g/L, about 5 g/L to about 250 g/L, about 5 g/L to about 100 g/L, about 5 g/L to about 50 g/L, about 25 g/L to about 1000 g/L, about 25 g/L to about 750 g/L, about 25 g/L to about 500 g/L, about 25 g/L to about 300 g/L, about 25 g/L to about 250 g/L, about 25 g/L to about 100 g/L, about 50 g/L to about 1000 g/L, about 50 g/L to about 750 g/L, about 50 g/L to about 500 g/L, about 50 g/L to about 300 g/L, about 50 g/L to about 250 g/L, about 100 g/L to 1000 g/L, about 100 g/L to about 750 g/L, about 100 g/L to about 500 g/L, about 200 g/L to about 1000 g/L, about 200 g/L to about 750 g/L, about 200 g/L to about 500 g/L, about 300 g/L to about 1000 g/L, about 300 g/L to about 800 g/L, about 400 g/L to about 1000 g/L, or about 500 g/L to about 1000 g/L including values and ranges therebetween.

6.8. Method for Improving Anchorage Independent Growth

[0250] Provided herein are methods of improving anchorage independent growth in a cell line where the method includes introducing a coding sequence of any of the growth factor ligands described herein, a coding sequence of any of the growth factor receptors described herein, a coding sequence of any of the accessory protein described herein, or a combination thereof, into the cell line; and culturing the cell line in a cultivation infrastructure.

[0251] In some embodiments, a cell line's ability to grow as a non-adherent, anchorage independent cell line can be modulated by culturing the cell line with FGF2 and/or IGF1

growth factors. In some embodiments, introducing a polynucleotide comprising a coding sequence of FGF2 and/or IGF1 into a cell line results in a cell line with at least a portion of the cell line having anchorage independent growth. In some embodiments, introducing a polynucleotide comprising a coding sequence of an FGFR and/or an IGFR results in a cell line with at least a portion of the cell line having anchorage independent growth.

[0252] In some embodiments, introducing a polynucleotide comprising a coding sequence of FGF2 or a fragment thereof and/or a coding sequence of IGF1 or a fragment thereof results in an increase in the rate of cell proliferation and decrease in cell death, which promotes the cell line (e.g., an adherent cell line) to transition to a non-adherent form (e.g., a non-adherent cell line). In some embodiments, an increase in the rate of cell proliferation and decrease in cell death promotes transition to anchorage-independent growth from anchorage-dependent growth.

[0253] In some embodiments, increase in the rate of cell proliferation is at least 2.5%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, 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 100%, at least 150%, at least 200%, at least 250%, at least 300%, at least 350%, at least 400%, at least 450%, at least 500%, at least 550%, at least 600%, at least 650%, at least 700%, at least 750%, at least 800%, at least 850%, at least 900%, at least 950%, at least 1000%, including values and ranges therebetween, compared to a cell line not including a polynucleotide comprising a coding sequence of FGF2 and/or a coding sequence of IGF1. In some embodiments, the increase in the rate of cell proliferation is about 25-1000%, about 25-750%, about 25-500%, about 50-1000%, about 50-750%, about 50-500%, about 100-1000%, about 100-750%, or about 100-500%, including values and ranges therebetween, compared to a cell line not including a polynucleotide comprising a coding sequence of FGF2 and/or a coding sequence of IGF1.

[0254] In some embodiments, the methods provided herein that include introducing a polynucleotide comprising a coding sequence of FGF2 or a fragment thereof and/or a coding sequence of IGF1 or a fragment thereof into a cell line promote anchorage-independent growth of the cell line by decreasing cell-to-cell contact inhibition. In some embodiments, the decrease in contact inhibition provided by the present methods is about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%, including values and ranges therebetween,

compared to a cell line not including a polynucleotide comprising a coding sequence of FGF2 or a coding sequence of IGF1.

[0255] In some embodiments, the methods provided herein that include introducing a polynucleotide comprising a coding sequence of FGF2 or a fragment thereof and/or a coding sequence of IGF1 or a fragment thereof into a cell line promote anchorage-independent growth of the cell line by decreasing cell death. In some embodiments, the decrease in cell death provided by the present methods is about 2.5%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%, including values and ranges therebetween, compared to a cell line not including a polynucleotide comprising a coding sequence of FGF2 or a coding sequence of IGF1.

[0256] In some embodiments, introducing a polynucleotide comprising a coding sequence of FGFR or a fragment thereof or a coding sequence of an IGF1R or a fragment thereof results in an increase in the rate of cell proliferation and decrease in cell death, which promotes cell line (e.g., an adherent cell line) to transition to a non-adherent form (e.g., a non-adherent cell line). In some embodiments, an increase in the rate of cell proliferation and decrease in cell death promotes transition to anchorage-independent growth from anchorage-dependent growth.

[0257] In some embodiments, increase in the rate of cell proliferation is at least 2.5%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, 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 100%, at least 150%, at least 200%, at least 250%, at least 300%, at least 350%, at least 400%, at least 450%, at least 500%, at least 550%, at least 600%, at least 650%, at least 700%, at least 750%, at least 800%, at least 850%, at least 900%, at least 950%, at least 1000%, including values and ranges therebetween, compared to a cell line not including a polynucleotide comprising a coding sequence of IGF1. In some embodiments, the increase in the rate of cell proliferation is about 25-1000%, about 25-750%, about 25-500%, about 50-1000%, about 50-750%, about 50-500%, about 100-1000%, about 100-750%, or about 100-500%, including values and ranges therebetween, compared to a cell line not including a polynucleotide comprising a coding sequence of FGFR or a coding sequence of IGF1R.

[0258] In some embodiments, the methods provided herein that include introducing a polynucleotide comprising a coding sequence of FGFR or a fragment thereof or a coding

sequence of an IGFR or a fragment thereof into a cell line promote anchorage-independent growth of the cell line by decreasing cell-to-cell contact inhibition. In some embodiments, the decrease in contact inhibition provided by the present methods is about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%, including values and ranges therebetween, compared to a cell line not including a polynucleotide comprising a coding sequence of FGFR or a coding sequence of IGF1R.

[0259] In some embodiments, the methods provided herein that include introducing a polynucleotide comprising a coding sequence of FGFR or a fragment thereof or a coding sequence of an IGFR or a fragment thereof into a cell line promote anchorage-independent growth of the cell line by decreasing cell death. In some embodiments, the decrease in cell death provided by the present methods is about 2.5%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100%, including values and ranges therebetween, compared to a cell line not including a polynucleotide comprising a coding sequence of FGFR or a coding sequence IGF1R.

6.9. Methods for Producing Cell-Based Meat Suitable for Consumption

[0260] Provided herein are in vitro methods for producing cell-based meat suitable for consumption, comprising: (a) introducing into a cell line one or more of a polynucleotide comprising a coding sequence of a growth factor ligand or a fragment thereof, a polynucleotide comprising a coding sequence of a growth factor receptor, a polynucleotide comprising a coding sequence of an activated downstream growth factor target; (b) inducing myogenic specific differentiation, wherein the differentiated cells form myotubes and multinucleated myotubes; (c) culturing the myocytes and myotubes to generate skeletal muscle fibers, thereby producing a cell-based meat suitable for consumption. In some embodiments, the in vitro method for producing cell-based meat suitable for consumption includes a step of adapting the cells to be grown in suspension. In some embodiments, the in vitro method for producing cell-based meat suitable for consumption includes a step of culturing the cells in a cultivation infrastructure.

[0261] In some embodiments, provided herein is cell-based meat suitable for consumption produced by the in vitro methods described herein.

[0262] In some embodiments, the in vitro method for producing cell-based meat suitable for consumption includes maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling an inducible promoter, thereby enabling

expression of the growth factor ligand (e.g., any of the growth factor ligands described herein), growth factor receptor (e.g., any of the growth factor receptors described herein), or a combination thereof, at specified times during the in vitro method. In some embodiments of the in vitro method, the engineered cell line is maintained in culture medium comprising a molecule capable of controlling an inducible promoter prior, contemporaneously with, or after the step of inducing myogenic specific differentiation. In some embodiments of the in vitro method, the engineered cell line is maintained in culture medium comprising a molecule capable of controlling an inducible promoter prior to the step of inducing myogenic specific differentiation. In such cases, the expression of the growth factor ligand, growth factor receptor, or a combination thereof, can be decreased or eliminated prior to the inducing of myogenic specific differentiation.

[0263] In some embodiments, the in vitro method for producing cell-based meat suitable for consumption includes maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible tag, thereby inducing activity of the growth factor ligand/fusion protein (e.g., any of the growth factor ligands described herein), growth factor receptor/fusion protein (e.g., any of the growth factor receptors described herein), or a combination thereof, at specified times during the in vitro method. In some embodiments of the in vitro method, the engineered cell line is maintained in culture medium comprising a molecule capable of controlling an inducible tag prior, contemporaneously with, or after the step of inducing myogenic specific differentiation. In some embodiments of the in vitro method, the engineered cell line is maintained in culture medium comprising a molecule capable of controlling an inducible tag prior to the step of inducing myogenic specific differentiation. In such cases, the activity of the growth factor ligand, growth factor receptor, or a combination thereof, can be reduced or inhibited prior to the inducing of myogenic specific differentiation.

[0264] In some embodiments, the in vitro method for producing cell-based meat suitable for consumption includes maintaining the engineered cell line in a culture medium comprising a molecule controlling the degradation tag, thereby targeting the growth factor ligand/fusion protein (e.g., any of the growth factor ligands described herein), growth factor receptor/fusion protein (e.g., any of the growth factor receptors described herein), or a combination thereof, for degradation at specific times during the in vitro method. In some embodiments of the in vitro method, the engineered cell line is maintained in culture medium comprising a molecule capable of controlling a degradation tag prior, contemporaneously

with, or after the step of inducing myogenic specific differentiation. In some embodiments of the in vitro method, the engineered cell line is maintained in culture medium comprising a molecule capable of controlling a degradation tag contemporaneously with or after the step of inducing myogenic specific differentiation. In such cases, the activity of the growth factor ligand, growth factor receptor, or combination thereof, can be reduced or inhibited in the same step as or shortly after beginning the inducing of myogenic specific differentiation.

[0265] In some embodiments, the cell line is from a livestock, poultry, game or aquatic animal species. In some embodiments, the cell line is from a chicken, duck, or turkey. In some embodiments, the cell line is from a fish. In some embodiments, the cell line is from a livestock species. In some embodiments, the livestock species is porcine or bovine. In some embodiments, the cells are from any animal species intended for human or non-human dietary consumption. In some embodiments, the cells are myogenic cells. In some embodiments, the myogenic cells are myoblasts, myocytes, satellite cells, side population cells, muscle derived stem cells, mesenchymal stem cells, myogenic pericytes, or mesoangioblasts. In some embodiments, the cells are non-myogenic cells.

[0266] Non-limiting examples of myogenic differentiation are as described in WO2019014652A1 and WO2015066377A1, both of which are herein incorporated by reference in their entireties.

[0267] In some embodiments, the myogenic cells and/or skeletal muscle produced according to the methods described herein can be processed as a raw, uncooked food product (cultured meat) or as a cooked food product or as a cooked/uncooked food ingredient. In some embodiments, processing comprises withdrawal of the culture medium that supports the viability, survival, growth or expansion (e.g., increase in total protein content of the non-naturally occurring myogenic cells) and differentiation of the myogenic cells. Withdrawal may comprise physical removal of the culture medium or altering the composition of the culture medium, for example, by addition of components that would reduce or prevent further expansion and/or differentiation of the cell line or cells-derived from the cell line or by depletion of components that support expansion and/or differentiation of the cell line or cells derived from the cell line.

6.9.1. Inducible Promoter, Inducible Tag, and Degradation Tag

[0268] In some embodiments, activity and/or expression of the growth factor ligand (e.g., any of the growth factor ligands described herein), growth factor receptor (e.g., any of the

growth factor receptors described herein), or a combination thereof, is controllable. In some embodiments, control of the activity and/or expression of the growth factor ligand, growth factor receptor, or a combination thereof, is controlled using an inducible promoter, an inducible tag, and/or a degradation tag.

[0269] In some embodiments, expression of a growth factor ligand or a fragment thereof, growth factor receptor or a fragment thereof, or a combination thereof, is controlled using an inducible promoter where expression is induced in the presence of a molecule capable of inducing the inducible promoter. In some embodiments, the promoter is a positive inducible promoter (e.g., addition of a controllable molecule induces binding to the promoter thereby activating transcription). In some embodiments, the promoter is a negative inducible promoter (e.g., addition of a controllable molecule removes a repressor from the promoter thereby allowing transcriptional machinery to bind and activate transcription). Inducible promoters include, without limitation, chemically inducible promoters (e.g., tetracycline inducible (tetracycline response elements (TRE)/tetracycline activator), cumate inducible (cumate operator (CuO)/cumate activator), alcohol inducible (AlcA promoter/AlcR activator), and steroid-inducible (e.g., LexA promoter/XVE (synthetic) activator)); temperature inducible promoters (e.g., heat shock inducible (e.g., hsp70, hsp90), and light inducible promoters (e.g., FixK2 promoter/blue-light sensing protein YFI; Vivid (VVD)/light oxygen voltage (LOV)).

[0270] In some embodiments, the coding sequence of the growth factor ligand or a fragment thereof, growth factor receptor or a fragment thereof, or both are operably linked to the inducible promoter. To induce expression of the growth factor ligand, the growth factor receptor, or a combination thereof, the engineered cell line is maintained in a culture medium comprising a molecule capable of controlling the inducible promoter.

[0271] In some embodiments, activity of a growth factor ligand or a fragment thereof, a growth factor receptor or a fragment thereof, or a combination thereof, is controlled using an inducible tag where activity of the growth factor ligand and/or growth factor receptor is controlled by the presence or absence of a molecule capable of controlling the inducible tag. In such embodiments, the polynucleotide includes a coding sequence of an inducible tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the inducible tag and the growth factor ligand are a fusion protein. In such cases, the inducible tag prevents growth factor ligand activity in the absence of the controllable molecule. To enable activity of the growth factor ligand, the engineered cell line is

maintained in a culture medium comprising a molecule capable of controlling the inducible tag, thereby controlling the activity of the fusion protein.

[0272] In some embodiments, the inducible tag is a ESR1 ligand binding domain that is activated in the presence of the ESR1 agonist (e.g., 17- β Estradiol (E2)), thereby allowing the growth factor ligand to bind to its receptor and facilitate downstream signaling. In some embodiments, the inducible tag is an estrogen receptor binding domain that is activated in the presence of tamoxifen, thereby allowing the growth factor ligand to bind to its receptor and facilitate downstream signaling.

[0273] In some embodiments, the activity of a growth factor ligand or a fragment thereof, a growth factor receptor or a fragment thereof, or a combination thereof, is controlled using a degradation tag, where activity of the growth factor ligand and/or growth factor receptor is controlled by the presence or absence of a molecule capable of controlling the degradation tag. In some embodiments, the polynucleotide includes a coding sequence of the degradation tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the degradation tag and the growth factor ligand are a fusion protein. In such cases, the degradation tag targets the growth factor ligand for degradation upon addition of a molecule capable of controlling the degradation tag to the culture medium.

[0274] Non-limiting examples of degradation tags include: Anchor away (e.g., the FKBP12-rapamycin-binding-domain of FRAP (FRB) is fused to a specific protein of interest, while the FKBP12 is fused to the anchor protein, rapamycin bridges between the POI and the anchor protein, allowing functional inhibition of the target protein); auxin-inducible degron system; and dTag system (i.e., three major components: an FKBP12F36V-fused protein of interest, a small synthetic molecule, a defined degrader, and the endogenous E3 ligase complex).

6.10. Cultivation Infrastructure

[0275] In some embodiments, a cultivation infrastructure may be a tube, a cylinder, a flask, a petri-dish, a multi-well plate, a dish, a vat, a roller bottle, an incubator, a bioreactor, an industrial fermenter and the like.

[0276] In some embodiments, a cultivation infrastructure can be of any scale, and support any volume of cellular biomass and culturing reagents. In some embodiments, the cultivation infrastructure ranges from about 10 μ L to about 100,000 L. In some embodiments, the cultivation infrastructure is about 10 μ L, about 100 μ L, about 1 mL, about 10 mL, about 100

mL, about 1 L, about 10 L, about 100 L, about 1000 L, about 10,000 L, or even about 100,000 L.

[0277] In some embodiments, the cultivation infrastructure comprises a substrate. In some embodiments, a cultivation infrastructure may comprise a permeable substrate (e.g. permeable to physiological solutions) or an impermeable substrate (e.g. impermeable to physiological solutions).

[0278] In some embodiments, the cultivation infrastructure comprises a primary substrate, which can be a flat, concave, or convex substrate. In some embodiments, the cultivation infrastructure further comprises a secondary substrate, either introduced, or autologous, to direct cellular growth between the substrates, e.g. to direct attachment, proliferation and hypertrophy of cells on a plane perpendicular to the primary substrate.

[0279] In some embodiments, the cultivation infrastructure comprises a hydrogel, a liquid cell culture media, or soft agar.

[0280] In some embodiments, the cultivation infrastructure does not comprise a substrate to which cells can adhere. In some embodiments, the cultivation infrastructure comprises a suspension culture, e.g. supporting the growth of a self-adhering biomass, or single-cell suspension in a liquid medium.

[0281] In some embodiments, the cultivation infrastructure comprises adherent cells (i.e. those cells that adhere to a substrate). In some embodiments, the cultivation infrastructure comprises non-adherent cells (i.e. those cells that do not adhere to a substrate). In some embodiments, the cultivation infrastructure comprises both adherent and non-adherent cells.

6.11. Immortalization

[0282] In some embodiments, the method provided herein include a cell line immortalized prior, contemporaneously therewith, or after introducing into the cell any of the polynucleotides described herein.

[0283] In some embodiments, immortalization comprises transforming a cell with a telomerase reverse transcriptase (TERT) gene. As used herein, "TERT" refers to telomerase reverse transcriptase (TERT) gene or TERT polypeptide that is a ribonucleoprotein polymerase that maintains telomere ends by addition of the telomere repeat TTAGGG. Telomerase expression plays a role in cellular senescence, as it is normally repressed in postnatal somatic cells resulting in progressive shortening of telomeres. In some

embodiments, cells ectopically express the TERT polynucleotide. In some embodiments, the cells are genetically modified and carry stable integrations of one or more copies of the TERT polynucleotide. Exemplary methods for immortalizing a cell line are as described in WO2019014652A1, which is herein incorporated by reference in its entirety.

[0284] In some embodiments, increased expression of TERT may be achieved using different approaches. In some embodiments, increased expression of TERT may be achieved by ectopically expressing TERT. In some embodiments, increased expression of TERT may be achieved by introducing targeted mutations in the TERT promoter. In some embodiments, increased expression of TERT may be achieved by activating endogenous TERT expression by an engineered transcriptional activator. In some embodiments, increased expression of TERT may be achieved by transiently transfecting TERT mRNA.

[0285] The polynucleotide encoding TERT can be from any organism. The TERT polynucleotide can be from bacteria, plants, fungi, and archaea. The TERT polynucleotide can be from any animal, such as vertebrate and invertebrate animal species. The TERT polynucleotide can be from any vertebrate animal species such as mammals, reptiles, birds, amphibians, and the like. The TERT polynucleotide can be from any mammalian species, such as a human, murine, bovine, porcine, and the like.

[0286] In some embodiments, immortalization comprises transforming a cell with a polynucleotide encoding a cyclin- dependent kinase 4 (“CDK4”) protein. In some embodiments, immortalization comprises inactivating a gene encoding an inhibitor of cyclin- dependent kinase 4 (CDK4). Exemplary methods for immortalizing a cell line are as described in WO2017124100A1, which is herein incorporated by reference in its entirety.

6.12. Nucleic Acids/Vectors

[0287] Also provided herein are polynucleotides comprising coding sequences of any of the growth factor ligands described herein, any of the growth factor receptors described herein, any of the accessory proteins described herein, or a combination thereof.

[0288] Also provided herein is a construct (i.e., a vector) that includes any of the polynucleotides described herein. In some embodiments, any of the vectors described herein can be an expression vector. In some embodiments, an expression vector can include one or more promoter sequences (e.g., any of the promoter sequences described herein) operably linked to a coding sequence of any of the growth factor ligands described herein, any of the growth factor receptors described herein, any of the accessory proteins described herein, or a

combination thereof. Non-limiting examples of vectors include plasmids, transposons, cosmids, and viral vectors (e.g., any adenoviral vectors (e.g., pSV or pCMV vectors), adeno-associated virus (AAV) vectors, lentivirus vectors, and retroviral vectors), and any Gateway® vectors. In some embodiments, a vector includes sufficient cis-acting elements that supplement expression where the remaining elements needed for expression can be supplied by the host cell (e.g., the cell line).

[0289] In some embodiments, a vector includes a polynucleotide comprising a coding sequence of a single growth factor ligand or fragment thereof. In some embodiments, a vector includes a polynucleotide comprising a first coding sequence of a first growth factor ligand and a second coding sequence of a second growth factor ligand. In some embodiments, a vector (e.g., a construct) includes a polynucleotide comprising a first coding sequence of a first growth factor ligand, a second coding sequence of a second growth factor ligand, and a third coding sequence of a third growth factor ligand. In such embodiments where the construct includes coding sequences for two or more growth factor ligands, each of the two or more coding sequences are operably linked to a promoter sequence or to another coding sequence via a self-cleaving polypeptide or IRES. As used herein, the term “operably linked” is well known in the art and refers to genetic components that are combined such that they carry out their normal functions. For example, a coding sequence is operably linked to a promoter when its transcription is under the control of the promoter. In another example, a coding sequence can be operably linked to other coding sequences by a self-cleaving 2A polypeptide or an internal ribosome entry site (IRES). In such cases, the self-cleaving 2A polypeptide allows the second coding sequence to be under the control of the promoter operably linked to the first coding sequence. In some cases, the coding sequences described herein can be operably linked to any other coding sequence described herein using a self-cleaving 2A polypeptide or IRES.

[0290] In some embodiments, a vector includes a polynucleotide comprising a coding sequence of a single growth factor receptor or fragment thereof. In some embodiments, a vector includes a polynucleotide comprising a first coding sequence of a first growth factor receptor and a second coding sequence of a second growth factor receptor. In some embodiments, a vector (e.g., a construct) includes a polynucleotide comprising a first coding sequence of a first growth factor receptor, a second coding sequence of a second growth factor receptor, and a third coding sequence of a third growth factor receptor. In such embodiments where the construct includes coding sequences for two or more growth factor

receptors, each of the two or more coding sequences are operably linked to a promoter sequence or to another coding sequence via a self-cleaving polypeptide or IRES. In another example, a coding sequence can be operably linked to other coding sequences by a self-cleaving 2A polypeptide or an internal ribosome entry site (IRES). In such cases, the self-cleaving 2A polypeptide allows the second coding sequence to be under the control of the promoter operably linked to the first coding sequence. In some cases, the coding sequences described herein can be operably linked to any other coding sequence described herein using a self-cleaving 2A polypeptide or IRES.

[0291] In some embodiments, a single construct comprises a coding sequence of FGF2 or a fragment thereof, and a coding sequence of any of the FGFR described herein or a fragment thereof, and includes a self-cleaving 2A polypeptide or an IRES to operably link the coding sequences. In some embodiments, a single construct comprises a coding sequence of IGF1 or a fragment thereof, and a coding sequence of IGF1R or a fragment thereof, and includes a self-cleaving 2A polypeptide or an IRES to operably link the coding sequences. In some embodiments, a single construct comprises a coding sequence of PDGF or a fragment thereof, and a coding sequence of PDGFR or a fragment thereof, and includes a self-cleaving 2A polypeptide or an IRES to operably link the coding sequences.

[0292] Also provided herein are a set of vectors that include two or more vectors. For example, the set of vectors include a first vector comprising a coding sequence of FGF2 or a fragment thereof, and a second vector comprising a coding sequence of FGFR (e.g., any of the FGFRs described herein) or a fragment thereof. In another example, the set of vectors include a first vector comprising a coding sequence of IGF1 or a fragment thereof, and a second vector comprising a coding sequence of IGF1R or a fragment thereof. In yet another example, the set of vectors include a first vector comprising a coding sequence of PDGF (e.g., PDGFB) or a fragment thereof, and a second vector comprising a coding sequence of IGF-1R or a fragment thereof.

[0293] In some embodiments, a coding sequence of any one or more of the growth factor ligands described herein, any one or more of the growth factor ligands described herein, any of the accessory protein described herein, or a combination thereof, is operably linked to a promoter. In some embodiments, the promoter is a tissue-specific promoter. In some embodiments, the tissue-specific promoter is a muscle-specific promoter. In some embodiments, the muscle-specific promoter is selected from the group consisting of: skeletal β -action, myosin light chain 2a, dystrophin, SPc-512, muscle creatine kinase, and synthetic

muscle promoters. In some embodiments, the promoter is a constitutively active promoter. In some embodiments, the promoter is selected from the group consisting of: EF1 (e.g., EF1alpha), PGK, CMV, RSV, and β -actin. In some embodiments, the promoter is a EF1 (e.g., EF1alpha) promoter. In some embodiments, the promoter is a PGK promoter. In some embodiments, the vector comprises a selectable marker (e.g., puromycin).

[0294] In some embodiments, a vector comprises a polynucleotide comprising a first coding sequence (e.g., a coding sequence of any of the growth factor ligands, growth factor receptors, or accessory proteins described herein) operably linked to a first promoter and a polynucleotide comprising a second coding sequence (e.g., a coding sequence of any of the growth factor ligands, growth factor receptors, or accessory proteins described herein) operably linked to a second promoter.

[0295] In some embodiments, a vector system is used to integrate a polynucleotide comprising a coding sequence of any one or more of the growth factor ligands described herein, any one or more of the growth factor ligands described herein, any of the accessory protein described herein, or a combination thereof, into the genome of a cell line (e.g., any of the cell lines described herein). In some embodiments, the vector system used for integration is a vector phiC31 Integrase Vector System. Additional non-limiting examples of vectors systems that can be used to integrate a coding sequence of any one or more of the growth factor ligands described herein, any one or more of the growth factor ligands described herein, any of the accessory protein described herein, or a combination thereof, into the genome of a cell line (e.g., any of the cell lines described herein) include: a sleeping beauty transposon system (as described in U.S. Pat. No. 7985739), a piggyBac transposition system (as described in US20090042297), CRISPR/Cas-mediated knockin, TALEN-mediated knockin, and viral vector-mediated integration. In such embodiments where integration is mediated via a viral vector, non-limiting examples of viral vectors include adenovirus, adeno-associated virus, lentivirus, retrovirus (e.g., a gamma-retrovirus), or sendai virus.

[0296] SEQ ID NOs: 120-122 represent exemplary vector backbones used in this study: Sequences listed in SEQ ID NO: 61-119 were cloned into any one of vectors in SEQ ID NOs: 120-122 using EcoRI and KpnI restriction sites with a kozak sequence GCCACC inserted ahead of ATG start site. FC550A-eBFP2 was created by replacing mRuby sequence in FC550A-empty vector (EVmRuby) with eBFP2. In some embodiments, the polynucleotide sequence includes a sequence having at least 80% (e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%) sequence identity to a sequence selected from SEQ ID NOs: 61-119.

6.13. Methods of Transducing Cells

[0297] Methods of introducing nucleic acids and expression vectors into a cell (e.g., an immortalized cell) are known in the art. Non-limiting examples of methods that can be used to introduce a nucleic acid into a cell include lipofection, transfection, electroporation, microinjection, calcium phosphate transfection, dendrimer-based transfection, cationic polymer transfection, cell squeezing, sonoporation, optical transfection, impalefection, hydrodynamic delivery, magnetofection, viral transduction (e.g., adenoviral, retroviral, and lentiviral transduction), lipid nanoparticle (LNP) transfection, and nanoparticle transfection.

6.14. Kits

[0298] Also provided herein are kits comprising any of the cell lines, any of the cells derived from the cell lines, any of the polynucleotides described herein (e.g., any of the coding sequence of any one or more of the growth factor ligands described herein, any one or more of the growth factor ligands described herein, any of the accessory protein described herein, or a combination thereof). In some embodiments, the kit includes instructions for performing any of the methods described herein.

6.15. Cells/Cell lines

[0299] Also provided herein are cell line(s) for cultured food production. In some embodiments, the cell line(s) are capable of self-renewal. In some embodiments, the cell line(s) are immortalized cell line(s). In some embodiments, the cell lines are then differentiated to cell types of interest (e.g., myogenic cells).

[0300] Also provided herein are immortalized cells (e.g., any of the immortalized cells described herein). In some embodiments, the immortalized cells are fibroblasts. In some embodiments, the immortalized cells comprise any of the nucleic acids described herein that encode any of the myogenic regulatory factors described herein. In some embodiments, an immortalized cell is immortalized prior to performing the methods described herein. In some embodiments, the methods provided herein include a step of immortalizing a cell. In some embodiments, a cell is immortalized by transforming the cell with TERT.

[0301] Also provided herein are cells comprising any of the polynucleotides described herein that include any of the growth factor ligands described herein, any of the growth factor receptors described herein, any of the accessory proteins described herein, or a combination thereof.

[0302] Also provided herein are cells derived from the cell line(s). Non-limiting examples of cells derived from the immortalized cells (e.g., using the methods described herein) include myoblasts, myotubes, multinucleated myotubes, satellite cells, skeletal muscle fibers, or any combination thereof.

[0303] In some embodiments, the cell line is from a livestock, poultry, game or aquatic animal species. In some embodiments, the cell line or immortalized cell line are from a chicken, duck, or turkey. In some embodiments, the cell line or immortalized cell line are from a fish. In some embodiments, the cell line or immortalized cell line are from a livestock species. In some embodiments, the livestock species is porcine or bovine.

[0304] In some embodiments, the cell line is selected from any metazoan species. In some embodiments, the cell line is from any animal, such as vertebrate and invertebrate animal species. In some embodiments, the cell line is from any vertebrate animal species such as mammals, reptiles, birds, amphibians, and the like. In some embodiments, the cell line is from any mammalian species such as a human, murine, bovine, porcine, poultry, and the like. In some embodiments, the cell line is derived from a species selected from including without limitation, *Gallus gallus*, *Bos taurus*, *Sus scrofa*, *Meleagris gallopavo*, *Anas platyrhynchos*, *Salmo salar*, *Thunnus thynnus*, *Ovis aries*, *Coturnix coturnix*, *Copra aegagrus hircus*, or *Homarus americanus*.

[0305] In some embodiments, the cell line (e.g., a cell line that is ultimately immortalized) is isolated from *Gallus gallus* (chicken). In some embodiments, the cell is isolated from chicken skin. In some embodiments, the cell is isolated from chicken muscle. In some embodiment, the cell is isolated from a chicken (e.g., chicken skin or chicken muscle) and cultured until a monoculture of cells is established (e.g., a monoculture of fibroblasts originating from the isolated chicken cells).

[0306] In some embodiments, the cell line (e.g., a cell line that is ultimately immortalized) is selected from the group consisting of: a myoblast, an immortalized myoblast, an immortalized primary myoblast, a muscle satellite cell, and a muscle stem cell. In some embodiments, the immortalized cell is an immortalized myoblast or an immortalized primary myoblast.

[0307] In some embodiments, the cell line (e.g., a cell line that is ultimately immortalized) is a fibroblast. For example, the cell is an immortalized fibroblast.

[0308] In some embodiments, skeletal muscle satellite cells are isolated from a chicken. In adults these are quiescent mononucleated myogenic cells that act as a reserve population of cells, able to proliferate and/or differentiate upon stimulation and give rise to regenerated muscle and to more satellite cells.

[0309] In some embodiments, an immortalized cell is not a stem cell (e.g., a muscle stem cell or a muscle satellite cell). In some embodiments, an immortalized cell is not a pluripotent stem cell (e.g., an embryonic stem cell or an induced pluripotent stem cell).

[0310] Also provided herein are cell banks comprising immortalized cell lines (e.g., immortalized fibroblast cells lines) generated according to the methods described herein.

[0311] Also provided herein is cell-based meat suitable for consumption.

7. EXAMPLES

7.1. Summary of Experimental Observations.

[0312] Applicant evaluated cell lines harboring a polynucleotide comprising a coding sequence of FGF2, IGF1, and/or PDGF for cell proliferation, impact on adherence, and amount of FGF2, IGF1, PDGF secreted into the culture medium. Applicant evaluated whether cells engineered to express and secrete FGF2, IGF1, and/or PDGF ligands could be grown in serum-free media (serum is known to contain an assortment of growth factors) in the absence of exogenous growth factors (i.e., media not supplemented with FGF2, IGF1, and/or PDGF). Applicant further evaluated whether cells engineered to express FGF2, IGF1, and/or PDGF receptors could be grown in serum-free media in the absence of exogenous growth factors. Applicant additionally evaluated whether cells engineered with specific promoters to drive expression of the exogenous polynucleotides or signaling peptides fused to the FGF2, IGF1, and/or PDG ligands could be grown in serum-free media in the absence of exogenous growth factors and increase growth factor secretion, respectively. Applicant demonstrated that introducing the polynucleotide comprising a coding sequence of an FGF2, IGF1, and/or PDGF ligand, receptor, or activated receptor into an immortalized cell line and culturing the cell line in serum free media resulted in cell proliferation and packed cell volumes similar to positive control cell lines grown in serum and/or in culture medium supplemented with exogenous growth factors. As a negative control, cell lines grown without being engineered to express an exogenous polynucleotide, without serum, and without exogenous growth factors failed to proliferate over 72 hours and also exhibited decreases in population doubling times. Additionally, Applicant found that specific

promoters further improved cell line performance when introducing the polynucleotide comprising a coding sequence of an FGF2, IGF1, and/or PDGF ligand, receptor, or activated receptor into an immortalized cell line and culturing the cell line in serum free media without any addition of exogenous growth factors. In addition, Applicant demonstrated that cell lines harboring the polynucleotide comprising a coding sequence of an FGF2, IGF1, and/or PDGF ligand secreted these growth factors into the serum-free media and this secretion was increased further when a polynucleotide comprising a coding sequence for a signaling peptide was combined with a polynucleotide comprising a coding sequence for growth factor to provide a fusion protein coding sequence. Applicant has further found that species to species and cell to cell variability impacts the efficacy of this approach and of these gene targets. For instance, Applicant found that introduction of polynucleotides comprising coding sequences for FGF2 ligands (of salmon, chicken, and bovine varieties) into bovine cell lines failed to generate a growth factor independent cell line. Application further notes that, even within the same species, cells of a different type often respond differently to any given growth factor and may require different growth factor targets.

[0313] Applicant further tested the cell lines harboring a polynucleotide comprising a coding sequence of FGF2 for impact on anchorage-dependent growth. Applicant demonstrated that introducing the polynucleotide comprising a coding sequence of FGF2 into an immortalized cell line resulted in an increase in the number of non-adherent cells capable of anchorage-independent growth.

[0314] Applicant also evaluated cell lines harboring a polynucleotide comprising a coding sequence of IGF1 for cell proliferation rate (e.g., viable cell density (VCD)) and packed cell volumes (PCV), where PCV is used as a proxy for cell biomass. In particular, Applicant demonstrated that introducing the polynucleotide comprising a coding sequence of IGF1 into an immortalized cell line and culturing the cell line in serum-free media in the absence of exogenous IGF1 resulted in increased viable cell densities as compared to the controls. Applicant also showed the cells engineered to express IGF1 had greater PCVs as compared to controls.

[0315] Applicant also evaluated cell lines harboring a polynucleotide comprising a coding sequence of IGF1 and a polynucleotide encoding an FGF2 for cell proliferation rate (e.g., viable cell density (VCD)) and packed cell volumes (PCV), where PCV is used as a proxy for cell biomass. Applicant demonstrated that introducing the polynucleotide comprising a coding sequence of IGF1 and a polynucleotide sequence encoding an FGF2 into an

immortalized cell line and culturing the cell line in serum-free media in the absence of growth factors resulted in increased viable cell densities and PCVs as compared to controls.

[0316] Applicant also evaluated cell lines harboring a polynucleotide comprising a coding sequence of IGF1 and a polynucleotide encoding an FGF2 receptor for cell proliferation rate (e.g., viable cell density (VCD)) and packed cell volumes (PCV). Applicant demonstrated that introducing the polynucleotide comprising a coding sequence of IGF1 and a polynucleotide sequence encoding an FGF2 receptor into a cell line and culturing the cell line in serum-free media in the absence of growth factors resulted in increased viable cell densities and PCVs as compared to controls.

[0317] Lastly, Applicant also evaluated cell lines harboring a polynucleotide comprising a coding sequence of PDGF or a polynucleotide encoding an PDGF receptor for cell proliferation rate (e.g., viable cell density (VCD)) and packed cell volumes (PCV). Applicant demonstrated that introducing the polynucleotide comprising a coding sequence of PDGF or a polynucleotide sequence encoding an PDGF receptor into a cell line and culturing the cell line in serum-free media in the absence of growth factors resulted in increased viable cell densities and PCVs as compared to controls.

[0318] Overall, this work demonstrated the ability to engineer cells to have reduced dependence on exogenous growth factors without compromising the cell's ability to proliferate or differentiate into myogenic cells. In particular, this work demonstrated that engineering cells to express growth factor ligands and/or growth factor receptors results in engineered cells that (i) maintain cell proliferation rates similar to positive controls, (ii) have an increase in the number of non-adherent cells (i.e., cells that exhibit anchorage-independent growth) as compared to controls, and (iii) have an increase in packed cell volumes as compared to both positive and negative controls, all while cells are grown in the absence of one or more exogenous growth factors. These findings are important because manufacturing cells suitable for consumption requires vast amounts of exogenous growth factor ligands in order to sufficiently expand the cells and adapt them to the appropriate culture formats (e.g., suspension culture). The engineered cells provided herein supply their own source of growth factor signaling—thereby bypassing or at least reducing the need to supplement the cultures with exogenous growth factors. Moreover, by promoting anchorage independent growth, which is currently essential for manufacturing cell based meats suitable for consumption, the engineered cell lines provided herein increase the efficiency by which cell based meats suitable for consumption can be produced.

7.2. Methods

7.2.1. Cell Line Production.

[0319] In order to generate cell lines with integrated polynucleotides, a PhiC31 Integrase Expression Plasmid system was used (System Biosciences). Briefly, coding sequences of genes of interest (e.g., coding sequence of FGF2 or coding sequence of IGF1) were cloned into a PhiC31 dual promoter expression plasmid (System Biosciences, Cat No. FC550A-1). Cell lines were transfected with the plasmid containing the coding sequences of the gene(s) of interest (e.g., FGF2 or IGF1) and a plasmid containing an integrase (PhiC31 integrase, System Biosciences, Cat No. FC200PA-1) to integrate the coding sequences into the genome. In some cases, the Phi31 plasmids also included a red fluorescent protein as a reporter. Cell lines with integrated plasmids were selected using puromycin and assessed for transgene expression and/or fluorescent marker expression. Cell lines exhibiting stable expression were selected for further analysis.

7.2.2. Assessment of Secreted FGF2 or secreted IGF1

[0320] Engineered cells were serum starved and plated into serum free media (no FGF2) for 72 hours. FGF2 ELISA (DFB50 (R&D Biosystems Quantikine Human FGF basic Immunoassay kit) was used to determine the concentration of FGF2 in the supernatant.

[0321] Engineered cells were serum starved and plated into serum free media (no IGF1) for 72 hours. IGF1 ELISA ((R&D Biosystems) was used to determine the concentration of IGF1 in the supernatant.

7.2.3. Assessment of Cell Proliferation

[0322] A colorimetric assay (WST-1 based) was used to assess cell proliferation (Roche, Cat. No. 05 015 944 001). WST-1 assay used to measure cell proliferation based on the cleavage of tetrazolium salt (WST-1) to formazan by cellular mitochondrial dehydrogenases. Through a colorimetric measurement, the proliferation fold change can be calculated and utilized to determine which cell lines grew significantly more than the negative control, FC550A (grown in serum free media). Cells were serum starved and plated in adherent plates with serum free media. WST-1 measured after 48 hours in culture.

7.2.4. Assessment of Myogenicity

[0323] Using qRT-PCR (real-time quantitative reverse transcription). Messenger RNA (mRNA) is isolated from cells to examine gene expression with probes specifically designed

to amplify select target genes to characterize cell lines. Identical quantity of mRNA is reverse transcribed to generate cDNA. Each cDNA is submitted to quantitative PCR (qPCR) to assess the expression of myogenic factors relative to a housekeeping gene. Expression of MyoD, MyoG, and/or MyHC1e indicate myogenic cells. Additionally, high levels of MyHC1e are indicative of cells that can mature to form myotubes.

[0324] Using immunohistochemistry. Cells are seeded in a 96-well plate at a low density (5000 – 10,000 cells/cm²) to allow cells to grow in the presence or absence of different small molecule combinations. After 2 days of media exposure, cells are fixed with 4% paraformaldehyde (PFA) and washed. Cells are permeabilized with 0.05% PBS-T (triton-x), blocked with normal goat serum (Millipore Sigma) and are incubated with antibodies, and subsequently with secondary antibodies.

7.3. Example 1: Promoter screen identified hEF1 α as potent promoter for driving expression of growth factor ligand

[0325] This experiment was designed to evaluate promoters for their ability to drive expression of the growth factor ligands (and growth factor receptors).

[0326] For these experiments, vectors having bi-directional promoters were used (see, e.g., **FIG. 3A** and **3B**) to assess each promoter's ability to drive expression of FGF2. In particular, the constructs included hEF1 α and mPGK promoter sequences and a coding sequence of FGF2 or a luciferase reporter gene downstream of the promoter sequences. The vectors shown in **FIG. 3A** and **FIG. 3B** were transfected into chicken fibroblast cells. Promoter strength (i.e., the promoter's ability to drive expression of a luciferase reporter gene) was assessed by measuring relative light unit (RLU) fold change relative to mPGK-NLucP control (see **FIG. 4**). Promoter strength for driving expression of FGF2 was measured by determining the FGF2 concentration in the supernatant after 72 hours in culture.

[0327] Surprisingly, as shown in **FIG. 4**, the hEF1 α promoter produced statistically significantly greater levels of luciferase reporter gene expression. In particular, the hEF1 α promoter produced 43.9x higher expression of the luciferase reporter gene than the mPGK promoter. Statistically significant differences between the means were determined by a t-test with P-values indicated with asterisks. N=5. ** p <0.01.

[0328] As shown in **FIG. 5**, the hEF1 α promoter resulted in a mean of 64.8 pg/mL of FGF2 in the supernatant following 72 hours in culture compared to 0 pg/mL of FGF2 in the supernatant when expression of FGF2 was linked to the mPGK promoter.

[0329] This data showed that the hEF1alpha promoter resulted in greater than 60-fold increase in expression compared to the mPGK promoter. For at least these reasons, the hEF1alpha promoter was selected for use in the following experiments.

7.4. Example 2: Cells engineered to express FGF2 secrete FGF2 into culture media

[0330] This experiment was designed to assess performance of different FGF2 variants by measuring FGF2 concentration in the culture media 72 hours post transduction. For these experiments, chicken 1312 cells were transfected, selected using a cell sorter, and expanded prior to assessing FGF2 concentration in the cell culture media.

[0331] In particular, chicken 1312 cells seeded in a 6-well plate were transfected using Lipofectamine 3000 using a 1:1 ratio of diluted Lipofectamine 3000 mixture (e.g., 125 μ L Opti-Mem and 3.75 μ L Lipofectamine) to diluted DNA plasmid mixture (e.g., 125 μ L Opti-Mem + 5 μ L of P3000 reagent + 2.5 μ g of DNA plasmid). After 48-72 hours, cells were assessed for expression levels using microscopy and flow cytometry (data not shown).

[0332] A cell sorter was used to sort the mRuby⁺ cells, which served as a proxy for FGF2 expressing cells. Gates for sorting mRuby⁺ cells were set up using Naïve transfection (no transfection control) (data not shown).

[0333] Following sorting, cells were grown in a tissue culture treated 12 well plates. When cells reach 80-90% confluence, the cells were trypsinized and passaged. Cells were maintained in maintenance media (DMEM/F12 and 10% FBS and 1-2% chicken serum).

[0334] After the cells recovered from cell sorting, the cells were re-adapted to suspension culture and grown in 50mL TPP tubes or shake flasks. Cells were seeded at a density of 0.25 1E6 cells/mL and passaged every 3 days. Serum free and ACF media formulation (100ng/mL FGF2 and 10ng/mL IGF1) was added to the cultures for continuous growth.

[0335] To assess FGF2 concentration in the culture media, an ELISA (enzyme-linked immunoassay) was used. In particular, chicken 1312 cells transduced and sorted according to the above methods were plated in 48-well plates in replicate (N=2) at 60,000 cells/well in 400uL Serum Free media supplemented with 5ug/mL Fibronectin. Cells were left to grow at 39°C for about 72 hours. Supernatant was removed, spun at 300rcf for 5 minutes and moved to a clean Eppendorf tube. 100uL of each supernatant was assessed for each well – biological replicates were expanded to technical duplicates resulting in a final N=4 per condition. The results of the FGF2 ELISA are shown in **FIG. 6**.

[0336] Applicant also assessed whether secretion signal peptides (SSPs) could be used to enhance secretion of FGF2. Wild type FGF2 is secreted by a non-conventional secretion mechanism, which does not rely on SSPs. Therefore, Applicant hypothesized that using a SSP fused to the N-terminus of FGF-2 would enhance FGF2 secretion by using conventional secretion pathways (e.g., through the endoplasmic reticulum and golgi apparatus).

[0337] As shown in **FIG. 6**, cells engineered to express FGF2 wild type (FGF2-wt) or engineered to express FGF2 with an N-terminal secretion signal peptide (cchIL2co1-FGF2 and BM40-FGF2) secreted statistically significant levels of FGF2 into the media after 72 hours. Statistically significant differences between the means were determined by an ANOVA one-way test with Dunnett's exclusion (post hoc) with P-values indicated with asterisks. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0005$; **** $p < 0.0001$; and ns = not significant.

[0338] To assess proliferation of the chicken 1312 cells following transduction and sorting (according to the above methods), a WST-1 assay was used. The WST-1 assay used to measure cell proliferation based on the cleavage of tetrazolium salt (WST-1) to formazan by cellular mitochondrial dehydrogenases. Through a colorimetric measurement, the proliferation fold change can be calculated and utilized to determine which cell lines grew significantly more than the negative control, FC550A (grown in serum free media). Cells were serum starved and plated in adherent plates with serum free media. WST-1 measured after 48 hours in culture.

[0339] In particular, transfected and sorted chicken 1312 cells were plated in triplicate in 96-well plates in seeding media comprising Serum Free Media (no FGF2). As controls, transfected and sorted chicken 1312 cells were also plated in serum containing media and serum free media having 100ng/mL FGF2 (i.e., supplemental FGF2). Cells were grown for 48 hours in a stationary incubator at 39°C. N=3 additional wells with a media only were set up as negative controls. Following the 48-hour incubation, 10uL/well of WST-1 substrate (Roche scientific) was added to each well. Plates were incubated in a stationary incubator for 3 hours. Following incubation, plates were placed on a shaker to ensure mixing for 1 minute. Plates were read on a Cytation Image to determine absorbance (colorimetric output) at 450nm (630nm for wavelength correction).

[0340] As shown in **FIG. 7**, ggIL2-FGF2, containing a chicken IL2 secretion signal, had the highest fold change in proliferation compared to FC550A empty vector control (1.42). Statistically significant increases in proliferation were observed for FGF2-WT, Gluc-FGF2,

ggIL2-FGF2, hIL2-FGF2, hIL2co1-FGF2, and hIL6-FGF2. Controls grown in serum containing media resulted in the highest fold change (positive control). Statistically significant differences between the means were determined by an ANOVA one-way test with Dunnett's exclusion (post hoc) with P-values indicated with asterisks. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0005$; **** $p < 0.0001$; and ns = not significant.

[0341] Taken together, this data showed that cell lines engineered to express FGF2 result in robust production of FGF2, as measured by the concentration of FGF2 in the culture media (FIG. 6). Additionally, the data showed that cell lines engineered to express FGF2 can be grown in serum-free media without the need for supplementing the media with exogenous sources of FGF2 (FIG. 7).

7.5. Example 3: Cells engineered to express FGF2 exhibit significantly improved cell density

[0342] This experiment was designed to assess the impact of each FGF2 variant on cell density in adherent, serum-free cultures.

[0343] In particular, chicken cells transduced and sorted according to the methods described in Example 2 were plated in 48-well plates in replicates (N=2 wells) at 75,000 cells/well in 400uL serum-free media supplemented with 5ug/mL fibronectin. Additional controls included: cell lines not transfected and cell lines transfected with an FC550A empty vector; where the control cell lines were grown in serum-free media supplemented with 100ng/mL FGF2.

[0344] Cells were serum-starved and left to grow at 39°C for about 72 hours and Biospa imaging was performed every 12 hours to count cells. Cells were then harvested at the end of the experiment and final cell counts were analyzed using a ViCell BLU cell counter.

[0345] FIG. 8 shows representative images taken at 12 hours after initial seeding of control (FC550A) and FGF2-WT cells plated in serum free media with no exogenous FGF2. FIG. 9 shows representative images taken at 48 hours after initial seeding of control (FC550A) and FGF2-WT cells plated in serum free media with no exogenous FGF2.

[0346] As shown in FIG. 9, after 48 hours, multiple cell lines engineered to express FGF2 developed a secondary cell population that was not attached to the plate (identified by the Arrow in FIG. 9) while the FC550A empty vector control consisted only of cells that were adherent.

[0347] At the end of the 72-hour period, the cells were harvested and viable cell densities were calculated for each condition. As shown in **FIG. 10**, FGF2-WT transfected cells grew significantly better than the negative controls and similar to positive controls grown in serum free media with 100ng/mL FGF2. Many FGF-expressing lines were able to grow significantly better than the FC550A empty vector control (Blue bar). Interestingly, all FGF-STAB expressing cell lines were not significant. Statistically significant differences between the means were determined by an ANOVA one-way test with Dunnett's exclusion (post hoc) with P-values indicated with asterisks. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0005$; **** $p < 0.0001$; and ns = not significant.

[0348] This data showed that cell lines engineered to express FGF2 result in cell densities comparable to positive controls, indicating that these cell lines are suitable sources for generating cell-based meat.

7.5.1. Further Assessment of impact on cell density

[0349] In another experiment, to test impact on cell density, naive cells (none transfected controls) and cells engineered to express FGF2-WT or FGF2-WT with a secretion tag (e.g., a secretion tag selected from Secrecon, human IGN2A, human IL2, human IL2 variation 1, human IL2 variation 2, human IL6, BM40) were adapted into suspension format and seeded into a 4 passage proliferation study. Cells were grown in serum free, ACF media for 4 passages on a 2 day passaging cadence (seeding density ~400K/mL) as biological replicates. (N=2). Serum free, ACF media contained 10 ng/mL IGF1 and 0 ng/mL FGF2. VCDs measurements were taken on Day 0 and Day 2 for each passage to determine doubling times and maximum VCDs. Naïve and FGF-STAB variants were used as controls. As shown in **FIG. 11**, after 4 passages, each of the FGF2 variants tested showed statistically significant increases in VCD as compared to the controls. This data established that engineered cells (FGF2 and FGF2 with a secretion tag) were able to grow in suspension without media-supplemented with FGF2. Notably, cells engineered to express thermostable FGF-STAB sequences and naive cells did not proliferate. **FIG. 11** shows Viable Cell Density (VCD) of day 2, passage 4. One way ANOVA was performed with significance indicated as $P < 0.0001$ (****) and $P < 0.001$ (**) compared to naive control.

7.6. Example 4: Cells engineered to express FGF2 variants enabled cell proliferation without media-supplemented FGF2

[0350] Chicken cells were engineered to express chicken FGF2, bovine FGF2, salmon FGF2, heat stable variants of FGF2 (e.g., FGF2-Q68I-N114G and FGF2-Q68I-C99S-N114G), FGF2 having a secretion tag (e.g., ggIL2-FGF2 and hIL2-co1-ggFGF2(xMet)), FGF2 variants that preserve amino acids for non-canonical secretion (FGF2-C77-Y81), and FGF2-STAB variants (STAB-C77Y81, c96-STAB-Gen2-ggFGF2, STAB-Gen3-ggFGF2, and c96-STAB-Gen3-ggFGF2). Controls include cells transduced with an empty vector (EV) and untransfected controls (Naïve).

[0351] In a first set of experiments, cells engineered to express FGF2 and FGF2 variants described above were assessed for their ability to proliferate and enable biomass production in media not supplemented with FGF2.

[0352] For assessment of impact on proliferation, naïve and engineered cells were grown in suspension in ACF media (10ug/L IGF1) for 4 passages on a 2 day passaging cadence (initial seeding density 0.5Mcells/mL) as biological replicates (N=2). Positive controls included naïve and empty vector (EV) engineer cells grown with media supplemented FGF2. Statistics: One way ANOVA was performed to compare test groups against empty vector (EV) grown in FGF2-containing media (100µg/L): not significant (n.s.), $p<0.05$ (*), $p<0.001$ (**), $p<0.0001$ (***), and $p<0.0001$ (****).

[0353] FIG. 12 shows viable cell density data shown for cultures on day 2 of passage 4. This data showed that thermostable FGF2 sequence variations based on computationally designed STAB sequence were unable to promote cell growth in FGF2-free media (FIG. 14). In contrast, each of the other variants of FGF2 resulted in VCDs similar to the controls.

[0354] For assessment of impact on biomass production, naïve and engineered cells were grown in suspension for 5 passages on a 2 day passaging cadence in media containing IGF1 (10µg/L). Seeding density at each passage was 0.5M cells/mL; N=2. Naïve and empty vector negative controls grown without media-supplemented FGF2 and did not survive to passage 5 (data not shown). On Day 2 of passage 5, packed cell volume (PCV) was taken by spinning 500µL of culture at 1000xg for 5 minutes and collecting a PCV reading. The PCV reading can be converted to percent PCV by the following formula: % PCV = (PCV reading/sample volume)*100. Statistics: One way ANOVA was performed to compare test groups against empty vector (EV) grown in FGF2-containing media (100µg/L): Not significant (n.s.),

$p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***) $p < 0.0001$ (****). Biomass production data (i.e., percent packed cell volumes) is shown in **FIG. 13**.

[0355] **FIG. 13** shows percent packed cell volume for cultures on day 2 of passage 5. **FIG. 13** shows that media supplemented with FGF2 was not required for the eight engineered cell lines to achieve packed cell volumes similar to the controls. The lower PCV's observed for chicken, bovine, and salmon FGF2 cell lines may be attributed to variations in the polyclonal population.

[0356] The engineered cells lines were assessed for their ability to secrete FGF2. An ELISA was performed on spent media (supernatants) from cell lines grown in suspension media (10 μ g/L IGF1) with/without media supplemented FGF2 (100 μ g/L); biological replicates N=2. Positive controls included spent media from naive and empty vector (EV) cells grown in FGF2 supplemented media. Negative controls included base media (Media) and spent media from naive cells grown in media not supplemented with FGF2. On Day 2 of Passage 5, cells were spun at 300xg for 5 minutes and the supernatant was removed for use in FGF2-ELISA kit to evaluate the concentration of FGF2 in the supernatant. For each condition, biological replicates (N=2) and technical replicates (N=4) were analyzed. **FIG. 14** shows FGF2 concentration (pg/mL) in supernatants collected from the controls and the engineered cells.

[0357] Overall, this data showed that cells engineered to express FGF2 or variants of FGF2 could be grown in the absence of FGF2, exhibit robust growth as compared to controls, thereby showing that the engineered cells can be grown in culture media not supplemented with FGF2. Therefore, these cells lines are ideal for use in cell based meat products suitable for consumption because they can endure the requisite culture conditions (i.e., extensive passaging) needed to make these products all while reducing the costs associated with using the vast amounts of exogenous growth factors traditionally needed to make these products.

7.7. **Example 5: Cell lines engineered to express FGF receptor variants proliferate without media supplemented FGF2.**

[0358] Chicken cells were engineered to express FGF receptors, including FGF1 receptors, FGF2 receptors, FGF3 receptors, and FGF4 receptors. FGF1 receptors included: FGFR1C, FGFR1C-N546K, FGFR1C-V561M, and myrist-FGFR1C-K656E. FGF2 receptors included: FGFR2, FGFR2-N550K, FGFR2-K660E, and FGFR2-3xMuts. FGF3 receptors included:

FGFR3, FGFR3-N540K, FGFR3-K560E, FGFR3-N540K-K560E, and myrist-FGF3R-K560E. FGF4 receptors included: FGF4R, FGF4R-Y367C, and FGF4R-Y367C-K654E.

[0359] For assessment of impact the FGF receptors on proliferation, cells were grown over 4 passages in suspension culture with ACF media containing IGF1 (10ug/L) and with/without FGF2 (100ug/L) on a 2 day passaging cadence (seeding density 0.5Mcells/mL) as biological replicates (N=2). Viable Cell Density (VCD) was taken on day 2 of passage 4 of culture (see **FIG. 15**). One way ANOVA was performed to compare test groups against empty Vector (EV) grown in FGF2-containing media (100ug/L), Not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), and $p < 0.0001$ (****).

[0360] As shown in **FIG. 15**, three cell lines including myrist-FGFR1C-K656E, FGFR2 (wild type), myrist-FGFR3-K560E achieved higher viable cell densities in FGF2-free media than positive controls grown with FGF2. Multiple conditions archived growth comparable to Positive Controls including FGFR1C-N546K, FGFR1C-V561M, FGFR3-N540K, FGFR2-K650E, and FGFR3-N540K-K560E.

[0361] For assessment of impact of the FGF receptors on biomass production, cells were grown in suspension for 5 passages on a 2 day passaging cadence in media containing IGF1 (10μg/L). Seeding density at each passage was 0.5M cells/mL; N=2. Naive and empty vector negative controls grown without media-supplemented with FGF2 did not survive to passage 5 (data not shown). On Day 2 of passage 5, packed cell volume (PCV) was taken by spinning 500uL of culture at 1000xg for 5 minutes and collecting a PCV reading. The PCV reading can be converted to percent PCV by the following formula: % PCV = (PCV reading/sample volume)*100. One way ANOVA was performed to compare test groups against empty Vector (EV) grown in FGF2-containing media (100ug/L), Not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), and $p < 0.0001$ (****).

[0362] As shown in **FIG. 16**, shows that media supplemented with FGF2 was not required for the eight engineered cell lines to achieve packed cell volumes similar to the controls.

[0363] The engineered cells lines were assessed for their ability to secrete FGF2. An ELISA was performed on spent media (supernatants) from cell lines grown in suspension media (10μg/L IGF1) with/without media supplemented FGF2 (100μg/L); biological replicates N=2. Positive controls included spent media from naive and empty vector (EV) cells grown in FGF2 supplemented media. Negative controls included base media (Media) and spent media from naive cells grown in media not supplemented with FGF2. On Day 2 of

Passage 5, cells were spun at 300xg for 5 minutes and the supernatant was removed for use in FGF2-ELISA kit to evaluate the concentration of FGF2 in the supernatant. For each condition, biological replicates (N=2) and technical replicates (N=4) were analyzed. **FIG. 17** shows FGF2 concentration (pg/mL) in supernatants collected from the controls and the engineered cells.

[0364] Overall, this data showed that cells engineered to express FGF1 receptor, FGF2 receptors, FGF3 receptors, or FGFR4 receptors (or variants thereof) could be grown in the absence of FGF2, exhibit robust growth as compared to controls, thereby showing that the engineered cells can be grown in culture media not supplemented with FGF2. Therefore, these cells lines are ideal for use in cell-based meat products and cell-based food products suitable for consumption because they can endure the requisite culture conditions (i.e., extensive passaging) needed to make these products all while reducing the costs associated with using the vast amounts of exogenous growth factors traditionally needed to make these products.

7.8. Summary of Examples 2-5

[0365] Overall, this data suggests that cell lines engineered to express FGF2-WT, or cells engineered to express FGF2-WT with various secretion signals, and grown in the absence of FGF2, exhibit robust growth as compared to controls, thereby showing that the engineered cells can be grown in culture media not supplemented with FGF2. Therefore, these cells lines are ideal for use in cell-based meat products and cell-based food products suitable for consumption because they can endure the requisite culture conditions (i.e., extensive passaging) needed to make these products all while reducing the costs associated with using the vast amounts of exogenous growth factors traditionally needed to make these products.

7.9. Example 6: Cells engineered to express IGF1 and IGF1 receptors (or variants thereof) significantly improve cell density and packed cell volumes

[0366] [498] This example was designed to assess how expression of exogenous IGF1 impacted cell density and packed cell volume. This experiment was also designed to assess how cells characterized as IGF1^{low} or IGF1^{high} contributed to cell density and packed cell volume.

7.9.1. Assessment of IGF1 and IGF1 receptor variants

[0367] In a first set of experiments, Chicken cells were engineered to express IGF1 WT (SEQ ID NO: 16), IGF1-trunc., IGF1R, or IGF1R-R1353H. These cells were grown in suspension with ACF media (100ug/L FGF2) without media supplemented IGF1. Cells were seeded at 0.5E6 cells/mL (N=2) and passaged every 2 days over 4 passages. Viable cell density (**FIG. 18**) and packed cell volume (PCV (**FIG. 19**)) were assessed to help determine how the engineered cells performed compared to controls.

[0368] Viable Cell Density (VCD) of day 2, passage 4 is provided in **FIG. 18**. One way ANOVA performed compared to IGF1 expressing cell line grown in IGF1-free media, Not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), and $p < 0.0001$ (****). As shown in **FIG. 18**, expression of IGF1 receptor variations or truncated IGF1 was not able to boost cell growth in IGF1-free media. In contrast, cells engineered to express wild type IGF-1 produced VCD similar to the controls (**FIG. 18**).

[0369] Packed cell volume (PCV) of day 2, passage 3 is provided in **FIG. 19**. PCV determined by spinning 500 μ L of culture at 1000xg for 5 minutes and collecting a PCV reading. The PCV reading was converted to percent PCV by the following formula: % PCV = (PCV reading/sample volume)*100. One way ANOVA performed compared to IGF1 expressing cell line grown in IGF1-free media, Not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), and $p < 0.0001$ (****). As shown in **FIG. 19**, expression of IGF1 receptor variations or truncated IGF1 was not able to boost cell growth in IGF1-free media. In contrast, cells engineered to express wild type IGF-1 produced PCV similar to the controls (**FIG. 19**).

[0370] This data showed that chicken cells engineered to express IGF1 yield produced the most favorable cell density and packed cell volume among the conditions tested. Chicken cells engineered to express IGF1 were selected for additional analysis.

7.9.2. Assessment of IGF1^{low} and IGF1^{high} cells

[0371] In another set of experiments, chicken cells were engineered to express either an FC550A empty vector ("EV") control or a Phi31 vector containing an IGF1 wild type (IGF1-WT) sequence (SEQ ID NO: 16). Transduced cells were sorted into "low" expressing cells and "high" expressing cells based on RFP expression. RFP expression served as a proxy for IGF1 expression. "Low-expression" cells and "high-expression" cells were separately plated in suspension format in TPP tubes. Controls included: cell lines not transfected ("Naïve")

and the EV control; where the control cell lines were grown in serum-free media supplemented with and without IGF1.

[0372] **FIGs. 20A-20B** shows growth curves over 3 passages for cell lines grown in ACF media supplemented with 0µg/L or 10µg/L IGF1. Here, cells were seeded at 0.5E6 cells/mL and passaged on a 2-day cadence. Cell counts were taken daily using ViCell BLU. Each condition was grown as a biological replicate (N=2).

[0373] As shown in **FIG. 20A**, cells engineered to expressed low levels of IGF1 (IGF1^{Low}) grown in 0 µg/L IGF1 had robust growth curves as compared to controls (i.e., Naïve and EV) not grown in the presence of IGF1. In fact, the cells engineered to express IGF1 (IGF1^{Low}) had growth curves similar to the controls (i.e., Naïve and EV) grown in 10 µg/L IGF1 (see **FIG. 20A**). This data suggests that IGF1^{Low} cells are able to produce enough of IGF1 such that supplementing the culture media with IGF1 is not required.

[0374] **FIG. 20B** show cells engineered to expressed high levels of IGF1 (IGF1^{High}) grown in 0 µg/L IGF1 had robust growth curves as compared to controls (i.e., Naïve and EV) not grown in the presence of IGF1. Similar to the IGF1^{Low} cells, the cells engineered to express high levels of IGF1 (IGF1^{High}) had growth curves similar to the controls (i.e., Naïve and EV) grown in 10 µg/L IGF1 (see **FIG. 20B**). This data suggests that IGF1^{High} cells are able to produce enough of IGF1 such that supplementing the culture media with IGF1 is not necessary.

[0375] The IGF1^{low} and IGF1^{high} cultures were assessed for their ability to secrete IGF1 into the culture medium. For these experiments, an ELISA was performed on spent media (supernatants) from cell lines grown in ACF media (100ug/L FGF2) with/without media supplemented IGF1 (10µg/L). Positive controls included spent media from Naïve cells, empty vector (EV) cells grown in IGF1 supplemented media, and EV cells grown in base media (100ug/L FGF2). Negative controls included base media (Media) and spent media from naive cells grown without IGF1. On Day 2 of Passage 3, cells were spun at 300xg for 5 minutes and the supernatant was removed for use in IGF1-ELISA kit to evaluate the concentration of IGF1 in the supernatant. For each condition, biological replicates (N=2) and technical replicates (N=4) were analyzed. One way ANOVA was performed to compare to IGF1 expressing cell lines to empty vector (EV) controls: not significant (n.s.), p<0.05 (*), p<0.001(**), p<0.0001(***)p<0.0001 (****).

[0376] **FIG. 21A** shows IGF1 ELISA data for IGF1^{low} cells. Supernatants from IGF1^{low} cells had 12.93 µg/L of IGF1 when grown in media not supplemented with IGF1 and 20.58 µg/L of IGF1 when grown in media supplemented with IGF1 (see **FIG. 21A**). **FIG. 21B** shows IGF1 ELISA data for IGF1^{high} cells. Supernatants from IGF1^{high} cells had 35.27 µg/L of IGF1 when grown in media not supplemented with IGF1 and 45.32 µg/L of IGF1 when grown in media supplemented with IGF1 (see **FIG. 21B**). Overall, this data showed robust IGF1 secretion into the culture media by the engineered cells, and the results were as expected with IGF1^{low} secreting lower amounts of IGF1 than IGF1^{high}.

[0377] IGF1^{low} cells were assessed for population doubling time (**FIG. 22**), viable cell density (**FIG. 23A**) and packed cell volume (**FIG. 23C**). IGF1^{high} cells were assessed for viable cell density (**FIG. 23B**) and packed cell volume (**FIG. 23D**).

[0378] **FIG. 22** shows doubling time (hours) for chicken cells engineered to express IGF1 (IGF1^{low}) grown in media supplement without (“-”) and with (“+”) IGF1. Cells were grown with or without 10µg/L IGF1 in ACF media (100ug/L FGF2) over 3 passages. Cells seeded at 0.5E6 cells/mL and passaged on a 2-day cadence (N=2). Doubling time was calculated by applying exponential growth equation $Y=Y_0*\exp(k*x)$ to proliferation profiles obtained on the third passage. Where Y₀ is the starting population, k is the rate constant, and Doubling Time (hr) is the time need for the population to double, calculated as $\ln(2)/k$. Where Y₀ is the starting population, k is the rate constant, and Doubling Time (hr) is the time need for the population to double, calculated as $\ln(2)/k$. One way ANOVA was performed: not significant (n.s.), p<0.05 (*), p<0.001(**), p<0.0001(***), and p<0.0001 (****). As shown in **FIG. 22**, the addition of media-supplemented IGF1 to IGF1^{Low} culture did not impact cell doubling time.

[0379] Further analysis of the suspension cultures at day 2 during the third passage revealed that both IGF1^{low} cells (**FIG. 23A**) and IGF1^{high} cells (**FIG. 23B**) had statistically significant differences in viable cell densities (VCD) as compared to the controls. In particular, IGF1^{Low} cells had statistically significant greater VCDs as compared to controls (i.e., Naïve and EV) grown in either 0 µg/L IGF1 or 10 µg/L IGF1 (see **FIG. 23A**). Similarly, IGF1^{High} cells had statistically significant greater VCDs as compared to both controls (i.e., Naïve and EV) grown in 0 µg/L IGF1 but was only statistically significant as compared to the EV control when controls were grown in 10 µg/L IGF1 (see **FIG. 23B**). Statistically significant differences between the means were determined by an ANOVA one-

way test with Dunnett's exclusion with P-values indicated with asterisks. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0005$; **** $p < 0.0001$; and ns = not significant.

[0380] Applicant then looked at Pack Cell Volumes (PCV), which is a proxy for cell biomass. PCV analysis for the suspension cultures at day 3 during the third passage revealed that both IGF1^{low} cells (**FIG. 23C**) and IGF1^{high} cells (**FIG. 23D**) had statistically significant differences in PCV as compared to the controls. To measure PCV, 500uL of culture volume was collected in a small PCV tube and centrifuged at 1000xg for 5 minutes. Each condition was measured in duplicate (biological replicates with technical replicates N=4).

[0381] As shown in **FIG. 23C**, IGF1^{low} cells had statistically significant greater PCVs as compared to controls (i.e., Naïve and EV) grown in either 0 µg/L IGF1 or 10 µg/L IGF1. IGF1^{high} cells had statistically significant greater PCVs as compared to both controls (i.e., Naïve and EV) grown in 0 µg/L IGF1 but was only statistically significant as compared to the EV control when controls were grown in 10 µg/L IGF1 (see **FIG. 23D**). Statistically significant differences between the means were determined by an ANOVA one-way test with Dunnett's exclusion with P-values indicated with asterisks. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0005$; **** $p < 0.0001$; and ns = not significant.

[0382] Overall, **FIGS. 23C-23D** show that cells engineered to express IGF1 (e.g., IGF1^{Low} and IGF1^{High}) actually outperformed (i.e., enable greater PCV) cells grown in the presence of IGF1. As PCV is a proxy for cell biomass, this data suggest that the engineered cells are ideal for use in cell-based meat products and cell-based food products suitable for consumption because they produce the amounts of cell biomass needed for these products and can do so in the absence of exogenous IGF1.

7.9.3. Assessment of impact of media supplemented IGF1 on IGF1^{low} cultures

[0383] **FIG. 26** shows doubling time (hours) for chicken cells engineered to express IGF-1 (IGF1^{low}) grown in media supplement without ("−") and with ("+") IGF1. Cells were grown with or without 10µg/L IGF1 in ACF media (100ug/L FGF2) over 3 passages. Cells seeded at 0.5E6 cells/mL and passaged on a 2-day cadence (N=2). Doubling time was calculated by applying exponential growth equation $Y=Y_0 \cdot \exp(k \cdot x)$ to proliferation profiles obtained on the third passage. Where Y_0 is the starting population, k is the rate constant, and Doubling Time (hr) is the time need for the population to double, calculated as $\ln(2)/k$. Where Y_0 is the starting population, k is the rate constant, and Doubling Time (hr) is the time need for the

population to double, calculated as $\ln(2)/k$. One way ANOVA was performed: not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), and $p < 0.0001$ (****). As shown in **FIG. 24**, the addition of media-supplemented IGF1 to IGF1^{Low} culture did not impact cell doubling time.

[0384] **FIG. 25** shows biomass (as PCV (g/L)) for chicken cells engineered to express IGF-1 (IGF1^{low}) grown in media supplement without (“-”) and with (“+”) IGF1. Cells were grown with or without 10 μ g/L IGF1 in ACF media (100 μ g/L FGF2) over 3 passages. Cells seeded at 0.5E6 cells/mL and passaged on a 2-day cadence (N=2). PCV was measured on Day 2 of Passage 3 using 500 μ L of culture volume and centrifuged at 1000xg for 5 minutes. One way ANOVA performed, Not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), $p < 0.0001$ (****). One way ANOVA was performed: Not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), $p < 0.0001$ (****). As shown in **FIG. 25**, the addition of media-supplemented IGF1 to IGF1^{Low} culture did not impact PCV.

[0385] Taken together, **FIGS. 20A-20B**, **FIG. 21A-21B**, **FIG. 22**, **FIGS. 23A-23D**, **FIG. 24**, and **FIG. 25** show that IGF1^{Low} and IGF1^{High} cells not only exhibit robust growth independent of exogenous IGF1 (i.e., media supplemented with IGF1) but also outperform (i.e., produce higher VCD) cells grown in the presence of IGF1. This data suggests these cells lines are ideal for use in cell-based meat products and cell-based food products suitable for consumption because they can endure the requisite culture conditions (i.e., extensive passage) needed to make these products--all while reducing the costs associated with using the vast amounts of exogenous growth factors traditionally needed to make these products.

7.10. Example 7: Cells engineered for complete growth factor-independence using IGF1 and FGF2

[0386] In this example chicken cells were engineered to assess whether expression of IGF1 WT and an FGF2 variant enables growth-factor independence (no requirement for growth factors in culture media).

[0387] Chicken cells engineered to express IGF1 WT (IGF1 amino acid sequence of were engineered with an FC550A empty vector (“EV”) control or a Phi31 vector containing one or more FGF2 variants, including chicken (Chicken FGF2), bovine (Bovine FGF2), salmon (Salmon FGF2), heat stable variants (FGF2-Q68I-N114G, FGF2-Q68I-C99S-N114G), secretion tagged variants (ggIL2-FGF2, hIL2-co1-ggFGF2(xMet)) or variants that preserve amino acids for non-canonical secretion (FGF2-C77-Y81)). Controls consisted of dual empty

vector (EVmRuby and EVeBFP2) that were used to construct the IGF1 and FGF2 variants, respectively, and were grown with or without growth factors IGF1 (10 μ g/L) and FGF2 (100 μ g/L) (see **FIG. 26**). Cells were grown in suspension over 4 passages using a 2 day passaging cadence at initial seeding density of 0.5E6 cells/mL (N=2). One way ANOVA performed compared to EV control in growth factor-free media, Not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), and $p < 0.0001$ (****).

[0388] As shown in **FIG. 26**, each cell line expressing IGF1 WT and a FGF2 variant resulted in increased viable cell density as compared to the controls. Overall, this data showed that cell lines engineered to express IGF1 WT and a FGF2 variant significantly increased the viable cell density as compared to controls.

7.11. Example 8: Cells engineered for complete growth factor-independence using IGF1 and a FGF2 Receptor

[0389] In this example chicken cells were engineered to assess whether expression of IGF1 WT and an FGF2 receptor variant enables growth-factor independence (no requirement for growth factors in culture media).

[0390] Chicken cells engineered to express IGF1 WT (IGF1 amino acid sequence of were transduced with an FC550A empty vector ("EV") control or a Phi31 vector containing one or more of: FGFR1c-N546K, FGFR1c-V561M, myrist-FGFR1c-K656E, FGFR3-N540K, FGFR3-K650E, FGFR3-N540K-K650E, or myrist-FGFR3-K650E. Controls consisted of dual empty vector (EVmRuby and EVeBFP2) that were used to construct the IGF1 and FGF2 variants, respectively, and were grown with or without growth factors IGF1 (10 μ g/L) and FGF2 (100 μ g/L) (see **FIG. 27**). Cells were grown in suspension over 3 passages using a 2 day passaging cadence at initial seeding density of 0.5E6 cells/mL (N=2). One way ANOVA was performed compared to EV control in growth factor-free media: not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), and $p < 0.0001$ (****).

[0391] As shown in **FIG. 27**, each cell line expressing IGF1 WT and a FGF receptor variant resulted in increased viable cell density as compared to the controls. Overall, this data showed that cell lines engineered to express IGF1 WT and a FGF receptor variant significantly increased the viable cell density as compared to controls.

7.12. Example 9: Cells engineered for complete growth factor-independence using FGF2 Receptors

[0392] In this example chicken cells were engineered to assess whether expression of an FGF2 receptor alone was sufficient to enable growth-factor independence (no requirement for growth factors in culture media).

[0393] Chicken cells were engineered to expressed FGFR2 and were grown in suspension in a 3 passage proliferation study on a 2-day passaging cadence and initial seeding density of 0.5E6 cells/mL (N=2). Cells were grown in media with or without IGF1 (10ug/L) and FGF2 (100ug/L) (see **FIG. 28**). Naïve (no transduced chicken cells) were used as controls. **FIG. 28** shows viable cell density at day 2 of passage 3. One way ANOVA performed compared to Naive controls, Not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***) $p < 0.0001$ (****).

[0394] As shown in **FIG. 28**, engineering the chicken cells to express FGFR alone was, to Applicant's surprise, sufficient to enable both FGF2 and IGF independent proliferation, albeit at slight lower levels than the naïve chicken cells grown in the presence of FGF2 and IGF1.

7.13. Example 10: Cells engineered for complete growth factor-independence using FGF2

[0395] In this example chicken cells were engineered to assess whether expression of an FGF2 variant alone was sufficient to enable growth-factor independence (no requirement for growth factors in culture media).

[0396] Chicken cells were engineered to express: FGF2 (wild type (FIG. 31A): chicken FGF2, bovine FGF2, salmon FGF2; heat stability point mutations (FIG. 31B): chicken FGF2-Q68I-N114G or chicken FGF2-Q68I-C99S-N114G; and FGF2 with a secretion signal or variant to preserve amino acid for non-canonical secretion (FIG. 31C): chicken FGF2-C77Y8a, ggIL2-ggFGF2, and hIL2-co1-(xMet)ggFGF2). These cells were grown in growth factor-free media (ACF media) over 4 passages on 2 day passaging cadence with initial seeding density of 0.5E6 cells/mL (N=2). Naive and empty vector (EV) controls were grown in growth factor containing media (10μg/L IGF1 and 100μg/L FGF2) or growth factor-free media (0μg/L IGF1 and 0μg/L FGF2). **FIGs. 29A-29C** shows viable cell density measurements taken over the course of about 200 hours in culture. Notably, controls grown in growth factor free media died by passage 3 (see **FIGs. 29A-29C**). **FIG. 30** shows summary of VCD data from **FIGs. 29A-29C** at passage 4 day 2 (N=2). One way ANOVA

was performed compared to empty vector control in growth factor containing media: not significant (n.s.), $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), and $p < 0.0001$ (****).

[0397] Overall, this data showed that chicken cells engineered to express FGF2 from different species (chicken, bovine, and salmon) can be used to maintain VCD (viable cell density) over 200 hours in culture as compared to controls, and in some instances, increase VCD compared to controls (**FIG. 29A** and **FIG. 30**). This data also showed that chicken cells engineered to express FGF2 variants that have amino acid substitutions that increase heat stability can be used to maintain VCD (viable cell density) over 200 hours in cultures as compared to controls, and in some instances, increase VCD compared to controls (**FIG. 29B** and **FIG. 30**). Lastly, this data showed that chicken cells engineered to express FGF2 designed with secretion signals or variants to preserve non-canonical secretion could be used to maintain VCD (viable cell density) over 200 hours in cultures as compared to controls, and in some instances, increase VCD compared to controls (**FIG. 29C** and **FIG. 30**).

7.14. Example 11: Cells engineered for complete growth factor-independence using FGF2 receptors alone

[0398] In this example chicken cells were engineered to assess whether expression of an FGF2 receptor variant alone was sufficient to enable growth-factor independence (no requirement for growth factors in culture media) (see **FIGS. 31A-31C** and **FIG. 32**).

[0399] In a first set of experiments, chicken cells were engineered to express an FGFR1c-N546K, FGF1Rc-V561M, and myrist-FGF1Rc-K656E and were grown in growth factor-free media over 4 passages on 2 day passaging cadence with initial seeding density of 0.5×10^6 cells/mL (N=2) (see **FIG. 31A**). Naive and empty vector (EV) controls were grown in growth factor containing media ($10 \mu\text{g/L}$ IGF1 and $100 \mu\text{g/L}$ FGF2) or growth factor-free media ($0 \mu\text{g/L}$ IGF1 and $0 \mu\text{g/L}$ FGF2).

[0400] **FIG. 31A** and **FIG. 32** show viable cell density (VCD) for chicken cells engineered to express an FGFR1c-N546K, FGF1Rc-V561M, and myrist-FGF1Rc-K656E over 4 passages. Controls grown in growth factor free media died by passage 3 (see **FIG. 31A**). **FIG. 31A** shows daily viable cell densities over 4 passages in ACF media. Overall, this data showed that chicken cells engineered to express these FGFR1c variants can be used to maintain VCD (viable cell density) over 200 hours similar to controls, and in some instances, increase VCD compared to controls.

[0401] In a second set of experiments, chicken cells were engineered to express FGFR2 and were grown in growth factor-free media over 4 passages on 2 day passaging cadence with initial seeding density of 0.5E6 cells/mL (N=2) (see **FIG. 31B**). Naive and empty vector (EV) controls were grown in growth factor containing media (10µg/L IGF1 and 100µg/L FGF2) or growth factor-free media (0µg/L IGF1 and 0µg/L FGF2).

[0402] **FIG. 31B** and **FIG. 32** show viable cell density (VCD) for chicken cells engineered to express an FGFR2 over 4 passages. Controls grown in growth factor free media died by passage 3 (see **FIG. 31B**). Overall, this data showed that chicken cells engineered to express FGFR2 can be used to maintain VCD (viable cell density) over 200 hours in culture similar to controls, and in some instances, increase VCD compared to controls.

[0403] In a third set of experiments, chicken cells were engineered to express FGFR3-N540K, FGFR3-K650E, FGFR3-N540K-K560E, or myrist-FGFR3-K650E and were grown in growth factor-free media over 4 passages on 2 day passaging cadence with initial seeding density of 0.5E6 cells/mL (N=2) (see **FIG. 31C**). Naive and empty vector (EV) controls were grown in growth factor containing media (10µg/L IGF1 and 100µg/L FGF2) or growth factor-free media (0µg/L IGF1 and 0µg/L FGF2).

[0404] **FIG. 31C** and **FIG. 32** show viable cell density (VCD) for chicken cells engineered to express these FGFR3 variants over 4 passages. Controls grown in growth factor free media died by passage 3 (see **FIG. 31C**). Overall, this data showed that chicken cells engineered to express FGFR3 (or variants thereof) can be used to maintain VCD (viable cell density) over 200 hours in culture similar to controls, and in some instances, increase VCD compared to controls.

[0405] To Applicant's surprise, expression of FGF2R receptors alone enabled the serum free proliferation of chicken cells without the need for IGF1 and FGF2 exogenous supplementation. Cell growth is typically limited in the absence of IGF1 and is needed to achieve robust cell proliferation and high cell densities.

7.15. Example 12: Cells engineered to express PDGF (or variants thereof) or PDGF receptor (or variants thereof) enabled tissue formation in growth factor-free media

[0406] This experiment was designed to assess how expressing PDGF (or PDGF variants) or PDGF receptor (or PDGF receptor variants) enabled tissue formation (as measured by Wet Mass per Area (µg/cm²) (see **FIG. 33**)).

[0407] In particular, chicken cells were transduced with either an FC550A empty vector (“EV”) control or a Phi31 vector containing PDGFRa-D842V, PDGF(WT) or PDGF-211*. Controls included: cell lines not transfected (“Naïve”) and the EV control. Engineered cells and controls were cultured in roller bottles over 14 day period in serum free media. Controls were grown with or without 50µg/L PDGF (N=4). Tissue was harvested after 14 days culture and weighed for wet mass and normalized to growth area.

[0408] FIGs. 33 shows chicken cells engineered to express PDGFRa-D842V, PDGF(WT) or PDGF-211* formed tissue without media supplemented growth factors and was comparable to positive controls. Overall, this data showed that chicken cells engineered to express PDGF (or a variant thereof) or a PDGF receptor (or a variant thereof) formed tissue when grown in media not supplemented with growth factors and did so in comparable volume to positive controls. Therefore, these cells lines are ideal for use in cell-based meat products and cell-based food products suitable for consumption because they can endure the requisite culture conditions (i.e., extensive passaging) needed to make these products all while reducing the costs associated with using the vast amounts of exogenous growth factors traditionally needed to make these products.

7.16. Example 13: Methods for producing cell-based meat suitable for consumption

[0409] The manufacturing of cultured muscle cells suitable for consumption, in one exemplary protocol, can comprise:

[0410] In exemplary first step, cells are engineered to express the coding sequence of a growth factor ligand (e.g., FGF2, IGF1, PDGF, or a combination thereof), a growth factor receptor or activated growth factor receptor (e.g., a FGFR, an IGF1R, or an PDGFR), where the cells are from a livestock, poultry, game, or an aquatic animal species. Engineered cells are adapted to suspension culture and cultured in a cultivation infrastructure (e.g., any of the cultivation infrastructures described herein), seeded onto a substrate consisting of peptide-coated tissue-culture treated plastic in a standard growth medium at a density of 7.5×10^3 cells/cm² and cultured at 37° C under 5% CO₂ atmospheric conditions. As cultures approach 80% confluence, cells are enzymatically dissociated and the cells are expanded. This process is repeated until the total number of cells harvested following dissociation exceeds about 1.0×10^8 cells, or more. The engineered cells are cryopreserved and stored in a cryopreserved cell bank. Cells harvested in quantities equal to or exceeding 1.0×10^8 cells.

[0411] In an exemplary second step, the cryopreserved cells are seeded and cultivated in a cultivation infrastructure. In accordance with the cultivation scale desired, one or more vials from the master cell bank is rapidly thawed to room temperature. The cryopreservation medium is removed from the cells by a 5-minute, 300×g centrifugation step. Cells are suspended in standard growth medium and seeded onto a gelatin-coated cultivation substrate in standard growth medium as before, except that, on the final passage prior to harvest, the cells are permitted to proliferate to 100% confluence on the cell culture substrate. The cells are adapted for suspension culture in growth media to facilitate expansion of the cells. Following expansion, the cells are adapted to adherent culture in a cultivation infrastructure. The growth medium is exchanged for differentiation medium, thereby inducing myogenic differentiation where the differentiated cells form myocytes and multinucleated myotubes; and the myocytes and myotubes are cultured to generate skeletal muscle fibers.

[0412] In an exemplary fourth step, the engineered cells are harvested for dietary consumption. After the cells have proliferated to confluence, the culture medium is removed, and the adherent cell cultures are rinsed with phosphate buffered saline. Next, the confluent biomass of adherent cells are mechanically, fluidically, enzymatically, or metabolically dissociated from the substrate by means of a scraping device, pressurized fluid, or a harvest media. The dissociated biomass is collected into centrifuge tubes, pelleted to remove excess liquid, and processed for food product preparation.

7.17. **Example 14: Procurement of engineered cells and growth of cells into a cell mass**

[0413] **FIGS. 34A-34D** and the following accompanying paragraphs describe procurement of cells and growth of cells into a cell mass in accordance with one or more embodiments. Generally, **FIGS. 34A-34D** illustrate a process of collecting cells from an animal, growing cells in a favorable environment, banking successful cells, and collecting cells into a cell mass followed by de-wetting and/or other treatments.

[0414] As illustrated by step 3402 in **FIG. 34A**, tissue is collected from a living animal via biopsy. In particular, stem cells, mesenchymal progeny, ectoderm lineage, and/or endoderm lineages can be isolated from the removed tissue. In some implementations of the present disclosure, tissue, such as fat and others, are processed to isolate stem cells, mesenchymal, ectoderm, and/or endoderm progeny or lineage cells. As illustrated, tissue 3404 is removed from an animal. In some examples, the tissue 3404 is removed from a living animal by taking

a skin sample from the living animal. For instance, skin or muscle samples may be taken from a chicken, cow, fish, shellfish or another animal.

[0415] Cells may be extracted from the tissue 3404 that was removed from the animal. More specifically, the tissue 3404 is broken down by enzymatic and/or mechanical means. To illustrate, **FIG. 34A** includes digested tissue 3406 that comprises the cells to be grown in cultivation.

[0416] Cells in the digested tissue 3406 may be proliferated under appropriate conditions to begin a primary culture. As illustrated in **FIG. 34A**, cells 3408 from the digested tissue 3406 are spread on a surface or substrate and proliferated until they reach confluence. As shown in **FIG. 34A**, in some cases, cells 3412 have reached confluence when they start contacting other cells in the vessel, and/or have occupied all the available surface or substrate.

[0417] In some examples, cells are stored and frozen (i.e., banked) at different steps along the cell culture process. Cryopreservation generally comprises freezing cells for preservation and long-term storage. In some implementations, tissue and/or cells are removed from a surface or substrate, centrifuged to remove moisture content, and treated with a protective agent for cryopreservation. For example, as part of cryopreservation, tissues and cells are stored at temperatures at or below -80C. The protective agent may comprise dimethyl sulfoxide (DMSO) or glycerol.

[0418] Cells stored through cryopreservation may be used to replenish working cell stock. For instance, while a portion of the digested tissue 3406 is used as the cells 3408 spread on a surface or substrate, the remaining or excess digested tissue 3406 is transferred to cryovials 3410 for storage. Furthermore, the cells 3412 may be banked once reaching confluence and stored in cryovials 3414.

[0419] Once the cells 3412 have reached confluence, or just before the cells 3412 have reached confluence (e.g., occupation of about 80% of the substrate), the disclosed process comprises a series of cell passage steps. During cell passage, the cells 3412 are divided into one or more new culture vessels for continued proliferation. To illustrate, the cells 3412 may be diluted or spread on one or more surfaces or substrates to form the cells 3418. The cells 3418 are then grown 3416 to confluence, or just before confluence.

[0420] The cycle of dividing the cells 3412 into the cells 3418 for continued proliferation in new culture vessels may be repeated for a determined number of cycles. Typically, cell

lines derived from primary cultures have a finite life span. Passaging the cells allows cells with the highest growth capacity to predominate. In one example, cells are passaged for five cycles to meet a desired genotypic and phenotypic uniformity in the cell population.

[0421] In some implementations, the disclosed method comprises immortalizing cells that have been grown and passaged for the determined number of cycles. For instance, the cells 3418 may be immortalized. As shown in **FIG. 34B**, cells 3420 have demonstrated a preferred growth capacity to proceed to immortalization. To achieve immortalization, the disclosed process transfects the cells 3420 with genes of interest. In one example telomerase reverse transcriptase (TERT) is introduced to the cells 3420. In some embodiments, the cells may be subjected to a selection process as known by those skilled in the art. The cells 3420 may then be passaged for a predetermined set of passaging cycles. In one example passaging cycle, the cells 3420 are grown to (or near) confluence 3424, then they are reseeded in new growth vessels, preserved in vials 3422, or some combination of both. The disclosed process may include any number of passaging cycles to ensure that the cells have reached immortality (e.g., can passage 60+ times without senescing), a target growth capacity, and/or a target quantity for banking. For example, cells may be passaged until they have reached a passage level of 100 (e.g., have been passaged for 100 passaging cycles). In another example, cells are passaged until they reach a population doubling level of 100.

[0422] Cells that have reached immortality or a target growth capacity by living through a target passage level may be adapted to suspension culture. In one example, a suspension culture media and agitation of cells in this suspension environment help cells to adapt and start proliferating in the new growth environment. The cells adapted to suspension 3426 may be stored in cryovials 3428 for cryopreservation and banking. Cells in suspension 3426 will begin to proliferate and the process begins a series of dilute and expand steps.

[0423] During dilution and expansion, cells are moved from growth vessels into newer, and progressively larger, growth vessels. For example, cells in suspension 3426 may begin in a single tube. The cells will proliferate and increase in cellular density. Once the cells have reached a target cell number (i.e., viable cell density (VCD) at desired volume), they are diluted and moved to a larger growth vessel. Optionally, the cells are banked in cryovials throughout expansion. For example, once cells in suspension reach a maximum VCD, the cells may begin to leave exponential growth due to overcrowding. After reaching a target density, the suspension cells may be transferred to a larger vessel 3430 and diluted with additional media. The dilute-and-expand steps are repeated using progressively larger vessels

(e.g., the vessel 3431 and the vessel 3432) and/or progressive dilution until the cells reach a production-ready volume. For example, cells may be production ready at about a 1,000 - 100,000 liter scale at 5 million cells per mL. The cells may be banked in cryovials at any of the dilution and expansion cycles.

[0424] As part of preparing cells to form cell-based-meat products, the disclosed process comprises growing the cells as an adherent culture. Generally, cells that are grown attached to a substrate form a texture that more closely resembles tissue found in conventional meat. Thus, the cells may be transferred from growth in suspension to growth in an adherent reactor. For example, the cells grown in suspension in the vessel 3432 may be transferred to growth on a substrate. **FIG. 34C** illustrates a bioreactor system comprising a plurality of adherent bioreactors 3448 connecting in parallel to a media vessel 3440. The media vessel 3440 holds the cells grown in suspension media. In some implementations, cells from the vessel 3432 are transferred directly to a cell culture media (or just “media”) vessel 3440. In one example, the media vessel 3440 comprises the vessel 3432. The adherent bioreactors 3448 may comprise pipe-based bioreactors. As shown, a plurality of valves 3444 is secured to the plurality of adherent bioreactors 3448 to enable individual use and access of each of the adherent bioreactors 3448. For instance, to limit flow to only a first bioreactor of the plurality of adherent bioreactors 3448, the valve 3444 of the first bioreactor is opened while the remaining valves 3444 are closed. Furthermore, the bioreactor system can include a directional valve 3442 for changing between flow directions.

[0425] In some implementations, and as illustrated in **FIG. 34C**, cells (e.g., adherent cells or suspension adapted cells) are prepared by flowing cells suspended in media (e.g., cell culture media) across substrates in the plurality of adherent bioreactors 3448. More particularly, cells from the media vessel 3440 may contact or land on the substrates in the plurality of adherent bioreactors 3448. Cells and media that flowed through the adherent bioreactors 3448 are cycled back to the media vessel 3440. The media and cells can be cycled through the adherent bioreactors 3448 until a target adherent cell density is reached. For instance, in some implementations, the disclosed method comprises measuring a cell density of outflow from the adherent bioreactors 3448 to infer an adherent cell density.

[0426] The cells grow into adherent tissue within the adherent bioreactors 3448. Once they have grown to a target density, either according to a learned timing or according to a measured fluctuation in cell metabolism of components such as glucose and oxygen, then the adherent tissue is ready for removal. The removal process of the disclosed method uses a

high-pressure flow to shear the adherent tissue off the substrate surfaces. In one example, wash buffer from a wash tank 3456 is flowed across the substrates in the adherent bioreactors 3448. The wash buffer and cell mixture are flowed through a filter 3452 where the cells are collected into one or more cell masses 3454.

[0427] The cell masses 3454 may be further processed to adjust moisture content. **FIG. 34D** illustrates an example apparatus for reducing moisture content in the cells. In particular, **FIG. 34D** illustrates a pressure apparatus 3460 that compresses the cell masses 3458a and 3458b. While **FIG. 34D** illustrates a mechanical method for adjusting moisture content of the cell masses 3458a and 3458b, other methods may be used to adjust moisture content. For example, the cell masses 3458a and 3458b may be mixed with a drying agent, vacuum dried, centrifuged, or otherwise dried. A moisture-adjusted-cell mass may be transferred to a container 3462 for additional processing. For example, the cell mass 3458a or 3458b may be removed from the container 3462 to be formed into a cell-based-meat product.

8. SEQUENCE APPENDIX

SEQ ID NO:	Description	Sequence
1	ggFGF2-Wild Type (chicken)	MAAGAAGSITLTPALPDDGGGGAFFPGHFKDPKRLYCKNGGFFLRINPDGRVDGVREKSDPHIKLQLQAEERGVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
2	ggFGF2STAB (Thermal Stabilized)	MAAGAAGSITLTPALPDDGGGGAFFPGHFKDPKRLYCKNGGFFLRINPDGRVDGTREKSDPFIKLQLQAEERGVSANRFLAMKEDGRLLYALKYATEECFFFERLENNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
3	BM40sp-ggFGF2	MRAWIFFLLCLAGRALAMAAGAAGSITLTPALPDDGGGGAFFPGHFKDPKRLYCKNGGFFLRINPDGRVDGVREKSDPHIKLQLQAEERGVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
4	ggIL2-ggFGF2	MMCKVLIFGCISVAMLMTTAYMAAGAAGSITLTPALPDDGGGGAFFPGHFKDPKRLYCKNGGFFLRINPDGRVDGVREKSDPHIKLQLQAEERGVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
5	Gluc-ggFGF2	MGVKVLFALICIAVAEAMAAGAAGSITLTPALPDDGGGGAFFPGHFKDPKRLYCKNGGFFLRINPDGRVDGVREKSDPHIKLQLQAEERGVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
6	cohIL2-ggFGF2	MYRMQLLSIALSLALVTNSMAAGAAGSITLTPALPDDGGGGAFFPGHFKDPKRLYCKNGGFFLRINPDGRVDGVREKSDPHIKLQLQAEERGVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
7	cohIL2co1-ggFGF2	MRRMQLLLIALSLALVTNSMAAGAAGSITLTPALPDDGGGGAFFPGHFKDPKRLYCKNGGFFLRINPDGRVDGVREKSDPHIKLQLQAEERGVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
8	cohIL2co2-ggFGF2	MRRMQLLLIALSLALVTNSMAAGAAGSITLTPALPDDGGGGAFFPGHFKDPKRLYCKNGGFFLRINPDGRVDGVREKSDPHIKLQLQAEERGVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*

SEQ ID NO:	Description	Sequence
		SANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
9	ggIL2-FGF2STAB	MMCKVLIFGCISVAMLMTTAYMAAGAAGSITTLPALPDDGGGGAFPPGHFKDPKRL YCKNGGFLLINPDGRVDGTREKSDPFIKLQLQAEERGVSIGKVSANRFLAMKEDGRLYALKYATEECFFFERLEENNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
10	hIL2-ggFGF2STAB	MYRMQLLSICIALSLALVTNSMAAGAAGSITTLPALPDDGGGGAFPPGHFKDPKRL YCKNGGFLLINPDGRVDGTREKSDPFIKLQLQAEERGVSIGKVSANRFLAMKEDGRLYALKYATEECFFFERLEENNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
11	ggIL6-ggFGF2	MNFTEGCEATGRRPGSAGSRRRRAPRPGPVALLPLLLPLLPAAAVPLPM AAGAAGSITTLPALPDDGGGGAFPPGHFKDPKRL YCKNGGFLLINPDGRVDGVREKSDPHIKLQLQAEERGVSIGKVSANRFLAMKEDGRLLALKCA TEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
12	hIL2-ggFGF2	MNSFSTSAFGPVAFSLGLLLVLPAAFPAPMAAGAAGSITTLPALPDDGGGGAFPPGHFKDPKRL YCKNGGFLLINPDGRVDGVREKSDPHIKLQLQAEERGVSIGKVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
13	hIL2-ggFGF2	MYRMQLLSICIALSLALVTNSMAAGAAGSITTLPALPDDGGGGAFPPGHFKDPKRL YCKNGGFLLINPDGRVDGTREKSDPFIKLQLQAEERGVSIGKVSANRFLAMKEDGRLYALKYATEECFFFERLEENNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
14	hIFNa2-ggFGF2	MALTFALLVALLVLSCKSSCSVGMVSKMAAGAAGSITTLPALPDDGGGGAFPPGHFKDPKRL YCKNGGFLLINPDGRVDGVREKSDPHIKLQLQAEERGVSIGKVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
15	secrecon-ggFGF2	MWWRLWWLLLLLLLLWPMVWAMAAGAAGSITTLPALPDDGGGGAFPPGHFKDPKRL YCKNGGFLLINPDGRVDGVREKSDPHIKLQLQAEERGVSIGKVSANRFLAMKEDGRLLALKCATEECFFFERLESNNYNTYRSRKYSWYVALKRTGQYKPGPKTGPQGKAILFLPMSAKS*
16	ggIGF1-WT	MEKINSLSLQVKKCCFDFLKVKMHTVSYIHFFYLGLCLLTSSAAAGPE TL CGAELVDALQFVCGDRGFYFSKPTGYGSSSRRLHHKGIVDECCFQSCD LRRLEMYCAPIKPPKSARSVRAQRHTDMPKAQKEVHLKNTSRGNTGNRN YRM*
17	ggIGF1-truncated	MGPETL CGAELVDALQFVCGDRGFYFSKPTGYGSSSRRLHHKGIVDECCFQSCD LRRLEMYCAPIKPPKS*
18	ggPDGFb	MCPQPARLEPGMNFVGFVAVILSLPLARLEGDPIEDIYEILGGSSVRSISDL QRALRIDSVEEDSSSLDLNATQPSQNHVSLSRERRSLDALAAEPAVLAEC KTRTVVFEISRDMVDSTNANFVWPPCVEVQRCGSCCNRNVQCRPMQIRVRHVQVNKIEFFQRKPIFKKVIIVPLEDHVQCRCEVVSRRPPSRNPASRE QRRFSPSFTTAAISQKRKRVRPPAQKRKHKKYKHVNDKKVLKEILIA*
19	ggPDGFb-211STOP	MCPQPARLEPGMNFVGFVAVILSLPLARLEGDPIEDIYEILGGSSVRSISDL QRALRIDSVEEDSSSLDLNATQPSQNHVSLSRERRSLDALAAEPAVLAEC KTRTVVFEISRDMVDSTNANFVWPPCVEVQRCGSCCNRNVQCRPMQIRVRHVQVNKIEFFQRKPIFKKVIIVPLEDHVQCRCEVVSRRPPSRNPASRE QRRFSPSFTTAAISQ*
20	F-9C-SRG	MADYKDDDDKKGGIIVAILLLIVMLAIEILLITLIIAVTSGGSG*
21	9C-SRG	MAKGGIIVAILLLIVMLAIEILLITLIIAVTSGGSG*
22	IL2 (human) ("hil2" or "hIL2") Signal peptide	MYRMQLLSICIALSLALVTNS
23	IL2-CO1 (human) ("hil2col1")	MRMQLLLIALSLALVTNS

SEQ ID NO:	Description	Sequence
	Signal peptide	
24	IL2-CO2 (human) ("hil2col2") Signal peptide	MRRMQLLLLLIALSLALVTNS
25	IL2 (chicken) ("ggil2" or "ggIL2") Signal peptide	MMCKVLIFGCISVAMLMTTAY
26	IFNa (human) ("hIFNA") Signal peptide	MALTFALLVALLVLSCSSCSVGMVSK
27	IL6 (human) ("hil6") Signal peptide	MNSFSTSAFGPVAFSLGLLLVLPAAFPAP
28	IL6 (chicken) ("ggil6") Signal peptide	MNFTEGCEATGRRPGSAGSRRRRAPRPGPVALLPLLLPLLLPPAAAVPLP
29	Gaussia Luciferase ("GLuc") Signal peptide	MGVKVLFALICIAVAEA
30	Secrecon Signal peptide	MWWRLWWLLLLLLLLWPMVWA
31	BM40 signal peptide	MRAWIFFLLCLAGRALA
	Signal peptide	
32	FGFR1-WT	MFTWRCLILWAVLVTATLSAARPAPTLPDQALPKANIEVESHAHPGDLLQLRCRLRDDVQSINWVRDGVQLPENNRRITRITGEEVEVRDAVPEDSGLYACMTNSPSGSETTYFSVNVSDALPSAEDDDDDSSSEEKADNTKPNQAVAPYWTYPEKMEKKLHAVPAAKTVKFKCPSGGTPNPTRLWLKNGKEFKPDHRIGGYKVRYATWSIIMDSVVP SDKGNYTCIVENKYGSINHTYQLDVVERSPHRPILQAGLPANKTV ALG SNVEFVCKVYSDPQPHIQWLKHIEVNGSKIGPDNL PYVQILKTAGVNTTDKEMEVLHLRNVSFEDAGEYTCLAGNSIGISHSAWLT VLEATEQSPAMMTSPLYLEIIYCTGAFLISCMVVTVIIYKMKSTTKKTD FNSQLAVHKLAKSIPLRRQVTVSADSSSSMNSGVMLVRPSRLSSSGTPMLAGVSEYELPEDPRWELPRDRLILGKPLGEGCFGQVVLAEI GLDKDKPNRVTKVAVKMLKSDATEKDLSDLISEMEMMKMIGKHKNII LLGACTQDGPLYVIVEYASKGNLREYLQARRPPGMEYCYNPTRIPEEQLSFKDLVSCAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFG LARDIHHIDYYKKTNGRLPVK WMAPEALFDRIYTHQSDVWSFGVLLWEIFTLGGSPYPGVPVEELFKLLKEGHRMDKPSNCTNELYMMMRDCWHAVPSQRPTFKQLVEDLDRIVAMTSNQEYLDLSVPLDQYSPGF PATRSSTCSSGEDSVF SHDPLDEPCLPRCPPHSHGALKRH*
33	FGFR1-N546K	MFTWRCLILWAVLVTATLSAARPAPTLPDQALPKANIEVESHAHPGDLLQLRCRLRDDVQSINWVRDGVQLPENNRRITRITGEEVEVRDAVPEDSGLYACMTNSPSGSETTYFSVNVSDALPSAEDDDDDSSSEEKADNTKPNQAVAPYWTYPEKMEKKLHAVPAAKTVKFKCPSGGTPNPTRLWLKNGKEFKPDHRIGGYKVRYATWSIIMDSVVP SDKGNYTCIVENKYGSINHTYQLDVVERSPHRPILQAGLPANKTV ALG SNVEFVCKVYSDPQPHIQWLKHIEVNGSKIGPDNL PYVQILKTAGVNTTDKEMEVLHLRNVSFEDAGEYTCLAGNSIGISHSAWLT VLEATEQSPAMMTSPLYLEIIYCTGAFLISCMVVTVIIYKMKSTTKKTD FNSQLAVHKLAKSIPLRRQVTVSADSSSSMNSGVMLVRPSRLSSSGTPMLAGVSEYELPEDPRWELPRDRLILGKPLGEGCFGQVVLAEI GLDKDKPNRVTKVAVKMLKSDATEKDLSDLISEMEMMKMIGKHKNII LLGACTQDGPLYVIVEYASKGNLREYLQARRPPGMEYCYNPTRIPEEQLSFKDLVSCAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFG LARDIHHIDYYKKTNGRLPVK WMAPEALFDRIYTHQSDVWSFGVLLWEIFTLGGSPYPGVPVEELFKLLKEGHRMDKPSNCTNELYMMMRDCWHAVPSQRPTFKQLVEDLDRIVAMTSNQEYLDLSVPLDQYSPGF PATRSSTCSSGEDSVF SHDPLDEPCLPRCPPHSHGALKRH*

SEQ ID NO:	Description	Sequence
		CAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFGLARDIHHI DYYKKTNGRLPVKWMapeALFDRIYTHQSDVWSFGVLLWEIFTLGGSP YPGVPVEELFKLLKEGHRMDKPSNCTNELYMMMRDCWHA VPSQRPTFK QLVEDLDRIVAMTSNQEYLDLSVPLDQYSPGFATRSTCSSGEDSVFSDH PLPDEPCLPRCPHSHGALKRH*
34	FGFR1-K656E	MFTWRCLILWAVLVTATLSAARPAPTLPDQALPKANIEVESHSAPGDL QLRCRLRDDVQSINWVRDGVQLPENNRTRITGEEVEVRDAVPEDSGLYA CMTNSPSGSETTYFSVNVSDALPSAEDDDDEDDSSSEEKADNTKPNQAV APYWTYPEKMEKKLHAVPAAKTVKFKCPSGGTPNPTLRWLKNGKEFKPD HRIGGYKVRYATWSIIMDSVVP SDKGNYTCIVENKYGSINHTYQLDVVER SPHRPILQAGLPANKTVALGSNVEFVCKVYSDPQPHIQWLKHIEVNGSKIG PDNLPLYVQILKTAGVNTTDKEMEVLHLRNVSFEDAGEYTCLAGNSIGISH HSAWLTVLEATEQSPAMMTSPLYLEIIYCTGAFLISCMVVTVIIYKMKSTT KKTDFNSQLAVHKLAKSIPLRRQVTVSADSSSMNSGVMLVRPSRLSSSG TPMLAGVSEYELPEDPRWELPRDRLILGKPLGEGCFGQVVLAEAIGLDKD KPNRVTKVAVKMLKSDATEKDLSLISEMEMMKMIGKHKNINLLGACT QDGPLYVIVEYASKGNLREYLQARRPPGMEYCYNPTRIPEEQLSFKDLVS CAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFGLARDIHHI DYYKKTNGRLPVKWMapeALFDRIYTHQSDVWSFGVLLWEIFTLGGSP YPGVPVEELFKLLKEGHRMDKPSNCTNELYMMMRDCWHA VPSQRPTFK QLVEDLDRIVAMTSNQEYLDLSVPLDQYSPGFATRSTCSSGEDSVFSDH PLPDEPCLPRCPHSHGALKRH*
35	FGFR1-N546K-K656E-S780A	MFTWRCLILWAVLVTATLSAARPAPTLPDQALPKANIEVESHSAPGDL QLRCRLRDDVQSINWVRDGVQLPENNRTRITGEEVEVRDAVPEDSGLYA CMTNSPSGSETTYFSVNVSDALPSAEDDDDEDDSSSEEKADNTKPNQAV APYWTYPEKMEKKLHAVPAAKTVKFKCPSGGTPNPTLRWLKNGKEFKPD HRIGGYKVRYATWSIIMDSVVP SDKGNYTCIVENKYGSINHTYQLDVVER SPHRPILQAGLPANKTVALGSNVEFVCKVYSDPQPHIQWLKHIEVNGSKIG PDNLPLYVQILKTAGVNTTDKEMEVLHLRNVSFEDAGEYTCLAGNSIGISH HSAWLTVLEATEQSPAMMTSPLYLEIIYCTGAFLISCMVVTVIIYKMKSTT KKTDFNSQLAVHKLAKSIPLRRQVTVSADSSSMNSGVMLVRPSRLSSSG TPMLAGVSEYELPEDPRWELPRDRLILGKPLGEGCFGQVVLAEAIGLDKD KPNRVTKVAVKMLKSDATEKDLSLISEMEMMKMIGKHKNINLLGACT QDGPLYVIVEYASKGNLREYLQARRPPGMEYCYNPTRIPEEQLSFKDLVS CAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFGLARDIHHI DYYKKTNGRLPVKWMapeALFDRIYTHQSDVWSFGVLLWEIFTLGGSP YPGVPVEELFKLLKEGHRMDKPSNCTNELYMMMRDCWHA VPSQRPTFK QLVEDLDRIVAMTSNQEYLDLSVPLDQYAPGFATRSTCSSGEDSVFSDH PLPDEPCLPRCPHSHGALKRH*
36	FGFR1-myrist-K656E	MGSSKSKPKDPSQRKMKSTTKTDFNSQLAVHKLAKSIPLRRQVTVSADS SSSMNSGVMLVRPSRLSSSGTPMLAGVSEYELPEDPRWELPRDRLILGKPL GEGCFGQVVLAEAIGLDKDKPNRVTKVAVKMLKSDATEKDLSLISEME MMKMIGKHKNINLLGACTQDGPLYVIVEYASKGNLREYLQARRPPGME YCYNPTRIPEEQLSFKDLVSCAYQVARGMEYLASKKCIHRDLAARNVLVT EDNVMKIADFGLARDIHHIDYYKKTNGRLPVKWMapeALFDRIYTHQSD VWSFGVLLWEIFTLGGSPYPGVPVEELFKLLKEGHRMDKPSNCTNELYM MMMRDCWHA VPSQRPTFKQLVEDLDRIVAMTSNQEYLDLSVPLDQYSPGF PATRSTCSSGEDSVFSDHPLPDEPCLPRCPHSHGALKRH*
37	FGF2-WT	MGLKSTWRYGNGPGTYSKKMVSWDSGCLICLVVVTMAGLSLARPSFNL VVEDATLEPEEPPTYQISQPDVHSALPGEPELRCQLKDAVMISWTKDG VPLGPDNRTVIIIGEYLQIKDASPRDSGLYACTAIRTLDSDTLFYFVNVTDAL SSGDDDDNDGSEDFVNDNSQMRAPYWTHTDKMEKRLHAVPAANTVKF RCPAMGNPTPTMRWLKNGKEFKQEHRIGGYKVRNQHWSLIMESVVP SDKGYTCIVENQYGSINHTYHLDVVERSPHRPILQAGLPANASAVVGDVE FVCKVYSDAQPHIQWIKHVERNGSKYGPDGLPYLQVLKAAGVNTDKEI EVLIRNVTFEDAGEYTCLAGNSIGISFHTAWLTVLPAPKEKEKEFPTSPDY L EIAIYCIGVFLIACMVLTVILCRMKNNTTKKPDFSSQPAVHKLTKRIPLRRQV

SEQ ID NO:	Description	Sequence
		SADSSSSMNSNTPLVRITTRLSTADAPMLAGVSEYELPEDPKWEFPRDKL TLGKPLGEGCFGQVVM AEAVGIDKDRPKEAVTVAVKMLKDDATEKDLS DLVSEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEYASKGNLREYLRA RRPPGMEYSFDINRVPEEQMTFKDLVSCTYQLARGMEYLASQKCIHRDLA ARNVLVTENNVMKIADFG LARDINNIDYKKTNGRLPVK WMAPEALFD RVYTHQSDVWSFGVLMWEIFTLGGSPYPGIPVEELFKLLKEGHRMDK PAN CTNELYMMMRDCWQAVPSQRPTFKQLVEDLDRILTLTTNEEYLDLSGPL EQYSPSYDPDTRSSCSSGDDSVFSPDPMPYEPCLPKYQHMNGSVKT*
38	FGF2-N550K	MGLKSTWRYGNGPGTYSKKMVS WDSGCLICLVVVTMAGLSLARPSFNL VVEDATLEPEEPPTKYQISQPDVHSALPGEPELRLCQLKDAVMISWTKDG VPLGPDNRTVIIGEYLQIKDASPRDSGLYACTAIRTLDSDTLFYFIVNVT DAL SSGDDDDNDGSEDFVND SNQMRAPYWTHTDKMEKRLHAVPAANTVKF RCPAMGNPTPTMRWLKNGKEFKQEHRIGGYKVRNQHWSLIMESVVPD KGNYTCIVENQYGSINHTYHLDVVERS PHRPILQAGLPANASAVVGGDVE FVCKVYSDAQPHIQWIKHVERNGSKY GPDGLPYLQVLKAAGVNTTDKEI EVLYIRNVT FEDAGEYTCLAGNSIGISFHTAWLTVLPAPEKEKEFPTSPDYL EIAIYCIGVFLIACMVLTVILCRMKN TTKKPDFSSQPAVHKLTKRIPLRRQV SADSSSSMNSNTPLVRITTRLSTADAPMLAGVSEYELPEDPKWEFPRDKL TLGKPLGEGCFGQVVM AEAVGIDKDRPKEAVTVAVKMLKDDATEKDLS DLVSEMEMMKMIGKHKNIKLLGACTQDGPLYVIVEYASKGNLREYLRA RRPPGMEYSFDINRVPEEQMTFKDLVSCTYQLARGMEYLASQKCIHRDLA ARNVLVTENNVMKIADFG LARDINNIDYKKTNGRLPVK WMAPEALFD RVYTHQSDVWSFGVLMWEIFTLGGSPYPGIPVEELFKLLKEGHRMDK PAN CTNELYMMMRDCWQAVPSQRPTFKQLVEDLDRILTLTTNEEYLDLSGPL EQYSPSYDPDTRSSCSSGDDSVFSPDPMPYEPCLPKYQHMNGSVKT*
39	FGF2-K660E	MGLKSTWRYGNGPGTYSKKMVS WDSGCLICLVVVTMAGLSLARPSFNL VVEDATLEPEEPPTKYQISQPDVHSALPGEPELRLCQLKDAVMISWTKDG VPLGPDNRTVIIGEYLQIKDASPRDSGLYACTAIRTLDSDTLFYFIVNVT DAL SSGDDDDNDGSEDFVND SNQMRAPYWTHTDKMEKRLHAVPAANTVKF RCPAMGNPTPTMRWLKNGKEFKQEHRIGGYKVRNQHWSLIMESVVPD KGNYTCIVENQYGSINHTYHLDVVERS PHRPILQAGLPANASAVVGGDVE FVCKVYSDAQPHIQWIKHVERNGSKY GPDGLPYLQVLKAAGVNTTDKEI EVLYIRNVT FEDAGEYTCLAGNSIGISFHTAWLTVLPAPEKEKEFPTSPDYL EIAIYCIGVFLIACMVLTVILCRMKN TTKKPDFSSQPAVHKLTKRIPLRRQV SADSSSSMNSNTPLVRITTRLSTADAPMLAGVSEYELPEDPKWEFPRDKL TLGKPLGEGCFGQVVM AEAVGIDKDRPKEAVTVAVKMLKDDATEKDLS DLVSEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEYASKGNLREYLRA RRPPGMEYSFDINRVPEEQMTFKDLVSCTYQLARGMEYLASQKCIHRDLA ARNVLVTENNVMKIADFG LARDINNIDYKKTNGRLPVK WMAPEALFD RVYTHQSDVWSFGVLMWEIFTLGGSPYPGIPVEELFKLLKEGHRMDK PAN CTNELYMMMRDCWQAVPSQRPTFKQLVEDLDRILTLTTNEEYLDLSGPL EQYSPSYDPDTRSSCSSGDDSVFSPDPMPYEPCLPKYQHMNGSVKT*
40	FGF2-N550K-N660E-S780A	MGLKSTWRYGNGPGTYSKKMVS WDSGCLICLVVVTMAGLSLARPSFNL VVEDATLEPEEPPTKYQISQPDVHSALPGEPELRLCQLKDAVMISWTKDG VPLGPDNRTVIIGEYLQIKDASPRDSGLYACTAIRTLDSDTLFYFIVNVT DAL SSGDDDDNDGSEDFVND SNQMRAPYWTHTDKMEKRLHAVPAANTVKF RCPAMGNPTPTMRWLKNGKEFKQEHRIGGYKVRNQHWSLIMESVVPD KGNYTCIVENQYGSINHTYHLDVVERS PHRPILQAGLPANASAVVGGDVE FVCKVYSDAQPHIQWIKHVERNGSKY GPDGLPYLQVLKAAGVNTTDKEI EVLYIRNVT FEDAGEYTCLAGNSIGISFHTAWLTVLPAPEKEKEFPTSPDYL EIAIYCIGVFLIACMVLTVILCRMKN TTKKPDFSSQPAVHKLTKRIPLRRQV SADSSSSMNSNTPLVRITTRLSTADAPMLAGVSEYELPEDPKWEFPRDKL TLGKPLGEGCFGQVVM AEAVGIDKDRPKEAVTVAVKMLKDDATEKDLS DLVSEMEMMKMIGKHKNIKLLGACTQDGPLYVIVEYASKGNLREYLRA RRPPGMEYSFDINRVPEEQMTFKDLVSCTYQLARGMEYLASQKCIHRDLA ARNVLVTENNVMKIADFG LARDINNIDYKKTNGRLPVK WMAPEALFD RVYTHQSDVWSFGVLMWEIFTLGGSPYPGIPVEELFKLLKEGHRMDK PAN

SEQ ID NO:	Description	Sequence
		CTNEL YMMMRDCWQAVPSQRPTFKQLVEDLDRILTLTTNEEYLDLSGPL EQYAPSYPDTRSSCSSGDDSVFSPDPMPEYCLPKYQHMNGSVKT*
41	FGFR3-WT	MSEAGGGAAAAASLPRSRAGGMRAAWGSVWCLCLAAAVGALPAARRR GAERSSGGQAAEYLRSETAFLEELVFGSGDTIELSCNTQSSSVSVFWKDG GIAPSNRTHIGQKLLKINVSYYDDSGLYSCKPRHSNEVLGNFTVRVTGVPF WTRPDKMEKKLLAVPAANTVRFRCPAGGNPTPTIYWLKNGKEFKGEHRI GGIKLRHQQWSLVMESVVPDRGNYTCVVENKYGNIRHTYQLDVLERSP HRPILQAGLPANQTVVVGSNVEFHCKVYSDAQPHIQWLKHVEVNGSKYG PDGTPYVTVLKSWSKNAEADANLNLNFTVEQDEGEYLCRANFVGIAEK PFWLHIRKPKPAEELMEMDDSGSVYAGILSYGTGLVLFILVLVIVICRMK MPNKKAMNTTTVQKVSKFPLKRQVTVSLESNSSMNSNTPLVRITRLSSSD GPMLANVSELELPDPKWELARSRLTLGKPLGEGCFGQVVMMAEIGIDKD KPNKAITVAVKMLKDDATDKDLSLVSEMEMMMKMGKHKNIINLLGACT QDGPLYVLVEYASKGNLREYLRARRPPGMDYSFDTCKLPEEQLTFFKDLVS CAYQVARGMEYLASQKCIHRDLAARNVLVTEDNVMKIADFGIARDVHNI DYYKKTNGRLPVK WMAPEALFDRVYTHQSDVWSFGVLLWEIFTLGGSP YPGIPVEELFKLLKEGHRMDK PANCTHDL YMIMREC WHAVPSQRPTFKQ LVEDLDRVL TMTSTDEYLDLSVPFEQYSPAGQDTHSTCSSGDDSVFAHDL LPDEPCLPKHVPCNGVIRT*
42	FGFR3- N540K	MSEAGGGAAAAASLPRSRAGGMRAAWGSVWCLCLAAAVGALPAARRR GAERSSGGQAAEYLRSETAFLEELVFGSGDTIELSCNTQSSSVSVFWKDG GIAPSNRTHIGQKLLKINVSYYDDSGLYSCKPRHSNEVLGNFTVRVTGVPF WTRPDKMEKKLLAVPAANTVRFRCPAGGNPTPTIYWLKNGKEFKGEHRI GGIKLRHQQWSLVMESVVPDRGNYTCVVENKYGNIRHTYQLDVLERSP HRPILQAGLPANQTVVVGSNVEFHCKVYSDAQPHIQWLKHVEVNGSKYG PDGTPYVTVLKSWSKNAEADANLNLNFTVEQDEGEYLCRANFVGIAEK PFWLHIRKPKPAEELMEMDDSGSVYAGILSYGTGLVLFILVLVIVICRMK MPNKKAMNTTTVQKVSKFPLKRQVTVSLESNSSMNSNTPLVRITRLSSSD GPMLANVSELELPDPKWELARSRLTLGKPLGEGCFGQVVMMAEIGIDKD KPNKAITVAVKMLKDDATDKDLSLVSEMEMMMKMGKHKNIINLLGACT QDGPLYVLVEYASKGNLREYLRARRPPGMDYSFDTCKLPEEQLTFFKDLVS CAYQVARGMEYLASQKCIHRDLAARNVLVTEDNVMKIADFGIARDVHNI DYYKKTNGRLPVK WMAPEALFDRVYTHQSDVWSFGVLLWEIFTLGGSP YPGIPVEELFKLLKEGHRMDK PANCTHDL YMIMREC WHAVPSQRPTFKQ LVEDLDRVL TMTSTDEYLDLSVPFEQYSPAGQDTHSTCSSGDDSVFAHDL LPDEPCLPKHVPCNGVIRT*
43	FGFR3- K650E	MSEAGGGAAAAASLPRSRAGGMRAAWGSVWCLCLAAAVGALPAARRR GAERSSGGQAAEYLRSETAFLEELVFGSGDTIELSCNTQSSSVSVFWKDG GIAPSNRTHIGQKLLKINVSYYDDSGLYSCKPRHSNEVLGNFTVRVTGVPF WTRPDKMEKKLLAVPAANTVRFRCPAGGNPTPTIYWLKNGKEFKGEHRI GGIKLRHQQWSLVMESVVPDRGNYTCVVENKYGNIRHTYQLDVLERSP HRPILQAGLPANQTVVVGSNVEFHCKVYSDAQPHIQWLKHVEVNGSKYG PDGTPYVTVLKSWSKNAEADANLNLNFTVEQDEGEYLCRANFVGIAEK PFWLHIRKPKPAEELMEMDDSGSVYAGILSYGTGLVLFILVLVIVICRMK MPNKKAMNTTTVQKVSKFPLKRQVTVSLESNSSMNSNTPLVRITRLSSSD GPMLANVSELELPDPKWELARSRLTLGKPLGEGCFGQVVMMAEIGIDKD KPNKAITVAVKMLKDDATDKDLSLVSEMEMMMKMGKHKNIINLLGACT QDGPLYVLVEYASKGNLREYLRARRPPGMDYSFDTCKLPEEQLTFFKDLVS CAYQVARGMEYLASQKCIHRDLAARNVLVTEDNVMKIADFGIARDVHNI DYYKETNGRLPVK WMAPEALFDRVYTHQSDVWSFGVLLWEIFTLGGSP YPGIPVEELFKLLKEGHRMDK PANCTHDL YMIMREC WHAVPSQRPTFKQ LVEDLDRVL TMTSTDEYLDLSVPFEQYSPAGQDTHSTCSSGDDSVFAHDL LPDEPCLPKHVPCNGVIRT*
44	FGFR3- N540K-K650E	MSEAGGGAAAAASLPRSRAGGMRAAWGSVWCLCLAAAVGALPAARRR GAERSSGGQAAEYLRSETAFLEELVFGSGDTIELSCNTQSSSVSVFWKDG GIAPSNRTHIGQKLLKINVSYYDDSGLYSCKPRHSNEVLGNFTVRVTGVPF WTRPDKMEKKLLAVPAANTVRFRCPAGGNPTPTIYWLKNGKEFKGEHRI

SEQ ID NO:	Description	Sequence
		GGIKLRHQQWSLVMESVVPDRGNYTCVVENKYGNIRHTYQLDVLERSP HRPILQAGLPANQTVVVGSNVEFHCKVYSDAQPHIQWLKHVEVNGSKY PDGTPYVTVLKSWSKNAEADANLNLNFVTEQDEGEYLCRANNFVGIAEK PFWLHIRKPKPAEELMEMDDSGSVYAGILSYGTGLVLFILVLVIVICRMK MPNKKAMNTTTVQKVSKFPLKRQVTVSLESNSSMNSNTPLVRITRLSSSD GPMLANVSELELPDPKWELARSRLTLGKPLGEGCFGQVVMMAEIGIDKD KPNKAITVAVKMLKDDATDKDLSLVSEMEMMKMIGKHKNIKLLGACT QDGPLYVLYEYASKGNLREYLRARRPPGMDYSFDTCKLPEEQLTFKDLVS CAYQVARGMEYLASQKCIHRDLAARNVLVTEDNVMKIADFGRLARDVHNI DYYKETTNGRLPVKWMapeALFDRVYTHQSDVWSFGVLLWEIFTLGGSP YPGIPVEELFKLLKEGHRMDKPANCTHDLYMIMRECWHAVPSQRPTFKQ LVEDLDRVLTMTSTDEYLDLVPFEQYSPAGQDTHSTCSSGDDSVFAHDL LPDEPCLPKHVPCNGVIRT*
45	FGFR3- myrist-K650E	MGSSKSKPKDPSQRRMKMPNKKAMNTTTVQKVSKFPLKRQVTVSLESNS SMNSNTPLVRITRLSSSDGPMLANVSELELPDPKWELARSRLTLGKPLGE GCFGQVVMMAEIGIDKDKPNKAITVAVKMLKDDATDKDLSLVSEMEM MKMIGKHKNIINLLGACTQDGPLYVLYEYASKGNLREYLRARRPPGMDY SFDTCKLPEEQLTFKDLVSCAYQVARGMEYLASQKCIHRDLAARNVLVTE DNVMKIADFGRLARDVHNIIDYYKETTNGRLPVKWMapeALFDRVYTHQ SDVWSFGVLLWEIFTLGGSPYPGIPVEELFKLLKEGHRMDKPANCTHDLYM IMRECWHAVPSQRPTFKQLVEDLDRVLTMTSTDEYLDLVPFEQYSPAGQ DTHSTCSSGDDSVFAHDLDPDEPCLPKHVPCNGVIRT*
46	FGFR4-WT	MLPLRLVLAGLLVAAGSAASHRGEMEPELFEPLLESEEEHLLLDPGNAL KLYCDVNQSGASVVWYKESRPLLPGRVRLQQSVLEIAEVAEYEDSGLYV CRARGTGEVLRNFTISVVDLSASGDDDESDGDGPHGDRSEEPVYVHRAP YWTHPHRMDKKLYAVPAGNTVKFRCPASGSPSPSIRWFKNGREFRGEHRI GGIRLRHQHWSLVMESVVPDRGNYTCLVENRFGSIRYSYLLDVLERSPH RPILQAGLPANTTALVGSDVEFFCKVYSDAQPHIQWLKHIEVNGSSYGPD GVPPYVQVLKTADINSSEVEVLYLRNVTMEDAGEYTCLAGNSIGLSYQSA WLTVLPEELVHEAEAPEAKYTDIIYTSGLAVAMALIIVVLCRMQTQSSK QPLEPMAVHKLSKFPLIRQFSLDSSSSGKSSTSLMRVTRLSSSCAPMLAGV VELDLPLDSKWEFPREKLVLGKPLGEGCFGQVVRAEAYGIDRQWPDRAV TVAVKMLKDNATDKDLADLISEMEMMKLMDKHKNIINLLGVCTQDGPL YVIVEFAAKGNLREYLRARRPPMPDYTFDITELHEEQCLFKDLVSCVYQV ARGMEYLESRRCIHRDLAARNVLVTAENVMKIADFGRLARDVHDIDYYKK TSNGRLPVKWMapeALFDRVYTHQSDVWSFGILMWEIFTLGGSPYPGIPV EELFKLLKEGHRMDCPNCTHELYMLMRECWHAVPSQRPTFKQLVEGLD KILAAISEEYLDLSPFEQYSPSCEDTTSTCSSDDSVFTHDPLPLAPCLFACP SGRT*
47	FGFR4- Y367C	MLPLRLVLAGLLVAAGSAASHRGEMEPELFEPLLESEEEHLLLDPGNAL KLYCDVNQSGASVVWYKESRPLLPGRVRLQQSVLEIAEVAEYEDSGLYV CRARGTGEVLRNFTISVVDLSASGDDDESDGDGPHGDRSEEPVYVHRAP YWTHPHRMDKKLYAVPAGNTVKFRCPASGSPSPSIRWFKNGREFRGEHRI GGIRLRHQHWSLVMESVVPDRGNYTCLVENRFGSIRYSYLLDVLERSPH RPILQAGLPANTTALVGSDVEFFCKVYSDAQPHIQWLKHIEVNGSSYGPD GVPPYVQVLKTADINSSEVEVLYLRNVTMEDAGEYTCLAGNSIGLSYQSA WLTVLPEELVHEAEAPEAKCTDIIYTSGLAVAMALIIVVLCRMQTQSSK QPLEPMAVHKLSKFPLIRQFSLDSSSSGKSSTSLMRVTRLSSSCAPMLAGV VELDLPLDSKWEFPREKLVLGKPLGEGCFGQVVRAEAYGIDRQWPDRAV TVAVKMLKDNATDKDLADLISEMEMMKLMDKHKNIINLLGVCTQDGPL YVIVEFAAKGNLREYLRARRPPMPDYTFDITELHEEQCLFKDLVSCVYQV ARGMEYLESRRCIHRDLAARNVLVTAENVMKIADFGRLARDVHDIDYYKK TSNGRLPVKWMapeALFDRVYTHQSDVWSFGILMWEIFTLGGSPYPGIPV EELFKLLKEGHRMDCPNCTHELYMLMRECWHAVPSQRPTFKQLVEGLD KILAAISEEYLDLSPFEQYSPSCEDTTSTCSSDDSVFTHDPLPLAPCLFACP SGRT*

SEQ ID NO:	Description	Sequence
48	FGFR4-K645E	MLPLRLVLAGLLVAAGSAASHRGEMEPLEFESPLLESEEEHLLLDPGNAL KLYCDVNQSGASVVWYKESRPLLPGPRVRLQQSVLEIAEVAYEDSGLYV CRARGTGEVLRNFTISVVDLASGDDDEDSDGDGPHGDRSEEPVYVHRAP YWTHPHRMDKKLYAVPAGNTVKFRCPASGSPSPSIRWFKNGREFRGEHRI GGIRLRHQHWSLVMEVVPVSDRGNYTCLVENRFGSIRYSYLLDVLERSPH RPILQAGLPANTTALVGSDVEFFCKVYSDAQPHIQWLKHIEVNGSSYGPD GVPPYVQVLKTADINSSEVEVLYLRNVTMEDAGEYTCLAGNSIGLSYQSA WLTVLPEELVHEAEAEPAKYTDIIYTSGSLAVAMALIIVVLCRMQTQSSK QPLEPMAVHKLSKFPLIRQFSLDSSSSGKSSTSLMRVTRLSSSCAPMLAGV VELDLPLDSKWEFPREKLVLGKPLGEGCFGQVVRAEAYGIDRQWPDRAV TVAVKMLKDNATDKDLADLISEMEMMKLMDKHKNINLLGVCTQDGPL YVIVEFAAKGNLREYLRARRPPMPDYTFDITELHEEQCLCFKDLVSCVYQV ARGMEYLESRRCIHRDLAARNVLVTAENVMKIADFLGARDVHDIDYYKE TSNGRLPVKWMPEALFDRVYTHQSDVWSFGILMWEIFTLGGSYPGIPV EELFKLLKEGHRMDCPSNCTHELYMLMRECWAHVPSQRPTFKQLVEGLD KILAAISEEYLDLSMPFEQYSPSCEDTTSTCSSDDSVFTHDPLPLAPCLFACP SGRT*
49	FGFR4-Y367C-K645E	MLPLRLVLAGLLVAAGSAASHRGEMEPLEFESPLLESEEEHLLLDPGNAL KLYCDVNQSGASVVWYKESRPLLPGPRVRLQQSVLEIAEVAYEDSGLYV CRARGTGEVLRNFTISVVDLASGDDDEDSDGDGPHGDRSEEPVYVHRAP YWTHPHRMDKKLYAVPAGNTVKFRCPASGSPSPSIRWFKNGREFRGEHRI GGIRLRHQHWSLVMEVVPVSDRGNYTCLVENRFGSIRYSYLLDVLERSPH RPILQAGLPANTTALVGSDVEFFCKVYSDAQPHIQWLKHIEVNGSSYGPD GVPPYVQVLKTADINSSEVEVLYLRNVTMEDAGEYTCLAGNSIGLSYQSA WLTVLPEELVHEAEAEPAKCTDIIYTSGSLAVAMALIIVVLCRMQTQSSK QPLEPMAVHKLSKFPLIRQFSLDSSSSGKSSTSLMRVTRLSSSCAPMLAGV VELDLPLDSKWEFPREKLVLGKPLGEGCFGQVVRAEAYGIDRQWPDRAV TVAVKMLKDNATDKDLADLISEMEMMKLMDKHKNINLLGVCTQDGPL YVIVEFAAKGNLREYLRARRPPMPDYTFDITELHEEQCLCFKDLVSCVYQV ARGMEYLESRRCIHRDLAARNVLVTAENVMKIADFLGARDVHDIDYYKE TSNGRLPVKWMPEALFDRVYTHQSDVWSFGILMWEIFTLGGSYPGIPV EELFKLLKEGHRMDCPSNCTHELYMLMRECWAHVPSQRPTFKQLVEGLD KILAAISEEYLDLSMPFEQYSPSCEDTTSTCSSDDSVFTHDPLPLAPCLFACP SGRT*
50	ggIGFR1-WT	MKSGAGGGTLAVFCGLLLAFAALCLCPTNGEICGPNVDIRNDIHELKRLE NCTVVEGFLQILLISKAEDYRNFRFPKLTVITDYLLLFVAGLESLSDLFPN LTVIRGRNLFYNYALVIFEMTNLKEIGLHNLRNITRGAIRIEKNSDLCYLST VDWSLILDAVSNNYIVGNKPPKECGDLCPGTMEEKPLCEKTSINNEYNYR CWTNHCQKMCPPSSCGKRACTDQNECCHPECLGSCTAPDNNTACVACR NYYYEGVCMPTCPPNTYKFEGWRCVTKEFCSKVPATETSDYERFVIHNDE CMAECPSGFIRNGSQSMFCSPCEGPCPKICEDGKTKTIDSVTSAQMLQGCT ILKGNLLINIRRGNNIAELENFMGLIETVTGYVKIRHSHALVSLSFLKNLR YILGEEQVDGNYSFYVLDNHNLLQQLWDWNHNLTIKEGKMYFAFNPKL CVSEIYRMEEVSGTKGRQSKGDINPRNNGERASCESHILRFVSNNTTLKNRI KLTWERYRPPDYRDLISFTVYYKEAPFKNVTEYDGGDACGSNSWNMVD VDLPPNKENDPGILLQGLKPWTQYAIYVKAATLTMMENHHIHGAKSEIVY IRTNAAVPSIPLDVISASNSSQLIVKWNPPSLPNGNLSYIYVRWQQQPQDS YLVRHNYCSKDKVPIRRYADGTIDTEEAETPTKPEGCGGEKGPCCACPKT EAEKQAEKEEAERYKVFENFLHNSIFVPRPDRKRRDVFRANATLATRNR NITGADHFTNASDAEESVEYPPFFETKVDGKERTVISHLPQFTLYRIDIHSC NHEADTLGCSASNFFVARTMPSEGADNIPGTVAWEAKEENTVYLKWLEP TNPNGLILMYEIKYGQHGEERECVSRQEYKKLGGAKLTHLNPNGYSAR VQATSLAGNGSWTEPVSYFYVQPKSANYDNFLHLIIVLPPIAFLLIIGLLIML YVFNNKRNDRDLGNGVLYASVNPEYFASDVYVPDEWEVPREKITMCRE LGQGSFGMVYEGIAKGVVKDEPETRVAIKTVNESASMRERIEFLNEASVM KEFNCHHVVRLLGVVSQGPQTLVIMELMTRGDLKSYLRSRDPDTESNPGQ APPTLKKMIQMAGEIADGMAYLNANKFVHRDLAARNCMVAEDFTVKIG

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		DFGMTRDIYETDY YRKGGKGLLPVRWMSPELKDGVFTTHSDVWSFGVV LWEIATLAEQPYQGMTNEQVLRVMEGGLLEKPDNCPDMLFELMRMCW QYNPKMRPSFLEIISIKDELDPAFKEVSFFYSEENKPPDTEELDLETENMES IPLDPSSTLQPTDKHSGHKAENGPVGVVLRASFEERQPYAHMNGGRKNER ALPLQSSAC*
51	ggIGFR1- H1353H	MKSGAGGGTLAVFCGLLLAFAALCLCPTNGEICGPNVDIRNDIHELKRLE NCTVVEGFLQILLISKAEDYRNFRFPKLT VITDYLLLFVAGLESLSDLFPN LTVIRGRNLFYNYALVIFEMTNLKEIGLHNLNRNITRGAIRIEKNSDLCYLST VDWSLILD AVSNNYIVGNKPPKECGDLCPGTMEKPLCEKTSINNEYNYR CWTTNHCQKMCPSSCGKRACTDQNECCHPECLGSC TAPDNNTACVACR NYYYEGVCMPTCPPNTYKFEGWRCVTKEFCSKVPATETSDYERFVIHNDE CMAECPSGFIRNGSQSMFCSPCEGPCPKICEDGKTKTIDSVTAQMLQGCCT ILKGNLLINIRRGNNIASLENFMGLIETVTGYVKIRHSHALVLSFLKLNLR YILGEEQVDGNYSFYVLDNHNLLQQLWDWNHNLTKIEGKMYFAFNPKL CVSEIYRMEEVSGTKGRQSKGDINPRNNGERASCESHILRFVSNTTLKNRI KLTWERYRPPDYRDLISFTVYYKEAPFKNVTEYDGGQACGSNSWNMVD VDLPPNKENDPGILLQGLKPWTQYAIYVKA VTLTMMENHHIHGAKSEIVY IRTNAAVPSIPLDVISASNSSQLIVKWNPSPNGNLSYIYVRWQQPQDS YL YRHNYCSKDKVPIRRYADGTIDTEEA TEPTKPEGCGGEKGPCCACPKT EAEKQAEKEEAEYRKVFENFLHNSIFVPRPDRKRRDVFRIANATLATNR NITGADHFTNASDAEESVEYPPFFETKVDGKERTVISHLQPF TLYRIDIHSC NHEADTLGCSASNFFVARTMPSEAGDNIPGTVAWEAKEENTVYLYKWLPEP TNPNGLLIMYEIKYQHGEEKREC VSRQEYKKLGGA KLTHLNPNGYSAR VQATSLAGNGSWTEPVSFYVQPKSANYDNFLHLIIVLP IAFLLIIGGLLIML YVFNKKRNSDRLGNGVLYASVNPEYFASDVYVPDEWEVPREKITMCRE LGQGSFGMVYEGIAKG VVKDEPETRVAIKTVNESASMRERIEFLNEASVM KEFNCHHVVRLLGVVSQGP TLVIMELMTRGDLKSYLRSLRPDTESNPGQ APPTLKKMIQMAIEADGMAYLNANKFVHRDLAARNCMVAEDFTVKIG DFGMTRDIYETDY YRKGGKGLLPVRWMSPELKDGVFTTHSDVWSFGVV LWEIATLAEQPYQGMTNEQVLRVMEGGLLEKPDNCPDMLFELMRMCW QYNPKMRPSFLEIISIKDELDPAFKEVSFFYSEENKPPDTEELDLETENMES IPLDPSSTLQPTDKHSGHKAENGPVGVVLRASFEERQPYAHMNGGRKNEH ALPLQSSAC*
52	gPDGFRA- WT	MGTPPRTFLILGCFLTGPLLTLCLPLPTIVPNRNEMVVQLNSNFTLKCSGD SEVSWQYPVTEGSHRIDIRHEENNSGLFVTVLEVGNASAAHTGMYVCYY NHTQVEDGEVEGKDIYIYVPDPMFVPSLPEDQFILVEEGDPTVIPCRTSD PSAEVTLVNSLDPVYAFYDSKQGFVGNFLAGPYTCKTMVKGVEFKSDE FLIYL RATSQLPVEIEALKTVYKTGETIVVT CVVFDNEVNLQWNPYKGV KEKGLIKLDDIKVPSQKL VYTLTIPDASVKDTGDYECTARHATKEVKENK KVVTIVHDKGFIHLEPQFSPL EAVNLHEVKNFVVDVQAYPAPKMYWLKD NVTLIENLTEIVTSSNRVQETRFQSVLKLIRAKEEDSGYYTLVAENEDEIKR YTFSLLIQVPALILDLMDHQSAGRQTVRCLAEGTPLPDVEWL VCKDIK KCSNDTSWTLTNNISDIHMEAHLDERNMVESQVTFQKVEETLAVRCVA RNDLGAVTRELKLVAPTLRSELTVAAA VLVLLVIVISLIVLVIIWKQKPRY EIRWRVIESISPDGHEYIYVDPMLPYDSRWEFPRDGLVLGRILGSGAFGK VVEGTAYGLSRSPVMKVAVKMLKPTARSSEKQALMSELKIMTHLGPLH NIVNLLGACTKSGPIYITEYCFYGD LVNYLHKNRDNFLSRHPEKPKKDLDI FGMNPADESTRSYVILSFENTGEYMDMKQADTTQYVPMLERKEGSKYS IQRSVYDRPASYKKKSLSESEVKNL SDDGSEGLSLLDLSFTYQVARGM EFLASKNCVHRDLAARNVLLAQGKIVKICDFGLARDIMHDSNYVSKGSTF LPVKWMAPEIFDNLYTTLSDVWSYGILLWEIFSLGGTPYPGMMVDSTFY NKIKSGYRMAKPDHATNEVYEIMVKCWNSEPEKRPSFYHLSEIVESLLPG EYKKS YEKIHLDFLKS DHPAVTRMRGDCDNAYIGVTYKNEDKIKDRESGF DEQRLSADSGYIIPLDIPVSEDELGKRNRHSSQTSEESA IETGSSSSSTFIKR EDETIEDIDMMDDIGIDSSDLVEDSFL*
53	gPDGFRA- D842V	MGTPPRTFLILGCFLTGPLLTLCLPLPTIVPNRNEMVVQLNSNFTLKCSGD SEVSWQYPVTEGSHRIDIRHEENNSGLFVTVLEVGNASAAHTGMYVCYY

SEQ ID NO:	Description	Sequence
		NHTQVEDGEVEGKDIIYIVDPDMPFVPSLPEDQFILVEEGDPTVIPCRTSD PSAEVTLVNSLDPVYAFYDSKQGFVGNFLAGPYTCKTMVKGVEFKSDE FLIYILRATSQLPVEIEALKTVYKTGETIVVTCVVFDENVVNLQWNYPGKV KEKGLIKLDDIKVPSQKLVIYTLTIPDASVKDTGDYECTARHATKEVKENK KVVITVHDKGFIHLEPQFSPLEAVNLHEVKNFVVDVQAYPAPKMYWLKD NVTLIENLTEIVTSSNRVQETRFQSVLKLIRAKEEDSGYYTLVAENEDEIKR YTFSLLIQVPALILDLMDDHQSGAGRQTVRCLAEGTPLPDVEWL VCKDIK KCSNDTSWTLTNNISDIHMEAHLDERNMVESQVTFQKVEETLAVRCVA RNDLGAVTREKLVAPTLRSELTVA AAVLVLLVIVISLIVLVIIWKQKPRY EIRWRVIESISPDGHEYIYVDPMQLPYDSRWEFPRDGLVLGRILGSGAFGK VVEGTAYGLSRSQPMKVAVKMLKPTARSSEKQALMSELKIMTHLGPHL NIVNLLGACTKSGPIYIITEYCFYGDLVNVLHKNRDNFLSRHPEKPKKDLDI FGMNPADESTRSYVILSFENTGEYMDMKQADTTQYVPMLEKEGSKYSYD IQRSVYDRPASYSKKKSLSESEVKNLLSDDGSEGLSLDLSTFYQVARGM EFLASKNCVHRDLAARNVLLAQGKIVKICDFGLARVIMHDSNYVSKGSTF LPVKWMAPEFIDNLYTTLSDVWSYGILLWEIFSLGGTPYPGMMVDSTFY NKIKSGYRMAKPDHATNEVYEIMVKCWNSEPEKRPSTFYHLSEIVESLLPG EYKKSIEKIHLDFLKSHPAVTRMRGDCDNAYIGVTYKNEDKIKDRESGF DEQRLSADSGYIIPDPIDPVSEDELGKRNHRHSSQTSEESAETGSSSSTFIKR EDETIEDIDMMDDIGIDSSDLVEDSFL*
54	ggPDGFRBW T	MLCPSLKASLQLLITGLLEVTSGGSLHIEPEDAELVRLHSTFSLVCYGD GTLVWERDGOPLTAVLEHRDGVFISNLTLRNVTRHRTGEYACFYSPDQAP ERAERKALYIYVPDPSLVFLPAITSEEFFIFITGYTEATIPCRVTNPQLVTL EKKVENPIATYDPQQGFGFFEDKTYCQAIVDDQEVDSDTFYVYRIQV SSVNVSISAVQTVVRQGENVTLMCTVSGNELVNFNWDYPRKQAGKAVEP VTDFLPGSTHDIRSILIIQNAELEDSTGYVCNVSEGYHEKTDRKDITVQVIE RGFVRFHHLASTVYAEVHKSHIIQVDVEAYPQPNIVWLKNNKTLTMESS SEFTITNRNLSETRYQTSVLVRVKQEEGGYYTIRASNEDDAQELSFHLQI NVPKVVLDKENSASSGEQTVTCSAEGMPQPEISWSTCSNIKWCGSQGQ PTQLLGNNSAEIGLHTNATYHAELQVYRVNSTLQLHRVDEPLLLRCTVQN FLGSNSQDITLVPNALPFKVVIISVILALLVLTVISLIIILWQKKPRYEIRW KVIESVSSDGHEYIYVDPMQLPYDSSWEVPRDKLVLGRTLGSAGFRVVE ATAHGLSHSQSTMKVAVKMLKSTARSSSEKQALMSELKIMSHLGPHLNIV NLLGACTKGGPIYIITEYCRYGDLVDYLHRNKHTFLQSYGEKARREAEY GNTIKEDHVQSHLSLVSVDGGYMDMSKDESLDYVPMSDMKGEVKYADI ESSNYGTPYELDSYSPAPERTDRVTLINEPLLSYMDLVGFSFQVANGME FLASKNCVHRDLAARNVLICEGKLVKICDFGLARDIMRDSNYISKGSTFLP LKWMAPEFIDNLYTTLSDVWSYGILLWEIFTLGGTPYPELPMNEQFYNAI KRGYRMSKPTHASDEIYDIMQKCWEEKFEIRPSFSQLVVLGMNLLVDCYR KRYQQVDEEFMKSDHPAVVRTRPTIPGLNNARLPPSSPTLYTAVHQNGGE NDYIIPDPKPDALCDLPQEASVSRASSMLNEANTSSTISCDSPGPRQDEE PECDLQLGCQELAPGHHEVEESFL*
55	ggPDGFRB- V536A	MLCPSLKASLQLLITGLLEVTSGGSLHIEPEDAELVRLHSTFSLVCYGD GTLVWERDGOPLTAVLEHRDGVFISNLTLRNVTRHRTGEYACFYSPDQAP ERAERKALYIYVPDPSLVFLPAITSEEFFIFITGYTEATIPCRVTNPQLVTL EKKVENPIATYDPQQGFGFFEDKTYCQAIVDDQEVDSDTFYVYRIQV SSVNVSISAVQTVVRQGENVTLMCTVSGNELVNFNWDYPRKQAGKAVEP VTDFLPGSTHDIRSILIIQNAELEDSTGYVCNVSEGYHEKTDRKDITVQVIE RGFVRFHHLASTVYAEVHKSHIIQVDVEAYPQPNIVWLKNNKTLTMESS SEFTITNRNLSETRYQTSVLVRVKQEEGGYYTIRASNEDDAQELSFHLQI NVPKVVLDKENSASSGEQTVTCSAEGMPQPEISWSTCSNIKWCGSQGQ PTQLLGNNSAEIGLHTNATYHAELQVYRVNSTLQLHRVDEPLLLRCTVQN FLGSNSQDITLVPNALPFKVVIISVILALLVLTVISLIIILWQKKPRYEIRW KAIESVSSDGHEYIYVDPMQLPYDSSWEVPRDKLVLGRTLGSAGFRVVE ATAHGLSHSQSTMKVAVKMLKSTARSSSEKQALMSELKIMSHLGPHLNIV NLLGACTKGGPIYIITEYCRYGDLVDYLHRNKHTFLQSYGEKARREAEY GNTIKEDHVQSHLSLVSVDGGYMDMSKDESLDYVPMSDMKGEVKYADI

SEQ ID NO:	Description	Sequence
		ESSNYGTPYELDSYSPSAPERTDRVTLINE SPLLSYMDLVGFSFQVANGME FLASKNCVHRDLAARNVLICEGKLVKICDFGLARDIMRDSNYISKGSTFLP LKWMAPE SIFNNLYTTLSDVWSFGILLWEIFTLGGTPYPELPMNEQFYNAI KRGYRMSKPTHASDEIYDIMQKCWEEKFEIRPSFSQLVVLGMNLLVDCYR KRYQQVDEEFMKSDHPAVVRTRPTIPGLNNARLPPSSPTLYTAVHQNGGE NDYIIPDPKPD AICDLPQEASVSRASSMLNEANTSSITSCDSPLGPRQDEE PECDLQLGCQELAPGHHEVEESFL*
56	ggPDGFRB-D850V	MLCPSLKASLQLLITGLLEVTSGGSGLHIEPEDAELVRLHSTFSLVCYGD GTLVWERDGOPLTAVLEHRDGVFISNLTNRNVTGRHTGEYACFYSPDQAP ERAERKALYIYVPDPSLVFLPAITSEEFFIFITGYTEATIPCRVTNPQLVTLTY EKKVENPIPATYDPQQGFGFFEDKTYQCQAI VDDQEVSDSTFYVYRIQV SSVNVSISAVQTVVRQGENVTLMCTVSGNELVNFNWDYPRKQAGKAVEP VTDFLPGSTHDIRSILIIQNAELED SGTYVCNVSEGYHEKTD RKDITVQVIE RGFVRFHTHLASTVYAEVHKSHIIQVDVEAYPQPNIVWLKNNKTLTMESS SEFTITNRNLSETRYQTSVLVVRVKQEEGGYYTIRASNEDDAQELSFHLQI NVPKVVLDKENS SASSGEQTVTCSAEGMPQPEISWSTCSNIKWCGSQGQ PTQLLGNN SAEIGLHTNATYHAELQVYRVNSTLQLHRVDEPLLLRCTVQN FLGSNSQDITLVPNALPFKVVIISVILALLVLTVISLIIILWQKKPRYEIRW KVIESVSSDGHEYIYVDPMLQPYDSSWEVPRDKLVLGRTLGS GAFGRVVE ATAHGLSHSQSTMKVAVKMLKSTAR SSEQALMSELKIMSHLGPHLNIV NLLGACTKGGPIYIITEYCRYGDLVDYLHRNKHTFLQSYGEKARREAE LY GNTIKEDHVQSHLSL SVESDGGYMDMSKDESLDYVPMSDMKGEVKYADI ESSNYGTPYELDSYSPSAPERTDRVTLINE SPLLSYMDLVGFSFQVANGME FLASKNCVHRDLAARNVLICEGKLVKICDFGLARDIMRDSNYISKGSTFLP LKWMAPE SIFNNLYTTLSDVWSFGILLWEIFTLGGTPYPELPMNEQFYNAI KRGYRMSKPTHASDEIYDIMQKCWEEKFEIRPSFSQLVVLGMNLLVDCYR KRYQQVDEEFMKSDHPAVVRTRPTIPGLNNARLPPSSPTLYTAVHQNGGE NDYIIPDPKPD AICDLPQEASVSRASSMLNEANTSSITSCDSPLGPRQDEE PECDLQLGCQELAPGHHEVEESFL*
57	F-9C-PRggPDGFRB	MADYKDDDDKKGGIIVAILLLIVMLAIEILLITLIIAVTSGGSGLHIEPEDA ELVRLHSTFSLVCYGDGTLVWERDGOPLTAVLEHRDGVFISNLTNRNVT GRHTGEYACFYSPDQAPER AERKALYIYVPDPSLVFLPAITSEEFFIFITGYT EATIPCRVTNPQLVTLTYEKKVENPIPATYDPQQGFGFFEDKTYQCQAI V DDQEVSDSTFYVYRIQVSSVNVSISAVQTVVRQGENVTLMCTVSGNELV NFNWDYPRKQAGKAVEPVTDFLPGSTHDIRSILIIQNAELED SGTYVCNV EGYHEKTD RKDITVQVIERGFVRFHTHLASTVYAEVHKSHIIQVDVEAYP QPNIVWLKNNKTLTMESSSEFTITNRNLSETRYQTSVLVVRVKQEEGGYY TIRASNEDDAQELSFHLQINVPKVVLDKENS SASSGEQTVTCSAEGMPQ EISWSTCSNIKWCGSQGQPTQLLGNN SAEIGLHTNATYHAELQVYRVNST LQLHRVDEPLLLRCTVQNFLGSNSQDITLVPNALPFKVVIISVILALLVLTVI SLIILILWQKKPRYEIRWKVIESVSSDGHEYIYVDPMLQPYDSSWEVPRDK LVLGRTLGS GAFGRVVEATAHGLSHSQSTMKVAVKMLKSTAR SSEQAL MSELKIMSHLGPHLNIVNLLGACTKGGPIYIITEYCRYGDLVDYLHRNKHT FLQSYGEKARREAE LYGNTIKEDHVQSHLSL SVESDGGYMDMSKDESLD YVPMSDMKGEVKYADIESSNYGTPYELDSYSPSAPERTDRVTLINE SPLLS YMDLVGFSFQVANGMEFLASKNCVHRDLAARNVLICEGKLVKICDFGLA RDIMRDSNYISKGSTFLPLK WMAPE SIFNNLYTTLSDVWSFGILLWEIFTLG GTPYPELPMNEQFYNAIKRGYRMSKPTHASDEIYDIMQKCWEEKFEIRPSF SQLVVLGMNLLVDCYRKRYQQVDEEFMKSDHPAVVRTRPTIPGLNNARL PPSSPTLYTAVHQNGGENDYIIPDPKPD AICDLPQEASVSRASSMLNEAN TSSTISCDSP LGPRQDEEPECDLQLGCQELAPGHHEVEESFL*
58	9C-PRggPDGFRB	MAKGGIIVAILLLIVMLAIEILLITLIIAVTSGGSGLHIEPEDAELVRLHST FSLVCYGDGTLVWERDGOPLTAVLEHRDGVFISNLTNRNVTGRHTGEYA CFYSPDQAPER AERKALYIYVPDPSLVFLPAITSEEFFIFITGYTEATIPCRVT NPQLVTLTYEKKVENPIPATYDPQQGFGFFEDKTYQCQAI VDDQEVSD TFYVYRIQVSSVNVSISAVQTVVRQGENVTLMCTVSGNELVNFNWDYPR KQAGKAVEPVTDFLPGSTHDIRSILIIQNAELED SGTYVCNVSEGYHEKTD

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		RKDITVQVIERGFVRFHThLASTVYAEVHKSHIIQVDVEAYPQPNIWVWLNKNTLTMESSSEFTITNRNLSETRYQTSVLVRVKQEEGGYYTIRASNEDDAQELSFHLQINVPKVVDLKENSSASSGEQTVTCSAEGMPQPEISWSTCSNKKWCGSQGQPTQLLGNNSAEIGLHTNATYHAEQVYRVNSTLQLHRVDEPLLRLCTVQNFLGSNSQDITLVPNALPFKVVIIISVILALLVLTVISLIIILWQKKPRYEIRWKVIESVSSDGHEYIYVDPMQLPYDSSWEVPRDKLVLGRTLGSGAFGRVVEATAHGLSHSQSTMKVAVKMLKSTARSEKQALMSELKIMSHLGPHLNIVNLLGACTKGGPIYIITEYCRYGDLVDYLHRNKHTFLQSYGEKARREAELYGNTIKEDHVQSHLSLSVESDGGYMDMSKDESLDYVPMSDMKGEVKYADIESSNYGTPYELDSYSPSAPERTDRVTLINEPLLSYMDLVGFSFQVANGMEFLASKNCVHRDLAARNVLICEGKLVKICDFGLARDIMRDSNYISKGSTFLPLKWMAPESIFNNLYTTLSDVWSFGILLWEIFTLGGTPYPELPMNEQFYNAIKRGYRMSKPTHASDEIYDIMQKCWEEKFEIRPSFSQLVVLMLGNLLVDCYRKRYQQVDEEFMKSDHPAVVVRTRPTIPGLNNARLPSSPTLYTAVHQNGGENDYIIPLPDPKPAICDLPQEASVSRASSMLNEANTSSITSCDSPLGPRQDEEPECDLQLGCQELAPGHHEVEESFL*
59	FGFBP	MWIKNVGLLCVLIILVSQMLLASCEKQKERRRGKQGIEHGGKKQAFESNPEREKGKPKGGKASPKGKFKSKENADCSWAVTDMSAATVHIECRNGDSAFWCEFGDPSACPHYAANQKSYWKQVSRSLKKQKQICQDPRSLKPKICRKGPRGAHLKLTRSSLLAAVDPAKGHPAHHAEDAQGPAASETGKQPEHSPPDCVEDVDYIDQRKVAEEYCPESSLSLCNFFITMVQDKKC
60	RASV12	MTEYKLVVVGAVGVGKSALTILQIQLNHVDEYDPTIEDSYRKQVVIDGETCLLDILDITAGQEEYSAMRDQYMRGTGEGFLCVFAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVGNKCDLPARTVETRAQDLARSYGIPYIETSAKTRQGVEDAFYTLVREIRQHKLRKLNPPDESGPGCMNCKCVIS*
61	Chicken FGF2 or FGF2-WT	ATGGCGGCAGGAGCAGCTGGTTCATACCAACCATGCCCCCCTCCCA GACGATGGGGGCGGAGGCGCATTTCCTCCAGGTCATTTCAAGGACCCC AAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTCTGAGGATAAACCTT GACGGACGGGTGGACGGCGTACGCGAGAAATCAGATCCACATATCAA GCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGG TTAGCGCTAACAGATTTTTGGCAATGAAGGAAGACGGTAGGCTCCTCG CGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAAT CTAACAACCTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACG TCGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAAAGACGGGT CCGGGGCAGAAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
62	BM40-FGF2	ATGGCGGCAGGAGCAGCTGGTTCATACCAACCATGCCCCCCTCCCA GACGATGGGGGCGGAGGCGCATTTCCTCCAGGTCATTTCAAGGACCCC AAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTCTGAGGATAAACCTT GACGGACGGGTGGACGGCGTACGCGAGAAATCAGATCCACATATCAA GCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGG TTAGCGCTAACAGATTTTTGGCAATGAAGGAAGACGGTAGGCTCCTCG CGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAAT CTAACAACCTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACG TCGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAAAGACGGGT CCGGGGCAGAAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
63	ggIL2-FGF2	ATGATGTGTAAAGTTCTTATCTTCGGATGCATCTCCGTAGCAATGCTCA TGACTACAGCTTACATGGCGGCAGGAGCAGCTGGTTCATACCAACAT TGCCCGCCCTCCCAGACGATGGGGGCGGAGGCGCATTTCTCCAGGTC ATTTCAAGGACCCCAAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTT GAGGATAAAACCTGACGGACGGGTGGACGGCGTACGCGAGAAATCAG ATCCACATATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCT CTATAAAAGGGGTAGCGCTAACAGATTTTTGGCAATGAAGGAAGACG GTAGGCTCCTCGCGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGA ACGGCTCGAATCTAACAACCTACAACACGTACCGCTCTCGCAAATACTC TGACTGGTACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCC AAAGACGGGTCCGGGGCAGAAAAGCTATCCTGTTCTTCCAATGTCCGC CAAGAGTTAG

SEQ ID NO:	Description	Sequence
64	GLuc-FGF2	ATGGGGGTCAAAGTGCTGTTTGCCTTGATCTGTATTGCTGTGGCCGAG GCAATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCCGCCCTC CCAGACGATGGGGGCGGAGGCGCATTTCTCCAGGTCAATTCAAGGAC CCCAAAAGGCTGTAAGTAAGAATGGTGGTTTTTCTGAGGATAAAC CCTGACGGACGGGTGGACGGCGTACGCGAGAAATCAGATCCACATAT CAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAG GGGTTAGCGCTAACAGATTTTGGCAATGAAGGAAGACGGTAGGCTCC TCGCGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCG AATCTAACAACTACAACACGTACCGCTCTCGCAAATACTCTGACTGGT ACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAAAGACG GGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGT TAG
65	hIL2-FGF2	ATGTATCGCATGCAACTGCTTTCATGCATTGCTCTTAGCCTGGCGCTGG TCACGAACCTCTATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGC CCGCCCTCCCAGACGATGGGGGCGGAGGCGCATTTCTCCAGGTCAATT TCAAGGACCCCAAAAGGCTGTAAGTAAGAATGGTGGTTTTTCTGA GGATAAACCTGACGGACGGGTGGACGGCGTACGCGAGAAATCAGAT CCACATATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCT ATAAAAGGGGTAGCGCTAACAGATTTTGGCAATGAAGGAAGACGG TAGGCTCTCGCGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGAA CGGCTCGAATCTAACAACTACAACACGTACCGCTCTCGCAAATACTCT GACTGGTACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCA AAGACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCC AAGAGTTAG
66	hIL2co1-FGF2	ATGAGAATGCAACTGCTCCTGCTTATAGCGCTCAGTTTGGCTCTCGTGA CCAACTCAATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCCG CCCTCCCAGACGATGGGGGCGGAGGCGCATTTCTCCAGGTCAATTCA AGGACCCCAAAAGGCTGTAAGTAAGAATGGTGGTTTTTCTGAGGA TAAACCCTGACGGACGGGTGGACGGCGTACGCGAGAAATCAGATCC CATATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATA AAAGGGGTAGCGCTAACAGATTTTGGCAATGAAGGAAGACGGTAG GCTCCTCGCGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGAACGG CTCGAATCTAACAACTACAACACGTACCGCTCTCGCAAATACTCTGAC TGGTACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAA GACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAA GAGTTAG
67	hIL2co2-FGF2	ATGAGGCGGATGCAATTGCTGCTGTTGATCGCACTCTCTGGCACTTG TACTAATAGTATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGC CCGCCCTCCCAGACGATGGGGGCGGAGGCGCATTTCTCCAGGTCAATT TCAAGGACCCCAAAAGGCTGTAAGTAAGAATGGTGGTTTTTCTGA GGATAAACCTGACGGACGGGTGGACGGCGTACGCGAGAAATCAGAT CCACATATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCT ATAAAAGGGGTAGCGCTAACAGATTTTGGCAATGAAGGAAGACGG TAGGCTCTCGCGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGAA CGGCTCGAATCTAACAACTACAACACGTACCGCTCTCGCAAATACTCT GACTGGTACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCA AAGACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCC AAGAGTTAG
68	ggIL6-FGF2	ATGAATTTTACAGAAGGGTGTGAAGCGACTGGCAGGAGACCAGGATC CGCCGGGTCAAGGAGAAGAAGGGCCCCCGGCTGGGCCTGTGCGGC TTCTTCCCCTGTTGCTTCCGCTGTTGCTTCCACCGGCAGCTGCGGTTCCC TTGCCCATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCCGCC CTCCCAGACGATGGGGGCGGAGGCGCATTTCTCCAGGTCAATTCAAG GACCCCAAAAGGCTGTAAGTAAGAATGGTGGTTTTTCTGAGGATA AACCTGACGGACGGGTGGACGGCGTACGCGAGAAATCAGATCCACA TATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAA AGGGGTAGCGCTAACAGATTTTGGCAATGAAGGAAGACGGTAGGCT

SEQ ID NO:	Description	Sequence
		CCTCGCGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTTCGAACGGCTC GAATCTAACAACACTACAACACGTACCGCTCTCGCAAATACTCTGACTGG TACGTCGCACTCAAACGCACTGGGCAGTATAAACCGGGGGCCAAAGAC GGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAG TTAG
69	hIFN2A- ggFGF2	ATGGCGCTCACGTTTGCCCTCTTGGTTGCGCTTCTCGTTCTTCTCTGCAA GAGTAGCTGTTCCGTGGGAATGGTATCCAAGATGGCGGCAGGAGCAG CTGGTTCCATAACCACTTGCCCGCCCTCCCAGACGATGGGGGCGGAG GCGCATTTCTCCAGGTCATTTCAAGGACCCCAAAAGGCTGTACTGTA AGAATGGTGGTTTTTCTGAGGATAAACCCCTGACGGACGGGTGGACG GCGTACGCGAGAAATCAGATCCACATATCAAGCTGCAGTTGCAAGCCG AGGAACGCGGGGTAGTCTCTATAAAAGGGGTTAGCGCTAACAGATTTT TGGCAATGAAGGAAGACGGTAGGCTCCTCGCGCTTAAGTGTGCCACCG AGGAGTGCTTCTTCTCGAACGGCTCGAATCTAACAACTACAACACGT ACCGCTCTCGCAAATACTCTGACTGGTACGTCGCACTCAAACGCACTG GGCAGTATAAACCGGGGGCCAAAGACGGGTCCGGGGCAGAAAGCTATC CTGTTCTTCCAATGTCCGCCAAGAGTTAG
70	secrecon- FGF2	ATGTGGTGGCGCTTGTGGTGGTTGCTGTTGTTGTTGCTGCTGTTGTGGC CTATGGTCTGGGCAATGGCGGCAGGAGCAGCTGGTTCCATAACCAT TGCCCGCCCTCCCAGACGATGGGGGCGGAGGCGCATTTCTCCAGGTC ATTTCAAGGACCCCAAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTCT GAGGATAAACCCCTGACGGACGGGTGGACGGCGTACGCGAGAAATCAG ATCCACATATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCT CTATAAAAGGGGTAGCGCTAACAGATTTTGGCAATGAAGGAAGACG GTAGGCTCCTCGCGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGA ACGGCTCGAATCTAACAACTACAACACGTACCGCTCTCGCAAATACTC TGACTGGTACGTCGCACTCAAACGCACTGGGCAGTATAAACCGGGGGCC AAAGACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGC CAAGAGTTAG
71	hIL6-FGF2	ATGAATAGCTTCAGTACGTCTGCGTTCCGACCTGTGGCTTTTAGCCTCG GACTGCTGCTCGTGCTGCCGGCGCGTTTTCCGGCACCCATGGCGGCAG GAGCAGCTGGTTCCATAACCACTTGCCCGCCCTCCCAGACGATGGGG GCGGAGGCGCATTTCTCCAGGTCATTTCAAGGACCCCAAAAGGCTGT ACTGTAAGAATGGTGGTTTTTCTGAGGATAAACCCCTGACGGACGGG TGGACGGCGTACGCGAGAAATCAGATCCACATATCAAGCTGCAGTTGC AAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGGTAGCGCTAAC AGATTTTGGCAATGAAGGAAGACGGTAGGCTCCTCGCGCTTAAGTGT GCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAATCTAACAACTAC AACACGTACCGCTCTCGCAAATACTCTGACTGGTACGTCGCACTCAAA CGCACTGGGCAGTATAAACCGGGGGCCAAAGACGGGTCCGGGGCAGAA AGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
72	FGF2-Q68I- N114G-FGF2	ATGGCGGCAGGAGCAGCTGGTTCCATAACCACTTGCCCGCCCTCCCA GACGATGGGGGCGGAGGCGCATTTCTCCAGGTCATTTCAAGGACCC AAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTGAGGATAAACCCCT GACGGACGGGTGGACGGCGTACGCGAGAAATCAGATCCACATATCAA GCTGCAGTTGATAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGGT TAGCGCTAACAGATTTTGGCAATGAAGGAAGACGGTAGGCTCCTCGC GCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAATCT AACGGCTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACGTC GCACTCAAACGCACTGGGCAGTATAAACCGGGGGCCAAAGACGGGTCC GGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
73	FGF2-Q68I- N114G-C99S- FGF2	ATGGCGGCAGGAGCAGCTGGTTCCATAACCACTTGCCCGCCCTCCCA GACGATGGGGGCGGAGGCGCATTTCTCCAGGTCATTTCAAGGACCC AAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTGAGGATAAACCCCT GACGGACGGGTGGACGGCGTACGCGAGAAATCAGATCCACATATCAA GCTGCAGTTGATAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGGT TAGCGCTAACAGATTTTGGCAATGAAGGAAGACGGTAGGCTCCTCGC

SEQ ID NO:	Description	Sequence
		GCTTAAGTCTGCCACCGAGGAGTGCTTCTTCTTCGAACGGCTCGAATCTAACGGCTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACGTCGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAAAGACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
74	hIL2-co1ggFGF2(x Met)	ATGAGAATGCAACTGCTCTGCTTATAGCGCTCAGTTTGGCTCTCGTGACCAACTCAGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCCCGCC TCCCAGACGATGGGGGCGGAGGCGCATTTCCTCCAGGTCAITTC AAGGACCCAAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTGAGGATAAACCTGACGGACGGGTGGACGGCGTACGCGAGAAATCAGATCCACATATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGGTTAGCGCTAACAGATTTTTGGCAATGAAGGAAGACGGTAGGCTCTCGCGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAATCTAACAACTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAAAGACGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
75	FGF2-C77Y81	ATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCCCGCCCTCCAGACGATGGGGGCGGAGGCGCATTTCCTCCAGGTCAITTC AAGGACCCAAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTGAGGATAAACCTGACGGACGGGTGGACGGCACCCGCGAGAAATCAGATCCACATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGGTTTGCCTAACAGATTTTGGCAATGAAGGAAGACGGTAGGCTCTCGCGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAATCTAACAACTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAAAGACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
76	FGF-STAB	ATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCCCGCCCTCCAGACGATGGGGGCGGAGGCGCATTTCCTCCAGGTCAITTC AAGGACCCAAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTGCTGATAAACCTGACGGACGGGTGGACGGCACCCGCGAGAAATCAGATCCATTCATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGGTTAGCGCTAACAGATTTTGGCAATGAAGGAAGACGGTAGGCTCTACGCGCTTAAGTATGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAAGAGAACAACCTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAAAGACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
		ATGATGTGTAAAGTTCTTATCTTCGGATGCATCTCCGTAGCAATGCTCATGACTACAGCTTACATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCCCGCCCTCCAGACGATGGGGGCGGAGGCGCATTTCCTCCAGGTCAITTC AAGGACCCAAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTGCTGATAAACCTGACGGACGGGTGGACGGCACCCGCGAGAAATCAGATCCATTCATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGGTTAGCGCTAACAGATTTTGGCAATGAAGGAAGACG GTAGGCTCTACGCGCTTAAGTATGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAAGAGAACAACCTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAAAGACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGC CAAGAGTTAG
77	ggIL2-FGF-STAB	ATGATGTGTAAAGTTCTTATCTTCGGATGCATCTCCGTAGCAATGCTCATGACTACAGCTTACATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCCCGCCCTCCAGACGATGGGGGCGGAGGCGCATTTCCTCCAGGTCAITTC AAGGACCCAAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTGCTGATAAACCTGACGGACGGGTGGACGGCACCCGCGAGAAATCAGATCCATTCATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGGTTAGCGCTAACAGATTTTGGCAATGAAGGAAGACG GTAGGCTCTACGCGCTTAAGTATGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAAGAGAACAACCTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACGTGCACTCAAACGCACTGGGCAGTATAAACCGGGGCCAAAGACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGC CAAGAGTTAG
78	hIL2-FGF-STAB	ATGTATCGCATGCAACTGCTTTTCATGCATTGCTCTTAGCCTGGCGCTGGTCACGAACTCTATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTG CCGCCCTCCAGACGATGGGGGCGGAGGCGCATTTCCTCCAGGTCAITTC AAGGACCCAAAAGGCTGTACTGTAAGAATGGTGGTTTTTCTGCTGATAAACCTGACGGACGGGTGGACGGCACCCGCGAGAAATCAGATCCATTCATCAAGCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGGTTAGCGCTAACAGATTTTGGCAATGAAGGAAGACG GTAGGCTCTACGCGCTTAAGTATGCCACCGAGGAGTGCTTCTTCTCGAACGGCTCGAAGAGAACAACCTACAACACGTACCGCTCTCGCAAATACTCTCGGCTCGAAGAGAACAACCTACAACACGTACCGCTCTCGCAAATACTCT

SEQ ID NO:	Description	Sequence
		GACTGGTACGTGCGACTCAAACGCACTGGGCAGTATAAACCGGGGGCCA AAGACGGGTCCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCC AAGAGTTAG
79	STAB-C77Y81	ATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCGCCCTCCCA GACGATGGGGGCGGAGGCGCATTTCCCTCCAGGTCATTTCAAGGACCCC AAAAGGCTGTACTGTAAGAATGGTGGTTTTTTCCTGAGGATAAACCCCT GACGGACGGGTGGACGGCGTACGCGAGAAATCAGATCCACATATCAA GCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGG TTTGCGCTAACAGATATTTGGCAATGAAGGAAGACGGTAGGCTCCTCG CGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTTCGAACGGCTCGAAT CTAACAACTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACG TCGCACTCAAACGCACTGGGCAGTATAAACCGGGGGCCAAAGACGGGT CCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
80	c96-STAB-Gen2-ggFGF2	ATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCGCCCTCCCA GACGATGGGGGCGGAGGCGCATTTCCCTCCAGGTCATTTCAAGGACCCC AAAAGGCTGTACTGTAAGAATGGTGGTTTTTTCCTGCTGATAAACCCCT GACGGACGGGTGGACGGCACCCGCGAGAAATCAGATCCATTCATCAA GCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGG TTAGCGCTAACAGATTTTGGCAATGAAGGAAGACGGTAGGCTCTACG CGCTTAAGTGTGCCACCGAGGAGTGCTTCTTCTTCGAACGGCTCGAAG AGAACAACCTACAACACGTACCGCTCTCGCAAATACTCTGACTGGTACG TCGCACTCAAACGCACTGGGCAGTATAAACCGGGGGCCAAAGACGGGT CCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
81	STAB-Gen3-ggFGF2	ATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCGCCCTCCCA GACGATGGGGGCGGAGGCGCATTTCCCTCCAGGTCATTTCAAGGACCCC AAAAGGCTGTACTGTAAGAATGGTGGTTTTTTCCTGCTGATAAACCCCT GACGGACGGGTGGACGGCACCCGCGACAAATCAGATCCATTCATCAA GCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGG TTAGCGCTAACAGATTTTGGCAATGAAGGAAGACGGTAGGCTCTACG CGATAAAGAATGCCACCGAGGAGTGCTTCTTCTTCGAACGGCTCGAAG AGAACAACCTACAACACGTACCGCTCTCGCAAATACCCTGACTGGTACG TCGCACTCAAACGCACTGGGCAGTATAAACCGGGGGCCAAAGACGGGT CCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
82	c96-STAB-Gen3-ggFGF2	ATGGCGGCAGGAGCAGCTGGTTCCATAACCACATTGCCGCCCTCCCA GACGATGGGGGCGGAGGCGCATTTCCCTCCAGGTCATTTCAAGGACCCC AAAAGGCTGTACTGTAAGAATGGTGGTTTTTTCCTGCTGATAAACCCCT GACGGACGGGTGGACGGCACCCGCGACAAATCAGATCCATTCATCAA GCTGCAGTTGCAAGCCGAGGAACGCGGGGTAGTCTCTATAAAAGGGG TTAGCGCTAACAGATTTTGGCAATGAAGGAAGACGGTAGGCTCTACG CGATAAAGTGTGCCACCGAGGAGTGCTTCTTCTTCGAACGGCTCGAAG AGAACAACCTACAACACGTACCGCTCTCGCAAATACCCTGACTGGTACG TCGCACTCAAACGCACTGGGCAGTATAAACCGGGGGCCAAAGACGGGT CCGGGGCAGAAAGCTATCCTGTTCTTCCAATGTCCGCCAAGAGTTAG
83	Bovine FGF2	ATGGCCGCCGGGAGCATCACACGCTGCCAGCCCTGCCGGAGGACGG CGGCAGCGGCGCTTTCCCGCCGGGGCACTTCAAGGACCCCAAGCGGCT GTACTGCAAGAACGGGGGCTTCTTCTGCGCATCCACCCGACGCGCG AGTGGACGGGGTCCGCGAGAAGAGCGACCCACACATCAAACTACAAC TTCAAGCAGAAGAGAGAGGGGGTGTGTCTATCAAAGGAGTGTGTGCA AACCGTTACCTTGCTATGAAAGAAGATGGAAGATTACTAGCTTCTAAA TGTGTTACAGACGAGTGTTTCTTTTGAACGATTGGAGTCTAATAACT ACAATACTTACCGGTCAAGGAAATACTCCAGTTGGTATGTGGCACTGA AACGAACTGGGCAGTATAAACTTGGACCCAAAACAGGACCTGGGCAG AAAGCTATACTTTTCTTCCAATGTCTGCTAAGAGCTGA
84	Salmon FGF2	ATGGCCACAGGAGAAATCACCACTCTACCCGCCACACCTGAAGATGGA GGCAGTGGCGGCTTCCCTCCAGGAACTTTAAGGATCCCAAGAGGCTG TACTGTAAAAACGGGGGCTACTTCTTGAGAATAAACTCTAATGGAAGC GTGGACGGGATCCGAGAGAAGAACGACCCCCACATCAAGCTTCAACT

SEQ ID NO:	Description	Sequence
		CCAGGCGACCTCAGTAGGGGAGGTAGTGATCAAAGGGGTCTCAGCCA ACCGTTATCTGGCCATGAATGGAGATGGAAGACTGTTTGGAACGAGAC GGACAACAGATGAATGCTACTTCATGGAGAGGCTGGAGAGTAACAAC TACAACACCTACCGCTCACGGAAGTACCCTGACATGTATGTGGCGCTG AAAAGGACTGGCCAGTACAAGTCAGGATCCAAAACCTGGACCGGGCCA AAAAGCCATTCTCTTTCTCCCCATGTCAGCCAGACGCTGA
85	RASv12	ATGACCGAGTACAAGCTGGTGGTAGTGGGAGCTGTAGGTGTCCGGAA GAGCGCTTTGACGATACAGCTCATTGAGAACCATTTTGTGTGATGAGTA CGACCCACAATAGAGGATTCTACAGAAAGCAAGTCGTCATCGATGG AGAGACCTGTTTGTGGACATCCTGGATACGGCGGGGAGGAGGAGT ACAGTGCCATGCGAGACCAGTACATGAGAACGGGGGAAGGATTCTGT TGCGTCTTTGCCATTAACAACACCAAGTCCTTTGAGGACATCCACCAGT ACAGGGAGCAGATCAAGAGGGTGAAAGACTCAGATGATGTCCCCATG GTGCTGGTGGGAAATAAATGTGATCTGCCAGCACGGACAGTGGAGAC CCGGCAAGCGCAGGACCTGGCCCGGAGTTACGGGATCCCCTACATAGA AACGTCGGCCAAAACAGACAGGGCGTCGAAGATGCCTTCTATACCTT AGTGCGGGAGATCCGTCAGCATAAACTGCGCAAGCTGAACCCACCAG ATGAGAGTGGCCCTGGCTGCATGAACTGTAAATGCGTGATATCGTGA
86	FGFR1-WT	ATGTTACGCTGGAGATGTCTCATCCTGTGGGCGGTACTGGTTACCGCA ACGTTGAGCGCAGCTAGGCCCGCCCCACGCTGCCTGACCAGGCTCTC CCTAAGGCGAATATAGAAGTAGAATCACATTCTGCACATCCAGGAGAC TTGTTGCAATTGCGGTGCGCTTGAGAGACGATGTCCAATCAATCAAT TGGGTACAGGACGGGGTCCAACCTCCGGAGAATAACCGGACAAGGAT TACTGGAGAGGAGTTGAAGTCAGGGACGCTGTTCCCGAAGATAGCG GCTTGACGCTTGATGACTAATTCCCCGTCAGGGTCAGAAACCACGT ATTTTTCTGTAAACGTTAGCGATGCTCTCCGAGTGCTGAAGACGATGA TGATGAAGACGATAGCAGCTCCGAAGAGAAAAGAGGCGGATAATACTA AACCAAATCAAGCTGTTGCACCATATTGGACCTACCCGAAAAAATGG AGAAAAAGTTGCAATGCTGTTCCGGCAGCCAAAACCGTAAATTCAGT GCCCCCTCCGGCGGTACCCCTAATCCAACCTCTGAGATGGTTGAAGAACG GTAAGGAGTTCAAACCGGATCACCGGATAGGTGGATATAAAGTTCCGGT ATGCGACCTGGTCCATTATTATGGACTCTGTGCTGCCCTCCGACAAAG GTAACCTACCTTGTATCGTCGAGAACAAGTACGGCAGCATCAATCATA CGTACCAACTGGACGTGGTAGAACGCACTCCACACCGCCCTCCCTCC AGGCCGGAATCCCTGCCAACAAAACAGTTGCGCTCGGCTCTAATGTTG AATTTGTGTGCAAAGTTTACTCAGACCCTCAACCTCATATCCAATGGCT TAAACATATCGAAGTCAACGGTAGTAAGATAGGTCCCAGAACCTGCC GTATGTCCAGATCCTTAAACTGCGGGGGTAAATACCACTGACAAGGA AATGGAGGTCTTGCATCTTCGCAACGTGAGCTTTGAAGATGCAAGGTGA GTATACTTGTTTGGCAGGTAATAGCATCGGAATCTCCACCATTCGCGC TGGCTGACAGTGCTGGAGGCCACGGAACAAAGTCCGGCCATGATGAC CAGTCCGTTGTATCTGGAAATTATCATTACTGTACAGGGGCCTTTCTC ATATCATGCATGGTCGTAACCGTGATTATATATAAAATGAAGAGCACA ACGAAGAAGACTGATTTTAATTCACAACTGGCGGTACATAAACTCGCA AAATCTATCCCATTGAGGCGGCAGGTTACAGTCTCCGCCGACAGCTCC AGCAGCATGAACTCAGGAGTGATGCTTGTTCGCCCCAGCAGACTGAGT TCTAGTGGGACTCCGATGCTTGCTGGAGTCAGTGAATACGAATTGCCG GAGGATCCGCGGTGGGAACCTCCTAGGGACCGCCTTATATTGGGCAAA CCCCCTCGGTGAGGGCTGTTTCGGACAGGTCTGTCTCGCAGAGGCCATC GGCCTTGACAAAGATAAGCCGAATAGAGTGACCAAGGTGGCGGTTAA AATGCTGAAATCAGACGCTACGGAAGGACCTCTCAGACCTCATCAG TGAAATGGAAATGATGAAATGATAGGGAAGCACAAAAACATCATCA ATTTGCTCGGAGCTTGTACCCAGGACGGTCCCCCTCTACGTGATCGTAG AATACGCTTCCAAGGTAACTGCGCGCAATATCTGCAAGCTCGGAGGC CGCCAGGTATGGAATACTGTTATAATCCGACACGGATTCCCAGGGAAC AGCTCTCTTTTAAAGATTTGGTTTCATGCGCGTATCAAGTGGCGAGGG GCATGGAGTATCTGGCGTCCAAGAAGTGCATTATAGGGACTTGGCTG

SEQ ID NO:	Description	Sequence
		CAAGAAATGTCTTGGTAACAGAAGACAACGTCATGAAGATCGCCGACT TCGGCCTTGCACGGGATATTCATCACATCGACTATTACAAAAAGACGA CGAACGGCCGCCTCCCAGTTAAGTGGATGGCCCCCGAAGCCCTGTTCG ATCGGATTTACACGCATCAATCCGACGTGTGGTCTTTCGGTGTCCGTCT TTGGGAGATATTTACACTCGGGGGATCACCCCTACCCCGGAGTACCGGT GGAGGAGTTGTTCAAACCTCTTAAAGAAGGTCACAGAATGGACAAACC CAGTAACTGCACTAACGAGCTGTATATGATGATGCGCGATTGCTGGCA CGCTGTTCCGTCACAACGGCCCACTTTTAAACAGCTCGTGGAGGATCTT GACAGAATCGTTCGCGATGACTAGCAACCAAGAGTATTTGGATTTGTCA GTCCCGCTTGACCAATATTTCCCCCGGTTTTCCGGCTACCCGCTCTTCTA CTTGTTCCAGCGGTGAGGATAGTGTATTTTCTCATGACCCACTTCCAGA TGAGCCGTGCTTGCCCTCGGTGTCTCCCCACTCCCATGGAGCGCTCAAA CGCCACTGA
87	FGFR1C-N546K	ATGTTACGTTGGAGATGTCTCATCCTGTGGGCGGTACTGGTTACCGCA ACGTTGAGCGCAGCTAGGCCCGCCCCACGCTGCCTGACCAGGCTCTC CCTAAGGCGAATATAGAAGTAGAATCACATTCTGCACATCCAGGAGAC TTGTTGCAATTGCGGTGCCGCTTGAGAGACGATGTCCAATCAATCAAT TGGGTACGGGACGGGGTCCAACCTCCGGAGAATAACCGGACAAGGAT TACTGGAGAGGAGGTTGAAGTCAGGGACGCTGTTCCCGAAGATAGCG GCTTGACGCTTGCATGACTAATTCCCCGTCAGGGTCAGAAACCACGT ATTTTCTGTAAACGTTAGCGATGCTCTCCGAGTGCTGAAGACGATGA TGATGAAGACGATAGCAGCTCCGAAGAGAAAAGAGGCGGATAAATACTA AACCAAATCAAGCTGTTGCACCATATTGGACCTACCCGAAAAAATGG AGAAAAAGTTGCATGCTGTTCCGGCAGCCAAAACCGTAAAATTCAGT GCCCCCTCCGGCGGTACCCCTAATCCAACCTCTGAGATGGTTGAAGAACG GTAAGGAGTTCAAACCGGATCACCGGATAGGTGGATATAAAGTTCCGT ATGCGACCTGGTCCATTATTATGGACTCTGTCGTGCCCTCCGACAAAG GTAACACTACCTTGTATCGTCGAGAACAAGTACGGCAGCATCAATCATA CGTACCAACTGGACGTGGTAGAACGCACTCCACACCGCCCCATCCCTCC AGGCCGGAATCCCTGCCAACAAAACAGTTGCGCTCGGCTCTAATGTTG AATTTGTGTGCAAAGTTTACTCAGACCCTCAACCTCATATCCAATGGCT TAAACATATCGAAGTCAACGGTAGTAAGATAGGTCCCCGACAACCTGCC GTATGTCCAGATCCCTAAAACTGCGGGGGTAAATACCACTGACAAGGA AATGGAGGTCTTGCATCTTCGCAACGTGAGCTTTGAAGATGCAGGTGA GTATACTTGTTTGGCAGGTAATAGCATCGGAATCTCCACCATTCGGCC TGGCTGACAGTGCTGGAGGCCACGGAACAAAGTCCGGCCATGATGAC CAGTCCGTTGTATCTGGAAATTATCATTACTGTACAGGGGCCTTTCTC ATATCATGCATGGTCGTAACCGTGATTATATATAAAATGAAGAGCACA ACGAAGAAGACTGATTTTAATTCACAACCTGGCGGTACATAAACTCGCA AAATCTATCCCATTGAGGCGGCAGGTTACAGTCTCCGCCGACAGCTCC AGCAGCATGAACTCAGGAGTGATGCTTGTTCGCCCCAGCAGACTGAGT TCTAGTGGGACTCCGATGCTTGCTGGAGTCAGTGAATACGAATTGCCG GAGGATCCGCGGTGGGAACCTCCTAGGGACCGCCTTATATTGGGCAAA CCCCCTCGGTGAGGGCTGTTTCGGACAGGTCGTGCTCGCAGAGGCCATC GGCCTTGACAAAGATAAGCCGAATAGAGTGACCAAGGTGGCGGTTAA AATGCTGAAATCAGACGCTACGGAAAAGGACCTCTCAGACCTCATCAG TGAAATGGAAATGATGAAAATGATAGGGAAGCACAAAAACATCATCA AGTTGCTCGGAGCTTGATCCAGGACGGTCCCCCTCTACGTGATCGTAG AATACGCTTCCAAAGGTAATCTGCGCGAATATCTGCAAGCTCGGAGGC CGCCAGGTATGGAATACTGTTATAATCCGACACGGATTCCCGAGGAAC AGCTCTCTTTTAAAGATTTGGTTTCATGCGCGTATCAAGTGGCGAGGG GCATGGAGTATCTGGCGTCCAAGAAGTGCAATTCATAGGGACTTGGCTG CAAGAAATGTCTTGGTAACAGAAGACAACGTCATGAAGATCGCCGACT TCGGCCTTGCACGGGATATTCATCACATCGACTATTACAAAAAGACGA CGAACGGCCGCCTCCCAGTTAAGTGGATGGCCCCCGAAGCCCTGTTCG ATCGGATTTACACGCATCAATCCGACGTGTGGTCTTTCGGTGTCTGCT TTGGGAGATATTTACACTCGGGGGATCACCCCTACCCCGGAGTACCGGT

SEQ ID NO:	Description	Sequence
		GGAGGAGTTGTTCAAACCTTCTTAAAGAAGGTCACAGAATGGACAAACC CAGTAACTGCACTAACGAGCTGTATATGATGATGCGCGATTGCTGGCA CGCTGTTCCGTCACAACGGCCCACTTTTAAACAGCTCGTGGAGGATCTT GACAGAATCGTCGCGATGACTAGCAACCAAGAGTATTTGGATTTGTCA GTCCCGCTTGACCAATATTCCCCCGGTTTTCCGGCTACCCGCTCTTCTA CTTGTTCCAGCGGTGAGGATAGTGTATTTTCTCATGACCCACTTCCAGA TGAGCCGTGCTTGCCCTCGGTGTCTCCCCACTCCCATGGAGCGCTCAAA CGCCACTGA
88	FGFR1C-V561M	GCCGCCACCATGTTACGTGGAGATGTCTCATCCTGTGGGCGGTACTG GTTACCGCAACGTTGAGCGCAGCTAGGCCCGCCCCACGCTGCCTGAC CAGGCTCTCCCTAAGGCGAATATAGAAGTAGAATCACATTCTGCACAT CCAGGAGACTTGTTGCAATTGCGGTGCCGCTTGAGAGACGATGTCCAA TCAATCAATTGGGTACGGGACGGGTCCAACCTCCGGAGAATAACCGG ACAAGGATTACTGGAGAGGAGGTTGAAGTCAGGGACGCTGTTCCCGA AGATAGCGGCTTGACGCTTGATGACTAATTCCCCGTACGGGTCAGA AACCACGTATTTTCTGTAAACGTTAGCGATGCTCTTCCGAGTGCTGAA GACGATGATGATGAAGACGATAGCAGCTCCGAAGAGAAAAGAGGCGGA TAATACTAAACCAAATCAAGCTGTTGCACCATATTGGACCTACCCCGA AAAAATGGAGAAAAAGTTGCATGCTGTTCCGGCAGCCAAAACCGTAA AATTCAAGTGCCCTCCGGCGGTACCCCTAATCCAACCTCTGAGATGGT TGAAGAACGGTAAGGAGTTCAAACCGGATCACCGGATAGGTGGATAT AAAGTTCGGTATGCGACCTGGTCCATTATTATGGACTCTGTCTGTCCT CCGACAAAGGTAACCTACACTTGATCGTCGAGAACAAAGTACGGCAGCA TCAATCATACGTACCAACTGGACGTGGTAGAACGCAGTCCACACCGCC CCATCCTCCAGGCCGGACTCCCTGCCAACAAAACAGTTGCGCTCGGCT CTAATGTTGAATTTGTGTGCAAAGTTTACTCAGACCCTCAACCTCATAT CCAATGGCTTAAACATATCGAAGTCAACGGTAGTAAGATAGGTCCCGA CAACCTGCCGTATGTCCAGATCCTTAAACTGCGGGGGTAAATACCAC TGACAAGGAAATGGAGGTCTTGCACTCTCGCAACGTGAGCTTTGAAGA TGCAGGTGAGTATACTTGTTTGGCAGGTAATAGCATCGGAATCTCCCA CCATTCCGCCTGGCTGACAGTGCTGGAGGCCACGGAACAAAGTCCGGC CATGATGACCAGTCCGTTGTATCTGGAAATTATCATTTACTGTACAGGG GCCTTTCTCATATCATGCATGGTCGTAACCGTGATTATATATAAAATGA AGAGCACAAACGAAGAAGACTGATTTTAATTCACAACTGGCGGTACATA AACTCGCAAAATCTATCCCATTGAGGCGGCAGGTTACAGTCTCCGCCG ACAGCTCCAGCAGCATGAACTCAGGAGTGATGCTTGTTCCGCCACGCA GACTGAGTTCTAGTGGGACTCCGATGCTTGCTGGAGTCAGTGAATACG AATTGCCGGAGGATCCGCGGTGGGAACCTCCTAGGGACCGCCTTATAT TGGGCAAAACCCCTCGGTGAGGGCTGTTTCGGACAGGTCTGTCTCGCAG AGGCCATCGGCCTTGACAAAGATAAGCCGAATAGAGTGACCAAGGTG GCGGTTAAATGCTGAAATCAGACGCTACGGAAGAGACCTCTCAGA CCTCATCAGTGAAATGGAAATGATGAAATGATAGGGAAGCACAAAA ACATCATCAATTTGCTCGGAGCTTGTAACCCAGGACGGTCCCCTCTACGT GATCATGGAATACGCTTCCAAAGGTAATCTGCGCGAATATCTGCAAGC TCGGAGGCCGCCAGGTATGGAATACTGTTATAATCCGACACGGATTCC CGAGGAACAGCTCTCTTTTAAAGATTTGGTTTCATGCGCGTATCAAGTG GCGAGGGGCATGGAGTATCTGGCGTCCAAGAAGTGCATTATAGGGA CTTGGCTGCAAGAAATGCTTGTTGTAACAGAAGACAACGTATGAAGAT CGCCGACTTCGGCCTTGACACGGGATATTCATCACATCGCACTATTACAA AAAGACGACGAACGGCCGCTCCAGTTAAGTGGATGGCCCCCGAAG CCCTGTTTCGATCGGATTTACACGCATCAATCCGACGTGTGGTCTTTTCGG TGTCTGCTTTGGGAGATATTTACACTCGGGGGATCACCCCTACCCCGG AGTACCGGTGGAGGAGTTGTTCAAACCTTCTTAAAGAAGGTCACAGAAT GGACAAACCCAGTAACCTGCACTAACGAGCTGTATATGATGATGCGCGA TTGCTGGCACGCTGTTCCGTACAAACGGCCCACTTTTAAACAGCTCGTG GAGGATCTTGACAGAATCGTCGCGATGACTAGCAACCAAGAGTATTTG GATTTGTCAGTCCCGCTTGACCAATATTCCCCCGGTTTTCCGGCTACCC

SEQ ID NO:	Description	Sequence
		GCTCTTCTACTTGTTCAGCGGTGAGGATAGTGTATTTTCTCATGACCC ACTTCCAGATGAGCCGTGCTTGCCTCGGTGTCTCCCCACTCCCATGGA GCGCTCAAACGCCACTGA
89	FGFR1C- K656E	ATGTTACAGTGGAGATGTCTCATCCTGTGGGCGGTACTGGTTACCGCA ACGTTGAGCGCAGCTAGGCCCGCCCCACGCTGCCTGACCAGGCTCTC CCTAAGGCGAATATAGAAGTAGAATCACATTCTGCACATCCAGGAGAC TTGTTGCAATTGCGGTGCCGCTTGAGAGACGATGTCCAATCAATCAAT TGGGTCAAGGACGGGGTCCAACCTCCGGAGAATAACCGGACAAGGAT TACTGGAGAGGAGGTTGAAGTCAGGGACGCTGTCCCCGAAGATAGCG GCTTGTACGCTTGCATGACTAATTCCCCGTCAGGGTCAGAAACCACGT ATTTTCTGTAAACGTTAGCGATGCTCTCCGAGTGCTGAAGACGATGA TGATGAAGACGATAGCAGCTCCGAAGAGAAAAGAGGCGGATAATACTA AACCAAATCAAGCTGTTGCACCATATTGGACCTACCCGAAAAAATGG AGAAAAAGTTGCATGCTGTTCGGCAGCCAAAACCGTAAAAATTCAAGT GCCCCCTCCGGCGGTACCCCTAATCCAACCTCTGAGATGGTTGAAGAACG GTAAGGAGTTCAAACCGGATCACCGGATAGGTGGATATAAAGTTCCGGT ATGCGACCTGGTCCATTATTATGGACTCTGTCGTGCCCTCCGACAAAAG GTAACACTACCTTGTATCGTCGAGAACAAGTACGGCAGCATCAATCATA CGTACCAACTGGACGTGGTAGAACGCACTCCACACCGCCCCATCCTCC AGGCCGGAATCCCTGCCAACAAAACAGTTGCGCTCGGCTCTAATGTTG AATTTGTGTGCAAAGTTTACTCAGACCCTCAACCTCATATCCAATGGCT TAAACATATCGAAGTCAACGGTAGTAAGATAGGTCCCCGACAACCTGCC GTATGTCCAGATCCTTAAAACTGCGGGGGTAAATACCACTGACAAGGA AATGGAGGCTTTCATCTTCGCAACGTGAGCTTTGAAGATGCAGGTGA GTATACTTGTGTTGGCAGGTAATAGCATCGGAATCTCCCACCATTCGGCC TGGCTGACAGTGCTGGAGGCCACGGAACAAAGTCCGGCCATGATGAC CAGTCCGTTGTATCTGGAAATTATCATTACTGTACAGGGGCCTTTCTC ATATCATGCATGGTCGTAACCGTGATTATATATAAAATGAAGAGCACA ACGAAGAAGACTGATTTTAATTCACAACTGGCGGTACATAAACTCGCA AAATCTATCCCATTGAGGCGGCAGGTTACAGTCTCCGCCGACAGCTCC AGCAGCATGAACTCAGGAGTGATGCTTGTTCGCCCCAGCAGACTGAGT TCTAGTGGGACTCCGATGCTTGCTGGAGTCAGTGAATACGAATTGCCG GAGGATCCGCGGTGGGAACTTCCTAGGGACCGCCTTATATTGGGCAAA CCCCCTCGGTGAGGGCTGTTTCGGACAGGTCTGTCTCGCAGGCGCATC GGCCTTGACAAAGATAAGCCGAATAGAGTGACCAAGGTGGCGGTTAA AATGCTGAAATCAGACGCTACGGAAGGACCTCTCAGACCTCATCAG TGAAATGGAATGATGAAATGATAGGGAAGCACAAAAACATCATCA ATTTGCTCGGAGCTTGTACCCAGGACGGTCCCCTCTACGTGATCGTAG AATACGCTTCCAAAGGTAATCTGCGCGAATATCTGCAAGCTCGGAGGC CGCCAGGTATGGAATACTGTTATAATCCGACACGGATTCCCGAGGAAC AGCTCTCTTTAAAGATTTGGTTTCATGCGCGTATCAAGTGGCGAGGG GCATGGAGTATCTGGCGTCCAAGAAGTGCAATTCATAGGGACTTGGCTG CAAGAAATGTCTTGGTAACAGAAGACAACGTCATGAAGATCGCCGACT TCGGCCTTGACAGGGATATTCATCACATCGACTATTACAAAGAGACGA CGAACGGCCGCTCCCAAGTTAAGTGGATGGCCCCGAAGCCCTGTTTCG ATCGGATTTACACGCATCAATCCGACGTGTGGTCTTTCCGTGTCTGCT TTGGGAGATATTTACACTCGGGGGATCACCTACCCCGGAGTACCGGT GGAGGAGTTGTTCAAACCTCTTAAAGAAGGTCACAGAATGGACAAACC CAGTAACTGCACTAACGAGCTGTATATGATGATGCGCGATTGCTGGCA CGCTGTTCCGTCACAACGGCCACTTTTAAACAGCTCGTGGAGGATCTT GACAGAATCGTCGCGATGACTAGCAACCAAGAGTATTTGGATTTGTCA GTCCCGCTTGACCAATATTCCTCCCGGTTTTCGGCTACCCGCTCTTCTA CTTGTTCACGCGTGAGGATAGTGTATTTTCTCATGACCCACTTCCAGA TGAGCCGTGCTTGCCTCGGTGTCTCCCCACTCCCATGGAGCGCTCAAA CGCCACTGA

SEQ ID NO:	Description	Sequence
90	FGFR1-N546K-K656E-S780A	ATGTTACAGTGGAGATGTCTCATCTGTGGGCGGTACTGGTTACCGCA ACGTTGAGCGCAGCTAGGCCCGCCCCACGCTGCCTGACCAGGCTCTC CCTAAGGCGAATATAGAAGTAGAATCACATTCTGCACATCCAGGAGAC TTGTTGCAATTGCGGTGCGCTTGAGAGACGATGTCCAATCAATCAAT TGGGTCAGGGACGGGGTCCAACCTCCGGAGAATAACCGGACAAGGAT TACTGGAGAGGAGGTTGAAGTCAGGGACGCTGTTCCCGAAGATAGCG GCTTGTACGCTTGCATGACTAATTCCCCGTCAGGGTCAGAAACACGCT ATTTTCTGTAAACGTTAGCGATGCTCTTCCGAGTGCTGAAGACGATGA TGATGAAGACGATAGCAGCTCCGAAGAGAAAAGAGGCGGATAATACTA AACCAAATCAAGCTGTTGCACCATAATTGGACCTACCCCGAAAAAATGG AGAAAAAGTTGCATGCTGTTCCGGCAGCCAAAACCGTAAAATTCAAGT GCCCCCTCCGGCGGTACTCCTAATCCAACCTCTGAGATGGTTGAAGAACG GTAAGGAGTTCAAACCGGATCACC GGATAGGTGGATATAAAGTTCCGT ATGCGACCTGGTCCATTATTATGGACTCTGTCTGCCCTCCGACAAAAG GTAAC TACACTTGTATCGTCGAGAACAAGTACGGCAGCATCAATCATA CGTACCAACTGGACGTGGTAGAACGCAGTCCACACCGCCCCATCCTCC AGGCCGGACTCCCTGCCAACAAAACAGTTGCGCTCGGCTCTAATGTTG AATTTGTGTGCAAAGTTTACTCAGACCCTCAACCTCATATCCAATGGCT TAAACATATCGAAGTCAACGGTAGTAAGATAGGTCCCGACAACTGCC GTATGTCCAGATCCTTAAAACTGCGGGGGTAAATACCACTGACAAGGA AATGGAGGTCTTGCATCTTCGCAACGTGAGCTTTGAAGATGCAGGTGA GTATACTTGTGTTGGCAGGTAATAGCATCGGAATCTCCCACCATTCGCGC TGGCTGACAGTGCTGGAGGCCACGGAACAAAAGTCCGGCCATGATGAC CAGTCCGTTGTATCTGGAAATTATCATTTACTGTACAGGGGCTTTTCTC ATATCATGCATGGTCGTAACCGTGATTATATATAAAATGAAGAGCACA ACGAAGAAGACTGATTTTAAATTCACAACCTGGCGGTACATAAACTCGCA AAATCTATCCCATTTGAGGCGGCAGGTTACAGTCTCCGCGACAGCTCC AGCAGCATGAACTCAGGAGTGATGCTTGTTCGCCCCAGCAGACTGAGT TCTAGTGGGACTCCGATGCTTGCTGGAGTCAGTGAATACGAATTGCCG GAGGATCCGCGGTGGGAACCTCCTAGGGACCGCCTTATATTGGGCAAA CCCCCTCGGTGAGGGCTGTTTCGGACAGGTGCTGCTCGCAGAGGCCATC GGCCTTGACAAAGATAAGCCGAATAGAGTGACCAAGGTGGCGGTTAA AATGCTGAAATCAGACGCTACGGAAAAGGACCTCTCAGACCTCATCAG TGAAATGGAAATGATGAAAATGATAGGGAAGCACAAAAACATCATCA AGTTGCTCGGAGCTTGTACCCAGGACGGTCCCCTCTACGTGATCGTAG AATACGCTTCCAAAGGTAATCTGCGCGAATATCTGCAAGCTCGGAGGC CGCCAGGTATGGAATACTGTTATAATCCGACACGGATTCCCGAGGAAAC AGCTCTCTTTTAAAGATTTGGTTTCATGCGCGTATCAAGTGGCGAGGG GCATGGAGTATCTGGCGTCCAAGAAGTGCATTATAGGGACCTGGCTG CAAGAAATGTCTTGGTAACAGAAGACAACGTCATGAAGATCGCCGACT TCGGCCTTGACACGGGATATTCATCACATCGACTATTACAAAGAGACGA CGAACCGGCCGCTCCAGTTAAGTGGATGGCCCCCGAAGCCCTGTTCG ATCGGATTTACACGCATCAATCCGACGTGTGGTCTTTCCGTGTCTGCT TTGGGAGATATTTACACTCGGGGGATCACCTACCCCGAGTACCGGT GGAGGAGTTGTTCAAACCTCTTAAAGAAGGTCACAGAATGGACAAACC CAGTAAGTGCATAACGAGCTGTATATGATGATGCGCGATTGCTGGCA CGCTGTTCCGTCACAACGGCCCACTTTTAAACAGCTCGTGGAGGATCTT GACAGAATCGTCGCGATGACTAGCAACCAAGAGTATTTGGATTTGTCA GTCCCGCTTGACCAATATGCCCGCGGTTTTCCGGCTACCCGCTCTTCTA CTTGTTCAGCGGTGAGGATAGTGTATTTTCTCATGACCCACTTCCAGA TGAGCCGTGCTTGCTCCTCGGTGTCTCCCACTCCCATGGAGCGCTCAAA CGCCACTGA
91	myrist-FGFR1C-K656E	ATGGGATCATCCAAGTCAAAACCGAAAGACCCGTCACAGAGAAAAAT GAAGAGCACAAACGAAGAAGACTGATTTTAAATTCACAACCTGGCGGTAC ATAAACTCGCAAAATCTATCCCATTTGAGGCGGCAGGTTACAGTCTCCG CCGACAGCTCCAGCAGCATGAACTCAGGAGTGATGCTTGTTCGCCCCA GCAGACTGAGTTCTAGTGGGACTCCGATGCTTGCTGGAGTCAGTGAAT

SEQ ID NO:	Description	Sequence
		ACGAATTGCCGGAGGATCCGCGGTGGGAACTTCCTAGGGACCGCCTTA TATTGGGCAAACCCCTCGGTGAGGGCTGTTTCGGACAGGTCGTGCTCG CAGAGGCCATCGGCCTTGACAAAGATAAGCCGAATAGAGTGACCAAG GTGGCGGTAAAAATGCTGAAATCAGACGCTACGGAAAAAGGACCTCTCA GACCTCATCAGTGAAATGGAAATGATGAAAAATGATAGGGAAGCACAA AAACATCATCAATTTGCTCGGAGCTTGTACCCAGGACGGTCCCTCTA CGTGATCGTAGAATACGCTTCCAAAGGTAATCTGCGCGAATATCTGCA AGCTCGGAGGCCGCCAGGTATGGAATACTGTTATAATCCGACACGGAT TCCCGAGGAACAGCTCTCTTTTAAAGATTTGGTTTCATGCGCGTATCAA GTGGCGAGGGGCATGGAGTATCTGGCGTCCAAGAAGTGCATTTCATAGG GACTTGGCTGCAAGAAATGTCTTGGTAACAGAAGACAACGTCATGAAG ATCGCCGACTTCGGCCTTGACGCGGATATTCATCACATCGACTATTACA AAGAGACGACGAACGGCCGCCTCCAGTTAAGTGGATGGCCCCCGAA GCCCTGTTTCGATCGGATTTACACGCATCAATCCGACGTGTGGCTTTTCG GTGTCTGCTTTGGGAGATATTTACACTCGGGGGATCACCTACCCCG GAGTACCGGTGGAGGAGTTGTTCAAACCTTCTTAAAGAAGGTCACAGAA TGGACAAACCCAGTAACTGCACTAACGAGCTGTATATGATGATGCGCG ATTGCTGGCACGCTGTTCCGTCACAACGGCCCACTTTTAAACAGCTCGT GGAGGATCTTGACAGAATCGTCGCGATGACTAGCAACCAAGAGTATTT GGATTTGTCAGTCCCGCTTGACCAATATTTCCCGCGTTCCTCCGGCTACC CGCTCTTCTACTTGTTCAGCGGTGAGGATAGTGATTTTCTCATGACC CACTTCCAGATGAGCCGTGCTTGCCTCGGTGTCTCCCCACTCCCATGG AGCGCTCAAACGCCACTGA
92	FGFR2-WT	ATGGGCCCTTAAGTCAACTTGGAGATACGGCAATGGCCCGGTACGTAC TCCAAGAAAATGGTATCTTGGGATTCCGGTTGTCTCATTTGTCTGGTAG TGGTTACCATGGCGGCCTGAGTCTGGCGAGACCCTCTTTAATCTGGT AGTTGAAGACGCTACCTTGAGGCCAGAAGAGCCGCCCACTAAGTATCA GATAAGTCAGCCTGATGTGCACTCCGCGCTTCCGGGAGAACCTCTCGA GTTGCGCTGTCAACTCAAGGATGCCGTGATGATCAGCTGGACGAAAGA TGGAGTGCCTCTTGGACCAGATAATCGCACTGTTATCATTGGTGAATA CTTGCAAATTAAGATGCATCACACGGGATTCTGGCCTTTACGCGTG CACAGCTATCAGGACGCTCGACTCCGATACACTCTATTTTATAGTCAAC GTTACCGATGCGTTGTCAAGCGGGGATGATGAGGACGACAACGACGG GTCAGAAGACTTCGTTAACGATTCCAATCAGATGAGAGTCCCTATTG GACCCACACTGACAAAATGGAAAAAAGGCTCCACGCTGTCCCGGTGCG GAATACTGTGAAGTTTAGATGTCCCGCAATGGGCAACCCACGCCAAC AATGCGGTGGTTGAAAAATGGTAAAGAGTTCAAACAGGAGCATCGGA TAGGTGGGTATAAAGTGAGAAATCAACATTGGAGCTTGATCATGGAGT CTGTAGTTCCTTCAGATAAAGGAAATTATACATGCATCGTCGAGAATC AATACGGCTCTATTAACCATACATATCACCTGGACGTCGTAGAGAGGA GTCCCCACAGGCCTATCCTGCAAGCGGGACTGCCGGCAAATGCTTCTG CAGTCGTGGGCGGTGACGTTGAGTTTCGTCTGTAAGGTGTACAGCGACG CACAACCACACATCCAATGGATAAAGCATGTTGAGAGAAATGGTTCAA AATATGGCCCGGACGGCTTGCCCTACCTTCAGGTGCTCAAAGCTGCGG GAGTCAACACTACTGATAAGGAAATCGAGGTGCTCTATATTAGGAACG TTACCTTTGAAGACGCCGCGAATACACCTGTCTCGCGGGAAACTCTA TCGGTATCTCATTTACACCGCATGGTTGACTGTGCTTCCAGCTCCGGA GAAAGAGAAGGAGTTTCCGACCTCCCTGATTACCTCGAAATAGCGAT CTATTGCATCGGAGTTTTTCTCATCGCGTGCATGGTTCTTACTGTGATA CTTTGTAGAATGAAGAACACCACCAAGAAACCGGATTTTTCTCCCAA CCGGCCGTCCACAAGTTGACGAAACGGATCCCATTGAGGCGCCAGGTG AGTGCTGACAGCTCAAGTTCAATGAACAGTAACACGCCGCTCGTGAGG ATCACTACTCGCTGAGCTCTACCGCGGATGCGCCAATGTTGGCAGGG GTCAGTGAGTACGAACTCCCGAAGATCCGAAGTGGGAGTTTCCGCGC GACAACTCACTCTTGGAAAACCGCTTGGAGAGGGATGCTTCGGACAG GTCGTAATGGCCGAGGCGGTTGGTATAGACAAAGATAGACCCAAAGA AGCTGTCACAGTAGCTGTAAAAATGCTTAAGGATGATGCCACTGAAAA

SEQ ID NO:	Description	Sequence
		AGATTTGAGCGACCTCGTAAGCGAGATGGAAATGATGAAAATGATAG GGAAGCACAAAAATATAATTAACCTCCTGGGGGCTGCACACAGGAC GGCCCGTTGTATGTCATCGTCGAATATGCCTCCAAAGGGAACCTCAGG GAGTACCTTAGAGCGCGCAGACCGCCGGGGATGGAGTATTCATTTGAC ATCAATCGGGTCCCCGAAGAACAAATGACTTTCAAAGACCTTGCTCC TGTACCTATCAACTCGCCCGCGGAATGGAATATTTGGCTAGTCAAAAA TGCATTACCGCGATCTTGCTGCACGGAACGTAACGTAAGTGAAGAAT AACGTTATGAAAATAGCGGATTTTCGGCCTCGCAAGGGACATAAACAAAC ATCGACTACTACAAAAAAACCACGAATGGCAGACTGCCAGTCAAGTG GATGGCGCCAGAAGCCCTTTTGGATAGAGTCTACACGCACCAAGTCAGA CGTGTGGTCCCTTGGAGTGCTCATGTGGGAAATCTTTACGCTGGGTGGT AGCCCTTACCCGGGGATTCCCGTGGAAGAACTTTTCAAGCTGTTGAAA GAGGGCCATCGGATGGACAAACCCGCAAAATGCACAAATGAATTGTAT ATGATGATGCGCGACTGTTGGCAAGCCGTGCCTTCACAGAGACCTACA TTCAAGCAGTTGGTGAAGACCTCGACCGGATCCTGACGCTTACAACG AACGAAGAATACCTGGACTTGTCTGGTCCCTTGGAGCAATACTACCA AGCTACCCCGATACTCGGTCTCTGTCTAGTGGCGACGATAGTGTCT TTTACCTGATCCAATGCCCTACGAACCGTGTCTGCCAAAGTACCAAC ACATGAACGGTTCAGTAAAGACCTGA
93	FGFR2-N550K	ATGGGCCTTAAGTCAACTTGGAGATACGGCAATGGCCCGGTACGTAC TCCAAGAAAATGGTATCTTGGGATTCCGGTTGTCTCATTTGTCTGGTAG TGGTTACCATGGCGGGCTGAGTCTGGCGAGACCTCTTTTAATCTGGT AGTTGAAGACGCTACCTTGGAGCCAGAAGAGCCGCCACTAAGTATCA GATAAGTCACCTGATGTGCACTCCGCGCTTCCGGGAGAACCTTCGA GTTGCGCTGTCAACTCAAGGATGCCGTGATGATCAGCTGGACGAAAGA TGGAGTGCCTCTTGGACCAGATAATCGCACTGTTATCATTGGTGAATA CTTGCAAATTAAGATGCATCACACCGGGATTCTGGCCTTTACGCGTG CACAGCTATCAGGACGCTCGACTCCGATACACTCTATTTTATAGTCAAC GTTACCGATGCGTGTCAAGCGGGGATGATGAGGACGACAAACGACGG GTCAGAAGACTTCGTTAACGATTCCAATCAGATGAGAGCTCCCTATTG GACCCACACTGACAAAATGGAAAAAAGGCTCCACGCTGTCCCGGCTGC GAATACTGTGAAGTTTAGATGTCCCGCAATGGGCAACCCACGCCAAC AATGCGGTGGTTGAAAAATGGTAAAGAGTTCAAACAGGAGCATCGGA TAGGTGGGTATAAAGTGAGAAATCAACATTGGAGCTTGATCATGGAGT CTGTAGTTCCTTCAGATAAAGGAAATTATACATGCATCGTCGAGAATC AATACGGCTCTATTAACCATAACATATCACCTGGACGTCGTAGAGAGGA GTCCCCACAGGCCTATCCTGCAAGCGGGACTGCCGGCAAATGCTTCTG CAGTCGTGGGCGGTGACGTTGAGTTCGTCTGTAAGGTGTACAGCGACG CACAACCACACATCCAATGGATAAAGCATGTTGAGAGAAATGGTTCAA AATATGGCCCGACGGCTTGCCCTACCTTCAGGTGCTCAAAGCTGCGG GAGTCAACACTACTGATAAGGAAATCGAGGTGCTCTATATTAGGAACG TTACCTTTGAAGACGCCGCGCAATACACCTGTCTCGCGGGAACTCTA TCGGTATCTCATTTCACACCGCATGGTTGACTGTGCTTCCAGCTCCGGA GAAAGAGAAGGAGTTTCCGACCTCCCTGATTACCTCGAAATAGCGAT CTATTGCATCGGAGTTTTTCTCATCGCGTGCATGGTTCTTACTGTGATA CTTTGTAGAATGAAGAACACCACCAAGAAACCGGATTTTTCTCCCAA CCGGCCGTCCACAAGTTGACGAAACGGATCCCATTTGAGGCGCCAGGTG AGTGCTGACAGCTCAAGTTCAATGAACAGTAACACGCCGCTCGTGAGG ATCACTACTCGGCTGAGCTCTACCGCGGATGCGCCAATGTTGGCAGGG GTCAGTGAGTACGAACCTCCCGGAAGATCCGAAGTGGGAGTTTCCGCGC GACAACTCACTCTTGGAAAACCGCTTGGAGAGGGATGCTTCGGACAG GTCGTAATGGCCGAGGCGGTTGGTATAGACAAAAGATAGACCCAAAGA AGCTGTCACAGTAGCTGTAATAATGCTTAAGGATGATGCCACTGAAAA AGATTTGAGCGACCTCGTAAGCGAGATGGAAATGATGAAAATGATAG GGAAGCACAAAAATATAATTAAGCTCCTGGGGGCTGCACACAGGAC GGCCCGTTGTATGTCATCGTCGAATATGCCTCCAAAGGGAACCTCAGG GAGTACCTTAGAGCGCGCAGACCGCCGGGGATGGAGTATTCATTTGAC

SEQ ID NO:	Description	Sequence
		ATCAATCGGGTCCCCGAAGAACAAATGACTTTCAAAGACCTTGTCTCC TGTACCTATCAACTCGCCCGCGGAATGGAATATTTGGCTAGTCAAAAA TGCATTACCGCGATCTTGTGTCACGGAACGTACTCGTCACTGAGAAT AACGTTATGAAAATAGCGGATTTCCGGCCTCGCAAGGGACATAAAACAAC ATCGACTACTACAAAAAAACCACGAATGGCAGACTGCCAGTCAAGTG GATGGCGCCAGAAGCCCTTTTGTATAGAGTCTACACGCACCAGTCAGA CGTGTGGTCCCTTGGAGTGTCTCATGTGGGAAATCTTTACGCTGGGTGGT AGCCCTTACCCGGGGATTCCCGTGGAAGAACTTTTCAAGCTGTTGAAA GAGGGCCATCGGATGGACAAAACCCGCAAATTGCACAAAATGAATTGTAT ATGATGATGCGCGACTGTTGGCAAGCCGTGCCTTACAGAGACCTACA TTCAAGCAGTTGGTCAAGACCTCGACCGGATCCTGACGTTACAACG AACGAAGAATACCTGGACTTGTCTGGTCCCTTGGAGCAATACTCACCA AGCTACCCCGATACTCGGTCACTTGTCTTAGTGGCGACGATAGTGTCT TTTCACCTGATCCAATGCCCTACGAACCGTGTCTGCCAAAGTACCAAC ACATGAACGGTTCAGTAAAGACCTGA
94	FGFR2-K660E	ATGGGCCTTAAGTCAACTTGGAGATACGGCAATGGCCCGGGTACGTAC TCCAAGAAAATGGTATCTTGGGATTCCGGTGTCTCATTTGTCTGGTAG TGGTTACCATGGCGGGCCTGAGTCTGGCGAGACCCTCTTTAATCTGGT AGTTGAAGACGCTACCTTGGAGCCAGAAGAGCCGCCCACTAAGTATCA GATAAGTCAGCCTGATGTGCACTCCGCGCTTCCGGGAGAACCCTCTCGA GTTGCCTGTCAACTCAAGGATGCCGTGATGATCAGCTGGACGAAAAGA TGGAGTGCCTCTTGGACCAGATAATCGCACTGTTATCATTGGTGAATA CTTGCAAATTAAAGATGCATCACACGGGATTCTGGCCTTTACGCGTG CACAGCTATCAGGACGCTCGACTCCGATACACTCTATTTTATAGTCAAC GTTACCGATGCGTTGTCAAGCGGGGATGATGAGGACGACAACGACGG GTCAGAAGACTTCGTTAACGATTCCAATCAGATGAGAGCTCCCTATTG GACCCACACTGACAAAATGGAAAAAGGCTCCACGCTGTCCCGGCTGC GAATACTGTGAAGTTTAGATGTCCCGCAATGGGCAACCCACGCCAAC AATGCGGTGGTTGAAAAATGGTAAAGAGTTCAAACAGGAGCATCGGA TAGGTGGGTATAAAGTGAGAAATCAACATTGGAGCTTGATCATGGAGT CTGTAGTTCCTTCAGATAAAGGAAATTATACATGCATCGTCGAGAATC AATACGGCTCTATTAACCATACATATCACCTGGACGTCGTAGAGAGGA GTCCCCACAGGCCTATCCTGCAAGCGGGACTGCCGGCAAATGCTTCTG CAGTCGTGGCGGTGACGTTGAGTTCGTCTGTAAGGTGTACAGCGACG CACAACCACACATCCAATGGATAAAGCATGTTGAGAGAAATGGTTCAA AATATGGCCCGGACGGCTTGCCCTACCTTCAGGTGCTCAAAGCTGCGG GAGTCAACACTACTGATAAGGAAATCGAGGTGCTCTATATTAGGAACG TTACCTTTGAAGACGCCGGCGAATACACCTGTCTCGCGGAAACTCTA TCGGTATCTCATTTACACCCGCATGGTTGACTGTGCTTCCAGCTCCGA GAAAGAGAAGGAGTTTCCGACCTCCCTGATTACCTCGAAATAGCGAT CTATTGCATCGGAGTTTTTCTCATCGCGTGCATGGTTCTTACTGTGATA CTTTGTAGAATGAAGAACACCAAGAAACCGGATTTTTCTCCCAA CCGGCCGTCCACAAGTTGACGAAACGGATCCCATGAGGCGCCAGGTG AGTGTGACAGCTCAAGTTCAATGAACAGTAACACGCCGCTCGTGAGG ATCACTACTCGGCTGAGCTCTACCGCGGATGCGCCAATGTTGGCAGGG GTCAGTGAGTACGAACTCCCGGAAGATCCGAAGTGGGAGTTTCCGCGC GACAAACTCACTCTTGGAAAACCGCTTGGAGAGGGATGCTTCGGACAG GTCGTAATGGCCGAGGCGGTTGGTATAGACAAAGATAGACCCAAAGA AGCTGTACAGTAGCTGTAAAAATGCTTAAGGATGATGCCACTGAAAA AGATTTGAGCGACCTCGTAAGCGAGATGGAAATGATGAAAATGATAG GGAAGCACAAAAATATAATTAACCTCCTGGGGGCTGCACACAGGAC GGCCCGTTGTATGTCATCGTCGAATATGCCTCCAAAGGGAACCTCAGG GAGTACCTTAGAGCGCGCAGACCGCGGGGATGGAGTATTCATTGAC ATCAATCGGGTCCCCGAAGAACAAATGACTTTCAAAGACCTTGTCTCC TGTACCTATCAACTCGCCCGCGGAATGGAATATTTGGCTAGTCAAAAA TGCATTACCGCGATCTTGTGTCACGGAACGTACTCGTCACTGAGAAT AACGTTATGAAAATAGCGGATTTCCGGCCTCGCAAGGGACATAAAACAAC

SEQ ID NO:	Description	Sequence
		ATCGACTACTACAAAGAAACCACGAATGGCAGACTGCCAGTCAAGTG GATGGCGCCAGAAGCCCTTTTGGATAGAGTCTACACGCACCAAGTCAGA CGTGTGGTCCTTTGGAGTGCTCATGTGGGAAATCTTTACGCTGGGTGGT AGCCCTTACCCGGGGATTCCCGTGGAAGAACTTTTCAAGCTGTTGAAA GAGGGCCATCGGATGGACAAACCCGCAAATTGCACAAATGAATTGTAT ATGATGATGCGCGACTGTTGGCAAGCCGTGCCTTCACAGAGACCTACA TTCAAGCAGTTGGTCGAAGACCTCGACCGGATCCTGACGCTTACAACG AACGAAGAATACCTGGACTTGTCTGGTCCCTTGGAGCAATACTACCA AGCTACCCCGATACTCGGTGCATCTTGCTCTAGTGGCGACGATAGTGTCT TTTACCTGATCCAATGCCCTACGAACCGTGTCTGCCAAAGTACCAAC ACATGAACGGTTCAGTAAAGACCTGA
95	FGFR2-N550K-N660E-S780A	ATGGGCCTTAAGTCAACTTGGAGATACGGCAATGGCCCGGGTACGTAC TCCAAGAAAATGGTATCTTGGGATTCCGGTTGTCTCATTTGTCTGGTAG TGGTTACCATGGCGGGCCTGAGTCTGGCGAGACCCTCTTTAATCTGGT AGTTGAAGACGCTACCTTGGAGCCAGAAGAGCCGCCCACTAAGTATCA GATAAGTCAGCCTGATGTGCACTCCGCGCTTCCGGGAGAACCTCTCGA GTTGCGCTGTCAACTCAAGGATGCCGTGATGATCAGCTGGACGAAAAGA TGGAGTGCCTCTTGGACCAGATAATCGCACTGTTATCATTGGTGAATA CTTGCAAATTAAGATGCATCACACGGGATTCTGGCCTTTACGCGTG CACAGCTATCAGGACGCTCGACTCCGATACACTCTATTTTATAGTCAAC GTTACCGATGCGTTGTCAAGCGGGGATGATGAGGACGACAACGACGG GTCAGAAGACTTCGTTAACGATTCCAATCAGATGAGAGCTCCCTATTG GACCCACACTGACAAAATGGAAAAAAGGCTCCACGCTGTCCCGGCTGC GAATACTGTGAAGTTTAGATGTCCCGCAATGGGCAACCCACGCCAAC AATGCGGTGGTTGAAAAATGGTAAAGAGTTCAAACAGGAGCATCGGA TAGGTGGGTATAAAGTGAGAAATCAACATTGGAGCTTGATCATGGAGT CTGTAGTTCCTTCAGATAAAGGAAATTATACATGCATCGTCGAGAATC AATACGGCTCTATTAACCATACATATCACCTGGACGTCGTAGAGAGGA GTCCCCACAGGCCTATCCTGCAAGCGGGACTGCCGGCAAATGCTTCTG CAGTCGTGGGCGGTGACGTTGAGTTCGTCTGTAAGGTGTACAGCGACG CACAACCACACATCCAATGGATAAAGCATGTTGAGAGAAATGGTTCAA AATATGGCCCGGACGGCTTGCCCTACCTTCAGGTGCTCAAAGCTGCGG GAGTCAACACTACTGATAAGGAAATCGAGGTGCTCTATATTAGGAACG TTACCTTTGAAGACGCGGCGAATAACACCTGTCTCGCGGAAACTCTA TCGGTATCTCATTTACACCCGCATGGTTGACTGTGCTTCCAGCTCCGGA GAAAGAGAAGGAGTTTCCGACCTCCCTGATTACCTCGAAATAGCGAT CTATTGCATCGGAGTTTTTCTCATCGCGTGCATGGTTCTTACTGTGATA CTTTGTAGAATGAAGAACACCACCAAGAAACCGGATTTTTCTCCCAA CCGGCCGTCCACAAGTTGACGAAACGGATCCCATTTGAGGCGCCAGGTG AGTGCTGACAGCTCAAGTTCAATGAACAGTAACACGCGCTCGTGAGG ATCACTACTCGGCTGAGCTCTACCGCGGATGCGCCAATGTTGGCAGGG GTCAGTGAGTACGAACCTCCCGGAAGATCCGAAGTGGGAGTTTCCGCGC GACAACTCACTCTTGGAAAACCGCTTGGAGAGGGATGCTTCGGACAG GTCGTAATGGCCGAGGCGGTTGGTATAGACAAAGATAGACCCAAAGA AGCTGTCACAGTAGCTGTAAAAATGCTTAAGGATGATGCCACTGAAAA AGATTTGAGCGACCTCGTAAGCGAGATGGAAATGATGAAAATGATAG GGAAGCACAAAAATATAATTAAGCTCCTGGGGGCCTGCACACAGGAC GGCCCGTTGTATGTCATCGTGAATATGCCTCCAAAGGGAACCTCAGG GAGTACCTTAGAGCGCGCAGACCGCGGGGATGGAGTATTCATTTGAC ATCAATCGGGTCCCCGAAGAACAAATGACTTTCAAAGACCTTGTCTCC TGTACCTATCAACTCGCCCGCGGAATGGAATATTTGGCTAGTCAAAAA TGCATTACCGCGATCTTGCTGCACGGAACGTACTCGTCACTGAGAAT AACGTTATGAAAATAGCGGATTTCCGGCCTCGCAAGGGACATAAACAAAC ATCGACTACTACAAAGAAACCACGAATGGCAGACTGCCAGTCAAGT GATGGCGCCAGAAGCCCTTTTGGATAGAGTCTACACGCACCAAGTCAGA CGTGTGGTCCTTTGGAGTGCTCATGTGGGAAATCTTTACGCTGGGTGGT AGCCCTTACCCGGGGATTCCCGTGGAAGAACTTTTCAAGCTGTTGAAA

SEQ ID NO:	Description	Sequence
		GAGGGCCATCGGATGGACAAACCCGCAAATTGCACAAATGAATTGTAT ATGATGATGCGCGACTGTTGGCAAGCCGTGCCTTCACAGAGACCTACA TTCAAGCAGTTGGTCGAAGACCTCGACCGGATCCTGACGCTTACAACG AACGAAGAATACTGGACTTGTCTGGTCCCTTGGAGCAATACGCACCA AGCTACCCCGATACTCGGTCATCTTGTCTAGTGGCGACGATAGTGTCT TTTACCTGATCCAATGCCCTACGAACCGTGTCTGCCAAAGTACCAAC ACATGAACGGTTCAGTAAAGACCTGA
96	FGFR3-WT	ATGTCAGAAGCTGGTGGCGGCGCCGCTGCCGACGCTCACTCCCGAGA TCAAGGGCCGGTGGCATGCGCGCGGCATGGGGATCCGTGTGGTGTG TGCTCGCGGCGGCTGTCTGGAGCTCTGCCGGCTGCAAGGCGCAGGGGA GCGGAACGGAGCGGTGGCCAGGCGGCGGAGTATCTCCGAGTGAAAC TGCAATTTCTTGAGGAGCTTGTCTTTCGGTTCAGGGGATACCATCGAGCTT TCCTGTAACACACAATCTTCAAGTGAAGCGTATTCTGGTTCAAAGAT GGTATAGGCATTGCGCCCACTAATAGAACACACATCGGGCAGAACTT TTGAAGATCATCAACGTTTCATATGATGATTCCGGACTGTACTCATGTA AGCCAAGGCACAGTAACGAGGTGCTTGGGAACTTCACAGTCAGGGTTA CAGGCGTACCATTCTGGACGAGGCCCGATAAGATGGAAAAAACTTT TGGCAGTGCCCGCAGCCAATACAGTGCGGTTCCGCTGCCCGCAGGTG GGAATCCGACGCCCCACAATTTATTGGCTGAAGAATGGCAAGGAGTTCA AAGGAGAACATAGGATCGGCGGAATCAAACCTGAGGCACCAGCAATGG TCTCTGGTGATGGAATCAGTAGTCCCATCTGACCGCGGTAACTACACG TGCGTAGTAGAAAACAAGTATGGGAATATTCGGCATACCTACCAGCTC GATGTGCTCGAGAGATCTCCTCACAGGCCTATCTTGCAAGGCTGGACTG CCAGCTAATCAAACAGTAGTTGTCTGGATCTAACGTGGAGTTCAGTGC AAAGTTTACTCAGACGCCCCAACCGCACATTCAATGGCTTAAACACGTG GAGGTAAACGGTAGCAAGTATGGACCTGATGGGACTCCCTATGTGACA GTCCTTAAGAGTTGGATTTCTAAGAATGCCGAGGCGGATGCGAACTTG AACCTGTTTAAACGTAACCGAGCAGGACGAGGGCGAATATCTTTGTCTG GCTAACAACTTCGTTGGAATAGCGGAGAAGCCCTTCTGGCTGCATATA CGGAAGCCAAAGCCGGCGGAGGAGTTGATGGAGATGGATGACTCCGG TTCCGTATACGCCGAATCCTTAGCTACGGAACCGGGCTGGTGCTGTTT ATCCTCGTTTTGGTTATTGTTATTATATGCCGCATGAAGATGCCAAACA AAAAGGCAATGAATACTACAACGTGTCAGAAAAGTGTCAAAATTTCCAC TTAAACGGCAAGTCACTGTCTCACTCGAATCTAACTTCCATGAACTC CAACACTCCGTTGGTGCGGATTACCAGATTGTCTCATCCGACGGTCCC ATGTTGGCAAATGTCAGTGAGCTGGAATTGCCGCCCCGATCCCAAATGG GAACTTGCAAGATCCCGGCTTACTCTCGGTAAGCCCTTGGGCGAAGGT TGCTTTGGACAAGTCGTCATGGCCGAAGCGATTGGAATCGATAAAGAC AAACCCAAACAAGGCTATAACGGTCGCAGTAAAAATGTTGAAAGATGA CGCGACCGACAAGGACCTGTCAGATCTGGTCTCAGAGATGGAATGAT GAAGATGATTGGTAAACACAAGAATATAATCAACTTGCTTGGAGCATG TACGCAAGACGGCCCTCTCTACGTTCTCGTGGAGTATGCCTCTAAGGG CAATTTGAGGGAGTACCTGAGAGCTCGCAGACCTCCGGGCATGGATTA TAGTTTCGACACTTGTAAGCTGCCGGAGGAGCAACTTACCTTCAAGGA TCTTGTAAGTTGCGCGTACCAGGTTGCAAGGGGGATGGAATACCTCGC CAGTCAAAAGTGCATACATAGAGATTGGCAGCGAGGAACGTGCTCGT GACTGAGGACAACGTCATGAAAATTGCGGACTTTGGGCTTGACCGGA TGTTCTATAACATCGATTACTACAAGAAACTACTAACGGACGGCTCCC TGTGAAGTGGATGGCTCCAGAAGCGCTTTTTGATAGAGTTACACACA TCAAAGTGACGTATGGAGTTTTGGAGTATTGCTCTGGGAGATTTTACC TTGGGAGGGTCTCCTTACCCTGGAATACCCGTGCAAGAGCTCTTAAAG CTGCTTAAAGAAGGCCACAGGATGGACAAGCCGCGCAACTGCACTCA TGATCTGTACATGATAATGAGAGAGTGCTGGCACGCCGTTCCCTCCCA GCGGCCGACATTCAAGCAGCTGGTGGAAGACCTTGATAGGGTACTAC TATGACGTCCACCGATGAGTATCTGGACTTGTCTGTTCATTGCAACAA TACTCTCCGGCCGGTCAGGATACGCATTCCACTTGCTCCAGTGGTGATG

SEQ ID NO:	Description	Sequence
		ATTCTGTCTTTGCACACGATCTTCTCCCAGACGAACCCTGTCTTCCTAA ACACGTACCGTGTAACGGTGTCTATAAGGACATAG
97	FGFR3- N540K	ATGTCAGAAGCTGGTGGCGGCGCCGCTGCCGCAGCCTCACTCCCGAGA TCAAGGGCCGGTGGCATGCGCGCGGCATGGGGATCCGTGTGGTGTG TGCCTCGCGGCGGCTGTGCGAGCTCTGCCGGCTGCAAGGCGCAGGGGA GCGGAACGGAGCGGTGGCCAGGCGGCGGAGTATCTCCGAGTGAAAC TGCATTTCTTGAGGAGCTTGTTTTCGGTTTCAGGGGATACCATCGAGCTT TCCTGTAACACACAATCTTCAAGTGTAAAGCGTATTCTGGTTCAAAGAT GGTATAGGCATTGCGCCCACTAATAGAACACACATCGGGCAGAAAATT TTGAAGATCATCAACGTTTCATATGATGATTCCGGACTGTACTCATGTA AGCCAAGGCACAGTAACGAGGTGCTTGGGAACTTCACAGTCAGGGTTA CAGGCGTACCATTCTGGACGAGGCCCGATAAGATGGAAAAAAACTTT TGGCAGTGCCCGCAGCCAATACAGTGCGGTTCCGCTGCCCGCAGGTG GGAATCCGACGCCCCACAATTTATTGGCTGAAGAATGGCAAGGAGTTCA AAGGAGAACATAGGATCGGCGGAATCAAACCTGAGGCACCAGCAATGG TCTCTGGTGATGGAATCAGTAGTCCCATCTGACCGCGGTAACTACACG TGCGTAGTAGAAAACAAGTATGGGAATATTCGGCATACCTACCAGCTC GATGTGCTCGAGAGATCTCCTCACAGGCCTATCTTGCAGGCTGGACTG CCAGCTAATCAAACAGTAGTTGTGCGATCTAACGTGGAGTCCACTGC AAAGTTTACTCAGACGCCCAACCGCACATTCAATGGCTTAAACACGTG GAGGTAAACGGTAGCAAGTATGGACCTGATGGGACTCCCTATGTGACA GTCCTTAAGAGTTGGATTTCTAAGAATGCCGAGGCGGATGCGAACTTG AACCTGTTTAAACGTAACCGAGCAGGACGAGGGCGAATATCTTTGTCGC GCTAACAACTCTGTTGGAATAGCGGAGAAAGCCCTTCTGGCTCATATA CGGAAGCCAAAGCCGGCGGAGGAGTTGATGGAGATGGATGACTCCGG TTCCGTATACGCCGAATCCTTAGCTACGGAACCGGGCTGGTGCTGTTT ATCCTCGTTTTGGTTATTGTTATTATATGCCGCATGAAGATGCCAAACA AAAAGGCAATGAATACTACAACCTGTGCAGAAAAGTGTCAAAATTTCCAC TTAAACGGCAAGTCACCTGTCTCACTCGAATCTAACTCTCCATGAACCTC CAACACTCCGTTGGTGCGGATTACCAGATTGTCTCATCCGACGGTCCC ATGTTGGCAAATGTCAGTGAGCTGGAATTGCCGCCCCGATCCCAAATGG GAACTTGCAAGATCCCGGCTTACTCTCGGTAAGCCCCCTGGGCGAAGGT TGCTTTGGACAAGTCGTCATGGCCGAAGCGATTGGAATCGATAAAGAC AAACCCAAACAAGGCTATAACGGTTCGAGTAAAAATGTTGAAAGATGA CGCGACCGACAAGGACCTGTCTAGATCTGGTCTCAGAGATGGAATGAT GAAGATGATTGGTAAACACAAGAATATAATCAAGTTGCTTGGAGCATG TACGCAAGACGGCCCTCTCTACGTTCTCGTGGAGTATGCCTCTAAGGG CAATTTGAGGGAGTACCTGAGAGCTCGCAGACCTCCGGGCATGGATTA TAGTTTCGACACTTGTAAGCTGCCGGAGGAGCAACTTACCTTCAAGGA TCTTGTAAGTTGCGCGTACCAGGTTGCAAGGGGGATGGAATACCTCGC CAGTCAAAAGTGCATACATAGAGATTGGCAGCGAGGAACGTGCTCGT GACTGAGGACAACGTCATGAAAATTGCGGACTTTGGGCTTGACGGGA TGTTTATAACATCGATTACTACAAGAAAATACTAACGGACGGCTCCC TGTGAAGTGGATGGCTCCAGAAGCGCTTTTTGATAGAGTTTACACACA TCAAAGTGACGTATGGAGTTTGGAGTATTGCTCTGGGAGATTTTACAC TTGGGAGGGTCTCCTTACCCTGGAATACCCGTGCAAGAGCTCTTTAAG CTGCTTAAAGAAGGCCACAGGATGGACAAGCCGGCGAACTGCACTCA TGATCTGTACATGATAATGAGAGAGTGCTGGCACGCCGTTCCCTCCCA GCGGCCGACATTCAAGCAGCTGGTGGAAAGACCTTGATAGGGTACTCAC TATGACGTCCACCGATGAGTATCTGGACTTGTCTGTTCCATTGCAACAA TACTCTCCGGCCGGTCAGGATACGCATTCCACTTGCTCCAGTGGTGATG ATTCTGTCTTTGCACACGATCTTCTCCCAGACGAACCCTGTCTTCCTAA ACACGTACCGTGTAACGGTGTCTATAAGGACATAG
98	FGFR3- K650E	ATGTCAGAAGCTGGTGGCGGCGCCGCTGCCGCAGCCTCACTCCCGAGA TCAAGGGCCGGTGGCATGCGCGCGGCATGGGGATCCGTGTGGTGTGTTG TGCCTCGCGGCGGCTGTGCGAGCTCTGCCGGCTGCAAGGCGCAGGGGA GCGGAACGGAGCGGTGGCCAGGCGGCGGAGTATCTCCGAGTGAAAC

SEQ ID NO:	Description	Sequence
		TGCATTTCTTGAGGAGCTTGTTTTCGGTTTCAGGGGATACCATCGAGCTT TCCTGTAACACACAATCTTCAAGTGTAAGCGTATTCTGGTTCAAAGAT GGTATAGGCATTGCGCCCAGTAATAGAACACACATCGGGCAGAACTT TTGAAGATCATCAACGTTTCATATGATGATTCCGGACTGTACTCATGTA AGCCAAGGCACAGTAACGAGGTGCTTGGGAACTTCACAGTCAGGGTTA CAGGCGTACCATTCTGGACGAGGCCGATAAGATGGAAAAAAAAACTTT TGGCAGTGCCCGCAGCCAATACAGTGCGGTTCCGCTGCCCGCAGGTG GGAATCCGACGCCACAATTTATTGGCTGAAGAATGGCAAGGAGTTCA AAGGAGAACATAGGATCGGCGGAATCAAACCTGAGGCACCAGCAATGG TCTCTGGTGATGGAATCAGTAGTCCCATCTGACCGCGGTAACTACACG TGCGTAGTAGAAAACAAGTATGGGAATATTCCGCATACCTACCAGCTC GATGTGCTCGAGAGATCTCCTCACAGGCCTATCTTGCAAGCTGGACTG CCAGCTAATCAAACAGTAGTTGTCGGATCTAACGTGGAGTTCCACTGC AAAGTTTACTCAGACGCCCAACCGCACATTCAATGGCTTAAACACGTG GAGGTAAACGGTAGCAAGTATGGACCTGATGGGACTCCCTATGTGACA GTCCTTAAGAGTTGGATTTCTAAGAATGCCGAGGCGGATGCGAACTTG AACCTGTTTAAACGTAACCGAGCAGGACGAGGGCGAATATCTTTGTGCG GCTAACAACTTCGTTGGAATAGCGGAGAAGCCCTTCTGGCTGCATATA CGGAAGCCAAAGCCGGCGGAGGAGTTGATGGAGATGGATGACTCCGG TTCCGTATACGCCGAATCCTTAGCTACGGAACCGGGCTGGTGCTGTTT ATCCTCGTTTTGGTTATTGTTATTATATGCCGCATGAAGATGCCAAACA AAAAGGCAATGAATACTACAACCTGTGCAGAAAGTGCAAAATTTCCAC TTAAACGGCAAGTCACTGTCTCACTCGAATCTAACTCTTCCATGAACCT CAACACTCCGTTGGTGCGGATTACCAGATTGTCCTCATCGACGGTCCC ATGTTGGCAAATGTCAGTGAGCTGGAATTGCCGCCGATCCCAAATGG GAACTTGCAAGATCCCGGCTTACTCTCGGTAAGCCCCTGGGCGAAGGT TGCTTTGGACAAGTCGTCATGGCCGAAGCGATTGGAATCGATAAAGAC AAACCAACAAGGCTATAACGGTCGCACTAAAAATGTTGAAAGATGA CGCGACCGACAAAGGACCTGTCAGATCTGGTCTCAGAGATGGAATGAT GAAGATGATTGGTAAACACAAGAATATAATCAACTTGCTTGGAGCATG TACGCAAGACGGCCCTCTCTACGTTCTCGTGGAGTATGCCTCTAAGGG CAATTTGAGGGAGTACCTGAGAGCTCGCAGACCTCCGGGCATGGATTA TAGTTTCGACACTTGTAAGCTGCCGGAGGAGCAACTTACCTTCAAGGA TCTTGTAAGTTGCGCGTACCAGTTGCAAGGGGGATGGAATACCTCGC CAGTCAAAAGTGATACATAGAGATTTGGCAGCGAGGAACGTGCTCGT GACTGAGGACAACGTGATGAAAATTGCGGACTTTGGGCTTGACGGGA TGTTTCATAACATCGATTACTACAAGGAACTACTAACGGACGGCTCCC TGTGAAGTGGATGGCTCCAGAAGCGCTTTTGTATAGAGTTTACACACA TCAAAGTGACGTATGGAGTTTGGAGTATTGCTCTGGGAGATTTTACC TTGGGAGGGTCTCCTTACCCTGGAATACCCGTCGAAGAGCTCTTTAAG CTGCTTAAAGAAGGCCACAGGATGGACAAGCCGGCGAACTGCACTCA TGATCTGTACATGATAATGAGAGAGTGCTGGCACGCCGTTCCCTCCCA GCGGCCGACATTCAAGCAGCTGGTGGAAAGACCTTGATAGGGTACTCAC TATGACGTCCACCGATGAGTATCTGGACTTGTCTGTTCCATTCCAACAA TACTCTCCGGCCGGTCAGGATACGCATTCCACTTGCTCCAGTGGTGATG ATTCTGTCTTTGCACACGATCTTCTCCAGACGAACCTGTCTTCCTAA ACACGTACCGTGTAACGGTGTCATAAGGACATAG
99	FGFR3-N540K-K650E	ATGTCAGAAGCTGGTGGCGGCGCGCTGCCGCAGCCTCACTCCCGAGA TCAAGGGCCGGTGGCATGCGCGCGCATGGGGATCCGTGTGGTGTG TGCTTCGCGGCGGCTGTCGGAGCTCTGCCGGCTGCAAGGCGCAGGGGA GCGGAACGGAGCGGTGGCCAGGCGGCGGAGTATCTCCGAGTGAAAC TGCAATTTCTTGAGGAGCTTGTTTTCGGTTTCAGGGGATACCATCGAGCTT TCCTGTAACACACAATCTTCAAGTGTAAGCGTATTCTGGTTCAAAGAT GGTATAGGCATTGCGCCCAAGTAATAGAACACACATCGGGCAGAACTT TTGAAGATCATCAACGTTTCATATGATGATTCCGGACTGTACTCATGTA AGCCAAGGCACAGTAACGAGGTGCTTGGGAACTTCACAGTCAGGGTTA CAGGCGTACCATTCTGGACGAGGCCGATAAGATGGAAAAAAAAACTTT

SEQ ID NO:	Description	Sequence
		TGGCAGTGCCCGCAGCCAATACAGTGCGGTTCCGCTGCCCCGCAGGTG GGAATCCGACGCCCACAATTTATTGGCTGAAGAATGGCAAGGAGTTCA AAGGAGAACATAGGATCGGCGGAATCAAACCTGAGGCACCAGCAATGG TCTCTGGTGATGGAATCAGTAGTCCCATCTGACCGCGGTAACATACACG TGCGTAGTAGAAAACAAGTATGGGAATATTCCGCATACCTACCAGCTC GATGTGCTCGAGAGATCTCCTCACAGGCCTATCTTGCAAGGCTGGACTG CCAGCTAATCAAACAGTAGTTGTCGGATCTAACGTGGAGTCCACTGC AAAGTTTACTCAGACGCCCCAACCGCACATTCAATGGCTTAAACACGTG GAGGTTAACGGTAGCAAGTATGGACCTGATGGGACTCCCTATGTGACA GTCCTTAAGAGTTGGATTCTAAGAATGCCGAGGCGGATGCCAACTTG AACCTGTTTAAACGTAACCGAGCAGGACGAGGGCGAATATCTTTGTGCG GCTAACAACTTCGTTGGAATAGCGGAGAAAGCCCTTCTGGCTGCATATA CGGAAGCCAAAGCCGGCGGAGGAGTTGATGGAGATGGATGACTCCGG TTCCGTATACGCGGAATCCTTAGCTACGGAACCGGGCTGGTGCTGTTT ATCCTCGTTTTGGTTATTGTTATTATATGCCGCATGAAGATGCCAAACA AAAAGGCAATGAATACTACAACCTGTGCAGAAAGTGTCAAAATTTCCAC TTAAACGGCAAGTCACTGTCTCACTCGAATCTAACTCTTCCATGAACCTC CAACACTCCGTTGGTGCGGATTACCAGATTGTCTCATCCGACGGTCCC ATGTTGGCAAATGTCAGTGAGCTGGAATTGCCGCCGATCCCAAATGG GAACTTGCAAGATCCCGGCTTACTCTCGGTAAGCCCTGGGCGAAGGT TGCTTTGGACAAGTCGTATGGCCGAAGCGATTGGAATCGATAAAGAC AAACCCAAACAAGGCTATAACGGTCCGACGTAAAAATGTTGAAAGATGA CGCGACCGACAAGGACCTGTCAGATCTGGTCTCAGAGATGGAATGAT GAAGATGATTGGTAAACACAAGAATATAATCAAGTTGCTGGAGCATG TACGCAAGACGGCCCTCTCTACGTTCTCGTGGAGTATGCCTCTAAGGG CAATTTGAGGGAGTACCTGAGAGCTCGCAGACCTCCGGGCATGGATTA TAGTTTCGACACTTGTAAGCTGCCGGAGGAGCAACTTACCTTCAAGGA TCTTGTAAGTTGCGCGTACCAGGTTGCAAGGGGGATGGAATACCTCGC CAGTCAAAAGTGCATACATAGAGATTGGCAGCGAGGAACGTGCTCGT GACTGAGGACAACGTATGAAAATTGCGGACTTTGGGCTTGACGGGA TGTTTATAACATCGATTACTACAAGGAACTACTAACGGACGGTCCC TGTGAAGTGGATGGCTCCAGAAGCGCTTTTGTATAGAGTTTACACACA TCAAAGTGACGTATGGAGTTTGGAGTATTGCTCTGGGAGATTTTACC TTGGGAGGGTCTCCTTACCCTGGAATACCCGTCGAAGAGCTCTTAAAG CTGCTTAAAGAAGGCCACAGGATGGACAAGCCGGCGAACTGCACTCA TGATCTGTACATGATAATGAGAGAGTGCTGGCACGCCGTTCCCTCCCA GCGGCCGACATTCAAGCAGCTGGTGGAAGACCTTGATAGGGTACTCAC TATGACGTCCACCGATGAGTATCTGGACTTGTCTGTTCCATTGCAACAA TACTCTCCGGCCGGTCAAGGATACGCATTCCACTTGCTCCAGTGGTGATG ATTCTGTCTTTGCACACGATCTTCTCCAGACGAACCCTGTCTTCCTAA ACACGTACCGTGTAACGGTGTCTATAAGGACATAG
100	myrist- FGFR3- K650E	ATGGGATCATCCAAGTCAAAACCGAAAGACCCGTCACAGAGACGCAT GAAGATGCCAAACAAAAAGGCAATGAATACTACAACCTGTGCAGAAAG TGTCAAAATTTCCACTTAAACGGCAAGTCACTGTCTCACTCGAATCTA ACTCTTCCATGAACTCCAACACTCCGTTGGTGCGGATTACCAGATTGTC CTCATCCGACGGTCCCATGTTGGCAAATGTCAGTGAGCTGGAATTGCC GCCCCGATCCCAAATGGGAACCTTGCAAGATCCCGGCTTACTCTCGGTAA GCCCCCTGGGCGAAGGTTGCTTTGGACAAGTCGTATGGCCGAAGCGAT TGGAATCGATAAAGACAAACCCAACAAGGCTATAACGGTCCGAGTAA AAATGTTGAAAGATGACGCGACCGACAAGGACCTGTGAGATCTGGTCT CAGAGATGGAAATGATGAAGATGATTGGTAAACACAAGAATATAATC AACTTGCTTGGAGCATGTACGCAAGACGGCCCTCTCTACGTTCTCGTG GAGTATGCCTCTAAGGGCAATTTGAGGGAGTACCTGAGAGCTCGCAGA CCTCCGGGCATGGATTATAGTTTCGACACTTGTAAGCTGCCGAGGAG CAACTTACCTTCAAGGATCTTGTAAGTTGCGCGTACCAGGTTGCAAGG GGGATGGAATACCTCGCCAGTCAAAAGTGCATACATAGAGATTTGGCA GCGAGGAACGTGCTCGTGACTGAGGACAACGTCATGAAAATTGCGGA

SEQ ID NO:	Description	Sequence
		CTTTGGGCTTGCACGGGATGTTTCATAACATCGATTACTACAAGGAAAC TACTAACGGACGGCTCCCTGTGAAGTGGATGGCTCCAGAAGCGCTTT TGATAGAGTTTACACACATCAAAGTGACGTATGGAGTTTTGGAGTATT GCTCTGGGAGATTTTACCTTGGGAGGGTCTCCTTACCCTGGAATACCC GTCGAAGAGCTCTTAAAGCTGCTTAAAGAAGGCCACAGGATGGACAA GCCGGCGAACTGCACTCATGATCTGTACATGATAATGAGAGAGTGCTG GCACGCCGTTCCCTCCCAGCGGCCGACATTCAAGCAGCTGGTGGAAGA CCTTGATAGGGTACTCACTATGACGTCCACCGATGAGTATCTGGACTT GTCTGTTCCATTCGAACAATACTCTCCGGCCGGTCAGGATACGCATTCC ACTTGCTCCAGTGGTGATGATTCTGTCTTTGCACACGATCTTCTCCAG ACGAACCTGTCTTCTTAAACACGTACCGTGTAAACGGTGCATAAGGA CATAG
101	FGFR4-WT	ATGCTTCCTCTGCGCCTGGTTCTCGCTGGCCTCTTGGTTCGACGGGTT CAGCGGCGAGTCATAGGGGAGAAATGGAGCCGGAACCTTTGAGTCTC CACTCTTGGAATCCGAAGAAGAACCTCCTTCTGGACCCAGGAAACG CATTGAAACTCTATTGTGACGTAAACCAGTCCGGAGCTAGTGTGGTTT GGTATAAGGAGAGTAGACCTCTGCTGCCAGGGCCCCGCGTCAGATTGC AACAAAGCGTTCTTGAAATAGCGGAAGTAGCTTACGAGGATTCGGCC TCTACGTCTGTAGAGCTCGCGGAACCGGTGAGGTCCCTTAGGAACTTCA CCATATCAGTTGTAGATTCACTTGCCTCAGGCGATGACGATGAAGACA GCGATGGGGATGGTCCACATGGAGACCGCTCTGAAGAACCAGTATAC GTTCACAGAGCACCTTATTGGACCCATCCACACAGGATGGATAAAAAA CTCTACGCTGTTCTGCGGGCAATACCGTGAAATTCCGCTGTCCAGCG AGTGGGTCTCCAAGCCGTCCATTAGATGGTTTAAAGAATGGCAGAGAG TTTCGCGGGGAGCACAGAATAGGGGGCATTAGGCTCCGGCATCAGCAT TGGTCACTCGTTATGGAGTCAGTCGTGCCGTCTGATAGGGGGAATTAC ACCTGCTTGGTAGAGAACCGGTTTGGTTCAATCCGTATAGTTATCTGC TGGATGTCTCGAACGCTCCCCACACAGACCCATCTTGCAAGCTGGAC TTCCAGCTAACACAACAGCTCTGGTAGGTTTCAGATGTGGAATTTTTCTG CAAGGTATACTCTGATGCTCAACCGCACATACAGTGGTTGAAACACAT TGAAGTTAACGGGTCTCATATGGGCCAGACGGTGTACCCTACGTGCA GGTACTGAAGACGGCCGACATTAATTCATCTGAGGTTGAGGTGCTGTA TTTGCGGAACGTCACAATGGAAGACGCCGGGGAGTATACTTGTCTTGC CGGTAATAGTATTGGGCTGTCTATCAGTCCGCGTGGCTCACCGTCTG CCAGAAGAGCTGGTTCATGAGGCTGAGGCACCTGAGGCGAAATACAC CGACATCATAATTTACACTTCCGGATCATTGGCCGTGGCAATGGCTCTT ATCATCGTCGTCTGTGTAGGATGCAAACCTCAGAGCTCTAAACAACCC CTTGAACCCATGGCAGTACACAAATTGAGCAAATTTCTCTTATTAGA CAGTTTTCCCTTGACTCAAGTAGCTCAGGGAATCTAGCACATCACTTA TGCGGGTGACGAGACTGTCTTCCAGCTGCGCGCCCATGTTGGCTGGGG TGGTGGAACCTTGATCTGCCTCTGGACAGCAAGTGGGAATTTCCGAGGG AGAAACTGGTTCTTGGGAAGCCGCTCGGCGAAGGCTGTTTTGGTCAGG TGGTCAGGGCGGAAGCGTACGGGATCGACAGACAGTGGCCTGATCGC GCAGTTACTGTGCGAGTAAAAATGCTGAAAAGACAACGCTACTGATAAG GATCTGGCAGACCTGATAAGTGAAATGGAGATGATGAAACTGATGGA CAAACACAAGAACATCATTAATCTTGGGTGTATGTACACAAGATGG GCCTCTGTATGTTATAGTAGAGTTTGCGGCCAAAGGCAACCTTCGGGA GTATCTTCGCGCTAGAAGACCGCCAATGCCCGACTACACGTTTCGATAT TACAGAACTCCATGAGGAACAACCTTGTTTTAAGGATCTTGTTAGCTGT GTGTATCAAGTCGCCCGGGGGATGGAGTATCTGGAATCAAGACGGTGT ATACACCGCGACCTCGCTGCCAGAAACGTTCTCGTCACGGCGGAAAAT GTGATGAAGATCGCCGACTTCGGACTTGCCAGGGATGTCCATGATATA GACTATTACAAAAAACATCTAATGGGCGGCTCCCTGTCAAGTGGATG GCGCCCGAAGCACTGTTTGACAGAGTATACACGCACCACTGACGTG TGGTCATTGTCATCTGATGTGGGAAATTTTACACTCGGTGGTTTAC CTTATCCTGGCATCCCTGTTGAGGAGCTTTTAAATTGCTCAAAGAGGG CCACAGAATGGACTGTCTAGTAACTGCACCCATGAGCTGTATATGCT

SEQ ID NO:	Description	Sequence
		CATGCGCGAGTGCTGGCATGCGGTGCCTAGTCAAAGGCCAACCTTCAA ACAGCTCGTCGAAGGCCTGGACAAGATTCTTGCTGCAATAAGCGAGGA GTACCTCGACTTGCTATGCCATTCGAGCAATACTCACCTTCTTGTA GACACGACGAGTACATGCAGCAGCGACGACTCTGTATTTACACACGAC CCTTTGCCCTTGCTCCTTGCTGTTTGCCTGTCTAGTGGCCGCACCTA G
102	FGFR4- Y367C	ATGCTTCCTCTGCGCCTGGTTCTCGCTGGCCTCTTGGTCGCAGCGGGTT CAGCGGCGAGTCATAGGGGAGAAATGGAGCCGGAACCTTTGAGTCTC CACTCTTGGAATCCGAAGAAGAACACCTCCTTCTGGACCCAGGAAACG CATTGAACTCTATTGTGACGTAAACAGTCCGGAGCTAGTGTGGTTT GGTATAAGGAGAGTAGACCTCTGCTGCCAGGGCCCCGCGTCAGATTGC AACAAGCGTTCTTGAAATAGCGGAAGTAGCTTACGAGGATTCCGGCC TCTACGTCTGTAGAGCTCGCGGAACCGGTGAGGTCCTTAGGAACTTCA CCATATCAGTTGTAGATTCACTTGCCTCAGGCGATGACGATGAAGACA GCGATGGGGATGGTCCACATGGAGACCGCTCTGAAGAACCAGTATAC GTTACAGAGCACCTTATTGGACCCATCCACACAGGATGGATAAAAAA CTCTACGCTGTTCTGCGGGCAATACCGTGAAATTCGCTGTCCAGCG AGTGGGTCTCCAAGCCCGTCCATTAGATGGTTTAAAGATGGCAGAGAG TTTCGCGGGGAGCACAGAATAGGGGGCATTAGGCTCCGGCATCAGCAT TGGTCACTCGTTATGGAGTCAGTCGTGCCGTCTGATAGGGGGAATTAC ACCTGCTTGGTAGAGAACCGGTTTGGTTCAATCCGTATAGTTATCTGC TGGATGTCTCGAACGCTCCCCACACAGACCCATCTTGCAAGCTGGAC TTCCAGCTAACACAACAGCTCTGGTAGGTTTCAAGTGTGGAATTTTCTG CAAGGTATACCTGATGCTCAACCGCACATACAGTGGTTAAACCAT TGAAGTTAACGGTCTCATATGGGCCAGACGGTGTACCCTACGTGCA GGTACTGAAGACGGCCGACATTAATTCATCTGAGGTTGAGGTGCTGTA TTTGCGGAACGTCACAAATGGAAGACGCCGGGGAGTATACTTGTCTTGC CGGTAATAGTATTGGGCTGTCTATCAGTCCGCGTGGCTCACCGTCTG CCAGAAGAGCTGGTTCATGAGGCTGAGGCACTGAGGCGAAATGTAC CGACATCATAATTTACACTTCCGGATCATTGGCCGTGGCAATGGCTCTT ATCATCGTCGTTCTGTGTAGGATGCAAACTCAGAGCTCTAAACAACCC CTTGAACCCATGGCAGTACACAAATTGAGCAAATTTCTCTTATTAGA CAGTTTTCCCTTGACTCAAGTAGCTCAGGGAAATCTAGCACATCACTTA TGCGGGTGACGAGACTGTCTTCCAGCTGCGCGCCCATGTTGGCTGGGG TGGTGGAACCTTGATCTGCCTCTGGACAGCAAGTGGGAATTTCCGAGGG AGAACTGGTTCTTGGGAAGCCGCTCGGCGAAGGCTGTTTTGGTCAGG TGGTCAGGGCGGAAGCGTACGGGATCGACAGACAGTGGCCTGATCGC GCAGTTACTGTGCGAGTAAAAATGCTGAAAGACAACGCTACTGATAAG GATCTGGCAGACCTGATAAGTGAAATGGAGATGATGAAATGATGGA CAAACACAAGAACATCATTAATCTCTTGGGTGTATGTACACAAGATGG GCCTCTGTATGTTATAGTAGAGTTTGGCGCCAAAGGCAACCTTCGGGA GTATCTTCGCGCTAGAAGACCGCCAATGCCCGACTACACGTTTCGATAT TACAGAACTCCATGAGGAACAACCTTGTTTTAAAGGATCTTGTAGCTGT GTGTATCAAGTCGCGCGGGGATGGAGTATCTGGAATCAAGACGGTGT ATACACCGCGACCTCGCTGCCAGAAACGTTCTCGTCACGGCGGAAAT GTGATGAAGATCGCCGACTTCGACTTGCCAGGGATGTCCATGATATA GACTATTACAAAAAACATCTAATGGGCGGCTCCCTGTCAAGTGGATG GCGCCCCAAGCACTGTTTGACAGAGTATACACGCACCACTGTGACGTG TGGTCATTTGGCATACTGATGTGGGAAATTTTACACTCGGTGGTTTAC CTTATCCTGGCATCCCTGTTGAGGAGCTTTTTAAATTGCTCAAAGAGGG CCACAGAATGGACTGTCTAGTAAGTGCACCCATGAGCTGTATATGCT CATGCGCGAGTGCTGGCATGCGGTGCCTAGTCAAAGGCCAACCTTCAA ACAGCTCGTCGAAGGCCTGGACAAGATTCTTGCTGCAATAAGCGAGGA GTACCTCGACTTGCTATGCCATTTCGAGCAATACTCACTTCTTGTA GACACGACGAGTACATGCAGCAGCGACGACTCTGTATTTACACACGAC CCTTTGCCCTTGCTCCTTGCTGTTTGCCTGTCTAGTGGCCGCACCTA G

SEQ ID NO:	Description	Sequence
103	FGFR4-K645E	ATGCTTCCTCTGCGCCTGGTTCTCGCTGGCCTCTTGGTCGCAGCGGGTT CAGCGGCGAGTCATAGGGGAGAAATGGAGCCGGAACCTCTTTGAGTCTC CACTCTTGGAATCCGAAGAAGAACACCTCCTTCTGGACCCAGGAAACG CATTGAAACTCTATTGTGACGTAAACCAGTCCGGAGCTAGTGTGGTTT GGTATAAGGAGAGTAGACCTCTGCTGCCAGGGCCCCGCGTCAGATTGC AACAAAGCGTTCTTGAAATAGCGGAAGTAGCTTACGAGGATTCCGGCC TCTACGTCTGTAGAGCTCGCGGAACCGGTGAGGTCTTAGGAACTTCA CCATATCAGTTGTAGATTCACTTGCCTCAGGCGATGACGATGAAGACA GCGATGGGGATGGTCCACATGGAGACCGCTCTGAAGAACCAGTATAC GTTACAGAGCACCTTATTGGACCCATCCACACAGGATGGATAAAAAA CTCTACGCTGTTCTGCGGGCAATACCGTGAAATTCGCTGTCCAGCG AGTGGGTCTCCAAGCCCGTCCATTAGATGGTTTAAAGAAATGGCAGAGAG TTTCGCGGGGAGCACAGAATAGGGGGCATTAGGCTCCGGCATCAGCAT TGGTCACTCGTTATGGAGTCAGTCGTGCCGTCTGATAGGGGGAATTAC ACCTGCTTGGTAGAGAACCGGTTTGGTTCAATCCGCTATAGTTATCTGC TGGATGTCCTCGAACGCTCCCCACACAGACCCATCTTGCAAGCTGGAC TTCCAGCTAACACAACAGCTCTGGTAGGTTTCAAGATGTGGAAATTTTCTG CAAGGTATACTCTGATGCTCAACCGCACATACAGTGGTTGAAACACAT TGAAGTTAACGGGTCTCATATGGGCCAGACGGGTGTACCCTACGTGCA GGTACTGAAGACGGCCGACATTAATTCATCTGAGGTTGAGGTGCTGTA TTTGCGGAACGTCACAATGGAAGACGCCGGGAGTATACTTGTCTTGC CGGTAATAGTATTGGGCTGTCTATCAGTCCGCGTGGCTCACCGTCCTG CCAGAAGAGCTGGTTTATGAGGCTGAGGCACCTGAGGCGAAATACAC CGACATCATAATTTACACTTCCGATCATTGGCCGTGGCAATTCCTCTT ATCATCGTCGTTCTGTGTAGGATGCAAACTCAGAGCTCTAAACAACCC CTTGAACCCATGGCAGTACACAAATTGAGCAAAATTCCTCTTATTAGA CAGTTTTCCCTTGACTCAAGTAGCTCAGGGAAATCTAGCACATCACTTA TGCGGGTGACGAGACTGTCTTCCAGCTGCGCGCCCATGTTGGCTGGGG TGGTGGAACCTTGATCTGCCTCTGGACAGCAAGTGGGAATTTCCGAGGG AGAAACTGGTTCTTGGGAAGCCGCTCGGCGAAGGCTGTTTTGGTCAGG TGGTCAGGGCGGAAGCGTACGGGATCGACAGACAGTGGCCTGATCGC GCAGTTACTGTGCGAGTAAAAATGCTGAAAGACAACGCTACTGATAAG GATCTGGCAGACCTGATAAGTGAAATGGAGATGATGAAACTGATGGA CAACACACAAGAATCATTAATCTCTTGGGTGTATGTACACAAGATGG GCCTCTGTATGTTATAGTAGAGTTTGGCGCCAAAGGCAACCTTCGGGA GTATCTTCGCGCTAGAAGACCGCCAATGCCCAGTACACGTTTCGATAT TACAGAACTCCATGAGGAACAACCTTGTTTTAAGGATCTTGTTAGCTGT GTGTATCAAGTCGCCCGGGGGATGGAGTATCTGGAATCAAGACGGTGT ATACACCGCGACCTCGCTGCCAGAAACGTTCTCGTACCGGCGGAAAT GTGATGAAGATCGCCGACTTCGGACTTGCCAGGGATGTCCATGATATA GACTATTACAAAGAAACATCTAATGGGCGGCTCCCTGTCAAGTGGATG GCGCCCGAAGCACTGTTTGACAGAGTATACACGCACCACTGTGACGTG TGGTCATTTGGCATACTGATGTGGGAAATTTTACACTCGGTGGTTTAC CTTATCCTGGCATCCCTGTTGAGGAGCTTTTAAATTTGCTCAAAGAGGG CCACAGAATGGACTGTCTAGTAACTGCACCCATGAGCTGTATATGCT CATGCGCGAGTGTGGCATGCGGTGCTAGTCAAAGGCCAACCTTCAA ACAGCTCGTCAAGGCCTGGACAAGATTCTTGCTGCAATAAGCGAGGA GTACCTCGACTTGCTATGCCATTTCGAGCAATACTCACCTTCTTGTA GACACGACGAGTACATGCAGCAGCGACGACTCTGTATTTACACACGAC CCTTTGCCCTTGCTCCTTGCTTGTGCTTGTCTAGTGGCCGCACCTA G
104	FGFR4-Y367C-K645E	ATGCTTCCTCTGCGCCTGGTTCTCGCTGGCCTCTTGGTCGCAGCGGGTT CAGCGGCGAGTCATAGGGGAGAAATGGAGCCGGAACCTCTTTGAGTCTC CACTCTTGGAATCCGAAGAAGAACACCTCCTTCTGGACCCAGGAAACG CATTGAAACTCTATTGTGACGTAAACCAGTCCGGAGCTAGTGTGGTTT GGTATAAGGAGAGTAGACCTCTGCTGCCAGGGCCCCGCGTCAGATTGC AACAAAGCGTTCTTGAAATAGCGGAAGTAGCTTACGAGGATTCCGGCC

SEQ ID NO:	Description	Sequence
		TCTACGTCTGTAGAGCTCGCGGAACCGGTGAGGTCCTTAGGAACTTCA CCATATCAGTTGTAGATTCACTTGCCTCAGGCGATGACGATGAAGACA GCGATGGGGATGGTCCACATGGAGACCGCTCTGAAGAACCAGTATAC GTTACACAGAGCACCTTATTGGACCCATCCACACAGGATGGATAAAAAA CTCTACGCTGTTCTGCGGGCAATACCGTGAAATTCCGCTGTCCAGCG AGTGGGTCTCCAAGCCCGTCCATTAGATGGTTTAAGAATGGCAGAGAG TTTCGCGGGGAGCACAGAATAGGGGGCATTAGGCTCCGGCATCAGCAT TGGTCACTCGTTATGGAGTCAGTCGTGCCGTCTGATAGGGGGAATTAC ACCTGCTTGGTAGAGAACCGGTTTGGTTCAATCCGCTATAGTTATCTGC TGGATGTCCTCGAACGCTCCCCACACAGACCCATCTTGCAAGCTGGAC TTCCAGCTAACACAACAGCTCTGGTAGGTTTCAAGATGTGGAATTTTCTG CAAGGTATACTCTGATGCTCAACCGCACATACAGTGGTTGAAACACAT TGAAGTTAACGGGTCTCATATGGGCCAGACGGTGTACCTACGTGCA GGTACTGAAGACGGCCGACATTAATTCATCTGAGGTTGAGGTGCTGTA TTTGCAGAACGTCACAATGGAAGACGCCGGGGAGTATACTTGTCTTGC CGGTAATAGTATTGGGCTGTCCTATCAGTCCGCGTGGCTCACCGTCTG CCAGAAGAGCTGGTTCATGAGGCTGAGGCACCTGAGGCGAAATGTAC CGACATCATAATTTACACTTCCGGATCATTGGCCGTGGCAATGGCTCTT ATCATCGTCGTTCTGTGTAGGATGCAAACTCAGAGCTCTAAACAACCC CTTGAACCCATGGCAGTACACAAATTGAGCAAAATTTCTCTTATTAGA CAGTTTTCCCTTGACTCAAGTAGCTCAGGGAAATCTAGCACATCACTTA TGCGGGTGACGAGACTGTCTTCCAGCTGCGCGCCCATGTTGGCTGGGG TGGTGGAACCTTGATCTGCCTCTGGACAGCAAGTGGGAATTTCCGAGGG AGAAACTGGTTCTTGGGAAGCCGCTCGGCGAAGGCTGTTTGGTCAAG TGGTCAGGGCGGAAGCGTACGGGATCGACAGACAGTGGCCTGATCGC GCAGTTACTGTGCGAGTAAAAATGCTGAAAGACAACGCTACTGATAAG GATCTGGCAGACCTGATAAGTGAAATGGAGATGATGAAACTGATGGA CAAACACAAGAACATCATTAACTCTTGGGTGTATGACACAAGATGG GCCTCTGTATGTTATAGAAGAGTTTGCAGGCAAGGCAACCTTCGGGA GTATCTTCGCGCTAGAAGACCGCCAATGCCCGACTACACGTTTCGATAT TACAGAACTCCATGAGGAACAACCTTGTTTTAAGGATCTTGTAGCTGT GTGTATCAAGTCGCCCGGGGGATGGAGTATCTGGAATCAAGACGGTGT ATACACCGCGACCTCGCTGCCAGAAACGTTCTCGTCACGGCGGAAAAT GTGATGAAGATCGCCGACTTCGGAATTGCCAGGGATGTCATGATATA GACTATTACAAAAAACATCTAATGGGCGGCTCCCTGTCAAGTGGATG GCGCCCGAAGCACTGTTTGACAGAGTATACACGCACCACTGTGACGTG TGGTCATTTGGCATACTGATGTGGGAAATTTTACACTCGGTGGTTCAC CTTATCCTGGCATCCCTGTTGAGGAGCTTTTAAATTGCTCAAAGAGGG CCACAGAATGGACTGTCTAGTAAGTGCACCCATGAGCTGTATATGCT CATGCGCGAGTGTGGCATGCGGTGCCTAGTCAAAGGCCAACCTTCAA ACAGCTCGTCAAGGCCTGGACAAGATTCTTGCTGCAATAAGCGAGGA GTACCTCGACTTGTCTATGCCATTGAGCAATACTCACCTTCTTGTAAG GACACGACGAGTACATGCAGCAGCGACGACTCTGTATTTACACACGAC CCTTTGCCCTTGCTCCTTGCTGTTTGCCTGTCTAGTGCCCGCACCTA G
105	IGF1(WT)	ATGGAAAAAATCAACAGTCTTTCAACACAATTAGTTAAGTGCTGCTTT TGTGATTTCTGAAGGTGAAGATGCACACTGTGCTTACATTCAATTCT TCTACCTTGGCCTGTGTTTGCTTACCTTAACCAGTTCTGCTGCTGCCGG CCAGAAAACACTGTGTGGTGCTGAGCTGGTTGATGCTCTTCAGTTCGTA TGTGGAGACAGAGGCTTCTACTTCAGTAAGCCTACAGGGTATGGATCC AGCAGTAGACGCTTACACCACAAGGGAATAGTGGATGAGTGCTGCTTC CAGAGTTGTGACCTGAGGAGGCTGGAGATGTAAGTGTGCTCCAATAAAG CCACCTAAATCTGCACGCTCTGTACGTGCTCAGCGCCACACTGATATG CCAAAAGCACAAAAGGAAGTGCATTTGAAGAATACAAGTAGAGGGAA CACAGGAAACAGAACTACAGAATGTAA
106	IGF1 Trunc (truncated)	GGCCAGAAACACTGTGTGGTGCTGAGCTGGTTGATGCTCTTCAGTTT GTATGTGGAGACAGAGGCTTCTACTTCAGTAAGCCTACAGGGTATGGA

SEQ ID NO:	Description	Sequence
		TCCAGCAGTAGACGCTTACACCACAAGGGAATAGTGGATGAGTGCTGCTCCAGAGTTGTGACCTGAGGAGGCTGGAGATGTACTGTGCTCCAATAAAGCCACCTAAATCTGCATAA
107	IGF1R	ATGAAATCTGGGGCTGGGGGAGGGACCCTCGCCGTATTCTGTGGGCTT TTGTTGGCGTTTCGCCGACTCTGTCTCTGTCCGACCAATGGTGAAATAT GCGGCCCCGAATGTGGATATTAGAAAACGATATTCACGAGCTCAAGAGGC TCGAAAATTGTACTGTAGTGGAGGGGTTTCTGCAAATACTGCTTATCA GTAAGGCGGAAGATTACCGCAACTTCCGCTTTCTAAGCTGACTGTGA TCACAGACTATCTCCTGTCTGTTTCAGAGTTGCCGGAAGTTGAATCCCTCTC AGATCTGTTTCTAACCCTCACAGTGATCAGGGGTAGAAAACCTGTTCTA CAACTATGCTCTCGTAATATTTGAGATGACGAACCTTAAGGAGATTGG ACTCCACAATCTTCGCAACATAACCAGGGGTGCTATAAGGATCGAAAA AAATAGCGACCTGTGCTATCTTTCTACAGTAGACTGGAGTCTCATATTG GACGCAGTATCCAACAACCTATATAGTTGGCAACAAGCCTCCCAAAGAA TGCGGTGATCTCTGTCTGGAACCTATGGAGGAAAAACCTCTCTGCGAA AAGACTAGTATAAACAACGAGTACAACCTATAGGTGTTGGACTACCAAC CACTGCCAGAAGATGTGCCCGAGCAGCTGCGGCAAGCGCGCGTGCAC CGATCAGAATGAATGCTGCCACCCCGAATGTCTTGGTAGCTGTACGGC TCCCGACAATAACACAGCCTGCGTTGCGTGTGCGAATTACTATTATGA GGGTGTCTGTATGCCTACCTGTCCGCCTAACACATATAAGTTTCGAGGG GTGGCGCTGCGTGACAAAAGAATTTGTTCCAAGGTCCCAGCAACGGA GACGTCTGACTATGAAAGGTTTGTAAATTCATAATGATGAATGTATGGC GGAATGCCCCATCTGGATTTATCAGGAACGGTAGTCAGAGCATGTTTTG CTCCCCATGTGAAGGCCATGTCCCAAATTTGTGAAGACGGGAAGAC GAAGACAATAGATAGCGTCACCTCTGCTCAAATGCTTCAGGGATGTAC CATCTTGAAAGGAAATCTCTTGATTAACATTCGCCGGGGTAATAATAT AGCAAGTGAGCTTGAAACCTTATGGGGCTCATAGAAACGGTAACCTGG GTATGTCAAGATCCGCCATAGTCATGCACTCGTGTCACTTTTATTCTTG AAGAATCTCCGCTATATACTCGGCGAAGAGCAAGTTGACGGCAACTAC TCATTTTACGTTCTCGATAATCATAATTTGCAGCAGCTTTGGGACTGGA ATCACCACAACCTTGACCATTAAAGAAGGAAAGATGTACTTCGCTTTCA ATCCGAAACCTTTGTGTATCCGAAATTTACCGCATGGAAGAGGTGTCTG GAACTAAAGGACGCCAGTCAAAAGGAGATATAAATCCCAGGAATAAT GGAGAAAGGGCGTCTGTGAGAGCCATATATTGAGATTCTGTAGCAAT ACCACGCTGAAGAACCGGATAAAACTCACCTGGGAGAGATACAGGCC CCCGGATTACCGGGACCTCATCTCTTTCACGGTTTATTACAAGGAGGCC CCCTTCAAAAACGTCACAGAGTACGATGGGCAAGATGCCTGCGGCTCC AACTCTTGGAAACATGGTCGACGTAGACTTGCCCCCTAACAAAAGAGAAT GACCTGGTATATTGCTTCAAGGACTTAAACCTTGGACGCAATACGCC ATATACGTCAAAGCCGTGACCCCTTACAATGATGGAAAACCAACATC CACGGGGCTAAATCCGAGATTGTTTATATAAGGACAAATGCAGCCGTC CCCAGCATACCTCTCGACGTAATATCTGCCTCTAATAGCAGCAGCCAG CTCATTGTGAAGTGGAATCCTCCTTCACTTCCCAACGGGAATCTGTCTT ATTACATTGTCCGCTGGCAACAACAACCTCAGGATTCTTATTTGTATCG GCATAACTACTGTAGTAAAGACAAGGTGCCGATTTCGCCGGTACGCGGA CGGTACTATTGACACGGAAGAAGCAACAGAGCCAACAAAACCCGAAG GATGCGGCGGTGAAAAAGGTCCGTGTTGTGCGTGCCCTAAGACCGAAG CTGAGAAGCAAGCTGAAAAGGAAGAAGCTGAATACCGCAAGGTGTTT GAGAACTTCTGCATAACTCCATCTTCGTTCTTCGCCCGATAGAAAAG AGGCGCGACGTGTTTCAGGATTGCTAACGCCACGCTCGCTACGAGGAAT CGGAACATTACTGGTGGGATCACTTCACCAATGCATCCGATGCGGAA GAGTCCGAAGTAGAGTACCCATTTTTTGAACGAAAGTCACGGGAAG GAGAGAACGGTAATATCTCATTTCAGCCCTTTTACCCTTTATAGAATAG ATATCCACAGCTGCAATCACGAAGCAGACACCCTTGGTGTAGTGCTT CTAACCTTCGTGTTTGCCCGCACGATGCCCTCTGAAGGCGCTGACAATAT ACCCGGAACCGTAGCATGGGAAGCGAAGGAGGAGAACACGGTTTATC TTAAATGGTTGGAACCCACCAACCTAACGGACTTATCTTGATGTACG

SEQ ID NO:	Description	Sequence
		AGATTAAATATGGACAACACGGGGAGGAAAAGAGGGAGTGTGTCACT AGGCAAGAATACAAAAAATTGGTGGCGCCAAATTGACACACTTGAA CCCTGGTAATTACAGCGCGCGCTGCAGGCGACTAGCTTGGCAGGTAA TGGTTCTTGGACTGAACCCGTCTCCTTCTATGTTTCAGCCCAAATCCGCA AATTACGACAACCTTCTCCATTTGATAATAGTCCTTCCAATAGCCTTCC TGTTGATAATAGGTGGCCTCCTCATTATGTTGTACGTCTTTAATAAGAA ACGGAACCTCTGACCGGCTCGGAAATGGTGTCTGTATGCAAGTGTTAA TCCAGAATATTTCTCTGCATCAGACGTTTATGTGCCGGACGAGTGGGA AGTGCCAAGGGAGAAAAATTACAATGTGCAGAGAACTCGGACAGGGTT CTTTTGGCATGGTTTACGAGGGCATCGCAAAAGGCGTGGTGAAGGACG AACCCGAGACGAGAGTTGCTATCAAAACAGTCAATGAGTCAGCTTCTA TGCGCGAACGGATTGAGTTTTTGAATGAGGCCAGTGTAATGAAGGAGT TTAACTGCCACCACGTCGTACGGTTGCTTGGCGTCGTGTCTCAAGGAC AGCCCAACCCTCGTTATTATGGAGTTGATGACCCGGGGGATCTCAAGT CCTACTTGAGGTCTCTTCGCCCTGACACTGAGTCAAACCCAGGGCAGG CACCTCCTACGCTGAAAAAAATGATACAAATGGCTGGAGAAATCGCCG ATGGGATGGCGTATCTCAACGCTAATAAGTTTGTACACCGCGATCTGG CCGCAAGAAATTGTATGGTCGAGAGGATTTTACTGTCAAGATCGGCG ATTTCCGGCATGACACGCGACATCTATGAGACCGACTACTATAGGAAGG GGGGGAAGGGTTTGCTCCCAGTAAGGTGGATGTCACCGGAGAGCCTCA AGGATGGGGTGTTCACGACTCACAGCGATGTCTGGTCTTTTGGAGTTG TACTCTGGGAAATAGCTACACTGGCAGAGCAACCTACCAAGGAATGA CAAATGAACAAGTCTCCGCTTTGTAAATGGAAGGGGGTCTTCTCGAAA AACCGGACAACTGCCAGACATGCTTTTCGAGCTGATGCTGCTGCTG GGCAGTACAATCCCAAAATGCGCCCGTCTTTTCTTGAAATAATCTCAA GCATCAAGGATGAACCTTGACCCGGCCTTTAAAGAAGTATCATTTTCT ATTCCGAAGAAAATAAACCGCCAGATACAGAAAGAACTCGACCTTGAG ACAGAAAACATGGAAAGTATTCCTCTCGATCCTTCTCAACTTTGCAG CCGACGGATAAACATTCTGGCCACAAGGCGGAAAAATGGCCCGGGGGT TGTAAGTACTCAGGGCATCATTTGAAGAAAGGCAGCCATACGCACATAT GAATGGGGGTGCAAGAACGAGCGGGCTTTGCCTCTTCCCCAATCTTC TGCATGCTAG
108	IGFR-R1353H	GAATTCATGAAATCTGGGGCTGGGGGAGGGACCCTCGCCGTATTCTGT GGGCTTTTGTGGCGTTTCGCCGCACTCTGTCTGTGTCGACCAATGGTG AAATATGCGGCCCGAATGTGGATATTAGAAACGATATTCAGGAGCTCA AGAGGCTCGAAAATTGTACTGTAGTGGAGGGGTTTCTGCAAATACTGC TTATCAGTAAGGCGGAAGATTACCGCAACTTCCGCTTTCCTAAGCTGA CTGTGATCACAGACTATCTCCTGCTGTTTCAGAGTTGCCGGACTTGAATC CCTCTCAGATCTGTTTCTTAACCTCACAGTGATCAGGGGTAGAAACCT GTTCTACAACATATGCTCTCGTAATATTTGAGATGACGAACCTTAAGGA GATTGGACTCCACAATCTTCGCAACATAACCAGGGGTGCTATAAGGAT CGAAAAAAATAGCGACCTGTGCTATCTTTCTACAGTAGACTGGAGTCT CATATTGGACGCAAGTATCCAACAACATATATAGTTGGCAACAAGCCTCC CAAAGAATGCGGTGATCTCTGTCTGGAACATATGGAGGAAAAACCTCT CTGCGAAAAGACTAGTATAAACAACGAGTACAACATATAGGTGTTGGAC TACCAACCACTGCCAGAAGATGTGCCCAGCAGCTGCGGCAAGCGCG CGTGCAACCGATCAGAATGAATGCTGCCACCCCGAATGTCTTGGTAGCT GTACGGCTCCCGACAATAACACAGCCTGCGTTGCGTGTGCGCAATTACT ATTATGAGGGTGTCTGTATGCCTACCTGTCCGCCTAACACATATAAGTT CGAGGGGTGGCGCTGCGTGACAAAAGAATTTTGTCCAAGGTCCCAGC AACGGAGACGTCTGACTATGAAAGGTTTGTAAATTCATAATGATGAATG TATGGCGGAATGCCCATCTGGATTTATCAGGAACGGTAGTCAGAGCAT GTTTTGCTCCCATGTGAAGGCCCATGTCCCAAAATTTGTGAAGACGG GAAGACGAAGACAATAGATAGCGTCACTTCTGCTCAAAATGCTTCAGGG ATGTACCATCTTGAAAGGAAATCTCTTGATTAAACATTTCGCCGGGGTAA TAATATAGCAAGTGAGCTTGAAAACCTTATGGGGCTCATAGAAACGGT AACTGGGTATGTCAAGATCCGCCATAGTCATGCACTCGTGTCACTTTCA

SEQ ID NO:	Description	Sequence
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109	PDGFRa(WT)	ATGGGTAATCCCCAAGGACGTTCTGATCCTGGGATGTTTTCTCACAG GACCGCTCCTAACACTTTGCCAGCTTCCTCTGCCGACTATTGTTCCCAA TAGAAATGAGATGGTTGTACAGCTGAATTCCAATTTACACTCAAATG CTCTGGAGACAGCGAAGTGAGCTGGCAGTACCCAGTGACCGAGGGAA GCCACAGGATAGACATCAGACACGAGGAGAACAACAGTGGCCTCTTC GTGACAGTGCTTGAAGTCGGAAATGCCTCAGCCGCTCACACGGGCATG TATGTTTGTATTATAACACACGCAAGTGGAGGATGGGGAAGTCGAG GGGAAGGACATCTACATCTATGTGCCTGACCCAGACATGCCTTTCGTT CCTTCCTTACCAGAAGACCAGTTCATCCTAGTAGAAGAAGGTGATCCC ACTGTTATCCCTTGTCGGACAAGTGACCCAAGTGCTGAGTCTTGAATTA GTTAACAGTTTAGACAAGCCTGTCTATGCTTCTATGACAGCAAAACAG GGCTTCGTAGGGAACCTCCTTGACAGGACCATAACATGCAAAACAATG GTTAAAGGCGTGGAGTTCAAGTCCGATGAGTTTCTCATCTATATTTTAA GAGCTACTTCACAGCTGCCGGTTGAAATTGAAGCTCTGAAAACCTGTCT ACAAAACAGGCGAGACCATCGTAGTAACCTGTGTGGTCTTTGACAATG AGGTGGTTAATTTACAGTGGAATTATCCCGGGAAAGTGAAAGAAAAA GGTCTGATAAACTTGATGATATCAAAGTCCCATCACAGAAGTTGGTT TACACGTTGACCATACCTGACGCATCAGTGAAAGACACAGGGGATTAT GAATGTACTGCCCCACATGCAACCAAGGAGGTTAAGGAAAAATAAGAA AGTAGTCATTACAGTTCATGACAAAGGGTTCATTCACTAGAGCTCA ATTTAGCCCTTTGGAAGCTGTCAATCTACATGAAGTCAAAAAATTTGTCT GTGATGTGCAGGCGTACCCCGCTCCAAAAATGTACTGGTTGAAGGAT AATGTGACTCTGATTGAAAACCTTACTGAGATTGTTACTAGTTCAAAC AGAGTCCAGGAAACACGGTTTCAAAGTGTACTAAAATTGATCCGGGCC AAGGAAGAAGACAGTGGGTACTATACTTTGGTTGCTGAAAATGAAGAT GAGATTAAGAGATACACCTTCTCGTTGCTAATACAAGTTCAGCCTTG ATCTTAGACCTCATGGACGACCACCAAGGCTCTGCTGGCAGGCAGACG GTGAGGTGCTTGGCTGAAGGTACCCCGCTTCCTGATGTGGAATGGTTG GTTTGCAAGGACATTAATAAAATGCAGCAATGACACTTCTGGACTCTT CTGACTAACAATATCTCTGATATACACATGGAAGCCACCTGGATGAG AGGAATATGGTGGAAGCCAGGTGACCTTCCAGAAGGTAGAAAGAAAC CCTGGCTGTGAGATGTGTAGCAAGAAACGACCTTGGAGCTGTACTCG GGAAGTGAACCTTGTGGCTCCACCTTGCGATCAGAACTGACGGTGGC TGCTGCTGTCTTAGTACTGCTGGTGATTGTGATAATTTCACTGATTGTC CTGGTCATCATCTGGAAACAGAAGCCAAGATATGAGATAAAGATGGAG AGTCATTGAGTCTATCAGCCCCGATGGCCATGAATACATTATGTGGA CCCAATGCAGCTACCTTATGACTCCAGATGGGAGTTTCTCGAGATGG GTTAGTGCTTGGTCGAATCCTTGGTTCTGGTGCATTTGGAAAAGTGGTG GAAGGGACAGCATATGGATTGAGTCGTTCTCAACCTGTGATGAAAGTA GCCGTGAAAATGCTGAAACCTACAGCTAGATCCAGTGAAAAACAGGC GCTCATGTCTGAACTGAAGATAATGACACATCTTGGGCCCCACCTGAA TATTGTGAACCTGCTTGGAGCTTGTACGAAATCAGGTCCTATTTACATA ATCACTGAATACTGCTTTTACGGTGATTGGTGAACTATCTGCACAAGA ACAGGGACAACCTCCTCAGCCGACATCCAGAGAAACCAAGAAAGAT CTGGATATTTTGGGATGAACCCAGCTGATGAAAGCACAAAGAAGCTAT GTGATTTTATCATTTGAAAACACCGGAGAATATATGGATATGAAACAA GCTGATACCACTCAGTATGTGCCAATGCTGGAAAGGAAGGAGGGATCT AAATACTCTGATATTCAGAGATCTGTATATGATCGACCTGCTTCATATA AGAAGAAATCTTTGTGAGAATCAGAAAGTAAAAAACCTTCTTTTCAGATG ACGGTTTCGGAGGGTCTAAGCCTACTGGATTGCTAAGCTTCACCTACC AGGTTGCACGGGGAATGGAATTCCTTGGCTTCTAAAAATTCGCTACACC GTGACTTGGCAGCTCGTAATGTCCTTCTGGCTCAAGGCAAAATCGTGA AGATCTGCGACTTTGGGTTGGCTAGAGACATCATGCATGATTCCAAT

SEQ ID NO:	Description	Sequence
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110	PDGFRa-D842V	ATGGGTACTCCCCAAGGACGTTCTGATCCTGGGATGTTTTCTCACAG GACCGCTCCTAACACTTTGCCAGCTTCCTCTGCCGACTATTGTTCCCAA TAGAAATGAGATGGTTGTACAGCTGAATTTCAATTTCACTCAAATG CTCTGGAGACAGCGAAGTGAGCTGGCAGTACCCAGTGACCGAGGGAA GCCACAGGATAGACATCAGACACGAGGAGAACAACAGTGGCCTCTTC GTGACAGTGCTTGAAGTCGGAATGCCTCAGCCGCTCACACGGGCATG TATGTTTGCTATTATAACCACACGCAAGTGGAGGATGGGGAAGTCGAG GGGGAAGGACATCTACATCTATGTGCCTGACCCAGACATGCCTTTTCGTT CCTTCCTTACGAGAAGACCAGTTCATCCTAGTAGAAGAAGTGATCCC ACTGTTATCCCTTGTGCGACAAGTGACCCAAGTGCTGAAGTGACTTTA GTTAACAGTTTAGACAAGCCTGTCTATGCTTTCTATGACAGCAAAACAG GGCTTCGTAGGGAACCTCCTTGCAGGACCATACACATGCAAAACAAATG GTTAAAGGCGTGGAGTTCAAGTCCGATGAGTTCCTCATCTATATTTTAA GAGCTACTTCACAGCTGCCGTTGAAAATTGAAGCTCTGAAAACCTGTCT ACAAAAACAGGCGAGACCATCGTAGTAACCTTGTGTGGTCTTTGACAATG AGGTGGTTAATTTACAGTGGAATTATCCCGGGAAAGTGAAAGAAAAA GGTCTGATAAAACCTTGATGATATCAAAGTCCCATCACAGAAGTTGGTT TACACGTTGACCATACCTGACGCATCAGTGAAAGACACAGGGGATTAT GAATGTACTGCCGACATGCAACCAAGGAGTTAAGGAAAAATAAGAA AGTAGTCATTACAGTTCATGACAAAGGGTTCAATTCATCTAGAGCCTCA ATTTAGCCCTTTGGAAGCTGTCAATCTACATGAAGTCAAAAATTTTGTC GTCGATGTGCAGGCGTACCCCGCTCCAAAAATGTACTGGTTGAAGGAT AATGTGACTCTGATTGAAAACCTTACTGAGATTGTTACTAGTTCAAAC AGAGTCCAGGAAACACGGTTTCAAAGTGTAATAAATTGATCCGGGCC AAGGAAGAAGACAGTGGGTACTATACTTTGGTTGCTGAAAATGAAGAT GAGATTAAGAGATACACCTTCTCGTTGCTAATACAAGTTCCAGCCTTG ATCTTAGACCTCATGGACGACCACCAAGGCTCTGCTGGCAGGCAGACG GTGAGGTGCTTGGCTGAAGGTACCCCGCTTCCTGATGTGGAATGGTTG GTTTGCAAGGACATTAAAAAATGCAGCAATGACACTTCCTGGACTCTT CTGACTAACAATATCTCTGATATACACATGGAAGCCCACCTGGATGAG AGGAATATGGTGGAAAGCCAGGTGACCTTCCAGAAGGTAGAAGAAAC CCTGGCTGTGAGATGTGTAGCAAGAAACGACCTTGGAGCTGTTACTCG GGAAGTGAACCTTGTGGCTCCACCTTGCGATCAGAAGTACGCGTGGC TGCTGTCTTGTAGTACTGCTGGTGATTGTGATAATTTCACTGATTGTC CTGGTCATCATCTGGAACAGAAAGCAAGATATGAGATAAGATGGAG AGTCATTGAGTCTATCAGCCCCGATGGCCATGAATACATTTATGTGGA CCAATGCAGCTACCTTATGACTCCAGATGGGAGTTTCTCGAGATGG GTTAGTGCTTGGTCGAATCCTTGGTTCTGGTGCATTTGGAAAAGTGGTG GAAGGGACAGCATATGGATTGAGTCGTTCTCAACCTGTGATGAAAGTA GCCGTGAAAATGCTGAAACCTACAGCTAGATCCAGTGAAAAACAGGC GCTCATGTCTGAACTGAAGATAATGACACATCTTGGGCCCCACCTGAA TATTGTGAACCTGCTTGGAGCTTGTACGAAATCAGGTCCTATTTACATA

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111	PDGFRb(WT)	ATGCTCTGTCCCTCTCTGAAGGCATCTCTGCAGCTCCTCATCCTCACTG GTCTGCTGGAGGTAACGCTCTGGAGGCAGCGGGCTGCACATCGAACCTG AAGATGCTGAGCTCGTCTTAGGCTCCACAGCACTTTCTCCCTCGTGTG CTATGGGGACGGCAGCTGGTCTGGGAGCGGGATGGTCAGCCTCTCAC TGCCGTGCTGGAGCACAGGGACGGGGTCTTCATCAGCAACCTCACCT CAGGAACGTGACAGGCCGTACACGGGGGAGTATGCGTGCTTCTACAG CCCTGACCAGGCTCCGGAGCGAGCAGAGAGGAAAGCCCTTTACATCTA TGTTCAGATCCCTCCTTAGTTTTCTCCCGCAATCACTTCTGAAGAG TTCTTCATCTTCATCACGGGCTACACAGAGGCCACCATCCCATGCCGTG TGACCAACCCAGAGCTGCAGGTGACCCTCTATGAAAAGAAAGTGGAG AATCCCATTCAGCTACTTATGACCCACAACAGGGCTTCAAAGGCTTC TTTGAGGACAAGACCTACTACTGCCAGGCAATCGTGGATGACCAAGAG GTGGATTACAGACACCTTCTATGTCTACCGGATCCAGGTCTCATCTGTGA ACGTCTCCATCAGCGCAGTGCAGACCGTAGTGCGGCAGGGAGAAAAT GTTACCCTGATGTGCACTGTCACTGGCAATGAGCTGGTCAATTTCAACT GGGATTATCCCCGCAAGCAGGCAGGGAAGGCTGTGGAGCCAGTGACC GATTTCTGCTGGATCCACCCATGACATCCGTTCCATCCTCATCATCC AGAATGCAGAGCTAGAGGACAGTGGGACCTACGTCTGCAATGTCTCTG AGGGCTACCATGAGAAGACAGACCGGAAAGACATCACGGTCCAAGTG ATCGAGCGTGGCTTTGTACGCTTCCACACCCACCTGGCCAGCACGGTG TATGCTGAGGTCCACAAGAGCCACATCATCCAGGTGGATGTGGAGGCC TACCCACAGCCAAACATTGTGTGGCTGAAGAAACAACAGACATTGACC ATGGAGAGCAGCAGCGAGTTCAACCATCAACACAGGAACCTGTGAGA AACCAGGATATCAGACGTCTCTGGTCTGGTGCCTGTGAAGCAGGAGGA AGGAGGATATTACACCATCCGAGCTTCCAATGAGGATGATGCACAAGA GCTGTCTTCCATCTGCAGATAAATGTGCCAGCCAAAGTGGTGGATCT CAAGGAAAAACAGCAGTGCCAGCAGCGGGGAGCAGACTGTAACGTGCT CTGCTGAAGGGATGCCCCAGCCAGAGATCACTTGGTCCACTGCAGCA ACATCAAATGGTGTGGCAGCCAGGGGCAACCCACCCAGCTGCTGGGG AACAACCTCTGCAGAGATTGGCCTGCACACTAATGCTACGTACCATGCA GAGCTGCAGGTGTACCGTGTGAACAGCACCCCTGCAGCTGCACAGGGTG

SEQ ID NO:	Description	Sequence
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112	PDGFRb-D850V	ATGCTCTGTCCCTCTCTGAAGGCATCTCTGCAGCTCCTCATCCTCACTG GTCTGCTGGAGGTAACGCTCTGGAGGCAGCGGGCTGCACATCGAACCTG AAGATGCTGAGCTCGTCTTAGGCTCCACAGCACTTCTCCCTCGTGTG CTATGGGGACGGCAGCTGGTCTGGGAGCGGGATGGTCAGCCTCTCAC TGCCGTGCTGGAGCACAGGGACGGGTCTTCATCAGCAACCTCACCT CAGGAACGTGACAGGCCGTCACACGGGGGAGTATGCGTGCTTCTACAG CCCTGACCAGGCTCCGGAGCGAGCAGAGAGGAAAGCCCTTTACATCTA TGTTCCAGATCCCTCCTTAGTTTTCTCCCCGCAATCACTTCTGAAGAG TTCTTCATCTTCATACGGGCTACACAGAGGCCACCATCCCATGCCGTG TGACCAACCCAGAGCTGCAGGTGACCCTCTATGAAAAGAAAGTGGAG AATCCCATTCAGCTACTTATGACCCACAACAGGGCTTCAAAGGCTTC TTTGAGGACAAGACCTACTACTGCCAGGCAATCGTGGATGACCAAGAG GTGGATTACAGACACCTTCTATGTCTACCGATCCAGGTCTCATCTGTGA ACGTCTCCATCAGCGCAGTGACAGCCGTAAGTGCAGGAGGGAGAAAAT GTTACCTGATGTGCACTGTCACTGGCAATGAGCTGGTCAATTTCAACT GGGATTATCCCCGCAAGCAGGCAGGGAAGGCTGTGGAGCCAGTGAAC GATTTCTTGGCTGGATCCACCCATGACATCCGTTCCATCCTCATCATCC AGAATGCAGAGCTAGAGGACAGTGGGACCTACGTCTGCAATGTCTCTG AGGGCTACCATGAGAAGACAGACCGGAAAGACATCACGGTCCAAGTG

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113	PDGFRb-V536A	ATGCTCTGTCCCTCTCTGAAGGCATCTCTGCAGCTCCTCATCCTCACTG GTCTGCTGGAGGTAACGCTCTGGAGGCAGCGGGCTGCACATCGAACCTG AAGATGCTGAGCTCGTCTTAGGCTCCACAGCACTTTCTCCCTCGTGTG CTATGGGGACGGCACGCTGGTCTGGGAGCGGGATGGTCAAGCTCTCAC TGCCGTGCTGGAGCACAGGGACGGGGTCTTTCATCAGCAACCTCACCTT CAGGAACGTGACAGGCCGTACACGGGGGAGTATGCGTGCTTCTACAG CCCTGACCAGGCTCCGGAGCGAGCAGAGAGGAAAGCCCTTACATCTA

SEQ ID NO:	Description	Sequence
		TGTTCCAGATCCCTCCTTAGTTTTCTCCCCGCAATCACTTCTGAAGAG TTCTTCATCTTCATCACGGGCTACACAGAGGCCACCATCCCATGCCGTG TGACCAACCCAGAGCTGCAGGTGACCCTCTATGAAAAGAAAGTGGAG AATCCCATTCAGCTACTTATGACCCACAACAGGGCTTCAAAGGCTTC TTTGAGGACAAGACCTACTACTGCCAGGCAATCGTGGATGACCAAGAG GTGGATTTCAGACACCTTCTATGTCTACCGGATCCAGGTCTCATCTGTGA ACGTCTCCATCAGCGCAGTGCAGACCGTAGTGCGGCAGGGAGAAAAT GTTACCCCTGATGTGCACTGTCACTGGCAATGAGCTGGTCAATTTCAACT GGGATTATCCCCGCAAGCAGGCAGGGAAGGCTGTGGAGCCAGTGACC GATTTTCCTGCCTGGATCCACCCATGACATCCGTTCCATCCTCATCATCC AGAATGCAGAGCTAGAGGACAGTGGGACCTACGTCTGCAATGTCTCTG AGGGCTACCATGAGAAGACAGACCGGAAAGACATCACGGTCCAAGTG ATCGAGCGTGGCTTTGTACGCTTCCACACCCACCTGGCCAGCACGGTG TATGCTGAGGTCCACAAGAGCCACATCATCCAGGTGGATGTGGAGGCC TACCCACAGCCAAACATTGTGTGGCTGAAGAAACAACAAGACATTGACC ATGGAGAGCAGCAGCGAGTTCACCATCACCAACAGGAACCTGTCTAGA AACCAGGTATCAGACGTCTCTGGTCTGGTGCCTGTGAAGCAGGAGGA AGGAGGATATTACACCATCCGAGCTTCCAATGAGGATGATGCACAAGA GCTGTCTTCCATCTGCAGATAAATGTGCCAGCCAAAGTGGTGGATCT CAAGGAAAAACAGCAGTGCCAGCAGCGGGGAGCAGACTGTAACGTGCT CTGCTGAAGGGATGCCCCAGCCAGAGATCAGTTGGTCCACTTGCAGCA ACATCAAATGGTGTGGCAGCCAGGGGCAACCCACCCAGCTGCTGGGG AACAACCTCTGCAGAGATTGGCCTGCACACTAATGCTACGTACCATGCA GAGCTGCAGGTGTACCGTGTGAACAGCACCCCTGCAGTCCAGGAGTG GATGAACCCCTGCTTCTGAGATGCACCGTGCAAACTTCTGGGCTCC AACTCCCAAGACATCACTCTGGTCCCAAATGCCTTGCCATTCAAAGTG GTCATCATCTCCGTCATCTGGCTCTGCTGGTCTCACCGTCATCTCCC TGATCATCTGATCATCTGTGGCAGAAAGAACTTCGTATGAGATCC GCTGGAAGGCCATCGAGTCACTGAGCTCCGATGGGCACGAGTACATCT ACGTGGATCCCATGCAGCTCCCTTATGACTCCAGCTGGGAGGTGCCCA GGGACAAGCTGGTGTAGGACGCACTCTTGGCTCCGGTGCCTTTGGAC GCGTGGTGGAGGCAACAGCGCATGGCCTGAGCCATTACAGTCCACCA TGAAAGTGGCAGTCAAGATGCTCAAGTCCACTGCACGGAGCAGTGAG AAGCAAGCCCTCATGTCTGAGCTGAAGATCATGAGCCACCTGGGACCT CACCTCAACATCGTCAACTTGCTGGGGGCCTGCACCAAAGGAGGGGCC ATCTATATCATCACCGAGTACTGCCGTTATGGGGACCTGGTGGACTAC CTGCACCGCAACAAGCACACCTTCTGTCAGTCTATGGCGAGAAGGGC CGCCGGGAGGCAGAGCTGTATGGGAATACCATCAAGGAGGACCAGT GCAGAGTCACCTCTCTTGTCTGTCGAGAGTGATGGGGCTACATGGA CATGAGCAAGGATGAGTCTCTGGATTACGTGCCCATGTCTGACATGAA GGGTGAAGTCAAGTATGCTGACATCGAGTCTTCTAACTATGGCACCCC ATATGAGCTGGACAGCTATTCCCCATCAGTCCGGAAAGAACAGACCG GGTGACACTGATAAATGAATCTCCAATCTCAGCTACATGGACTTGGT GGGCTTCAGCTTCCAGGTGGCCAATGGGATGGAGTTCTGGCTTCCAA AAATTGTGTGCATCGTGACCTGGCTGCCAGGAACGTCTCTCATCTGCGA GGGGAAGCTGGTGAAGATCTGTGACTTTGGTCTGGCAAGAGACATCAT GAGGGATTCCAATACATCTCCAAAGGCAGTACCTTCTTGCCCCCTTAA GTGGATGGCCCCAGAGAGCATCTTCAACAACCTCTACACCACCTAAG TGATGTGTGGTCTTTGGGATTCTCTCTGGGAGATATTCACTTAGGA GGGACTCCCTACCCTGAACTGCCTATGAACGAACAGTTCTACAATGCC ATCAAACGTGGCTATCGGATGTCCAAACCTACCCATGCTTCTGATGAA ATCTACGATATCATGCAGAAAGTGCTGGGAGGAGAAGTTTGAGATCAGA CCGTCTTCTCACAGCTGGTGGTGTCTATGGGAAACCTCTTGGTGGACT GCTACAGAAAGAGGTACCAACAGGTAGATGAAGAGTTCATGAAGAGC GACCACCCGCTGTTGTTCGCACAAGACCCACCATCCCCGGGCTGAAC AACGCCAGGCTCCCTCCAGCTCCCCCACCCTCTACACGGCTGTGCAC CAGAACGGGGGAGAGAACGACTACATCATCCCTCTTCTGACCCCAAG

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		CCTGATGCAATCTGTGACCTCCCTCAGGAGGCCCTCCGTCAGCCGTGCC AGCTCTATGCTGAATGAAGCCAACACATCATCTACAATATCCTGTGAC AGCCCCCTGGGCCCCCGGCAGGACGAGGAGCCAGAATGTGACCTGCA GCTGGGCTGCCAGGAGCTGGCCCCGGGTCAACCACGAGGTGGAGGAGA GCTTTCTGTAG
114	9C3-PDGFRb	ATGGCGAAAGGTGGCATAATCGTCGCGATCCTTCTCCTTATCGTTATGC TTGCTATAGAGATATTGCTTTTGATAACTCTTATCATTGCTGTAACGTC TGGAGGCAGCGGGCTGCACATCGAACCTGAAGATGCTGAGCTCGTCCT TAGGCTCCACAGCACTTCTCCCTCGTGTGCTATGGGGACGGCACGCT GGTCTGGGAGCGGGATGGTCAGCCTCTCACTGCCGTGCTGGAGCACAG GGACGGGGTCTTCATCAGCAACCTCACCCCTCAGGAACGTGACAGGCCG TCACACGGGGGAGTATGCGTGCTTCTACAGCCCTGACCAGGTCCGGA GCGAGCAGAGAGGAAAGCCCTTTACATCTATGTTCCAGATCCCTCCTT AGTTTTTCTCCCCGCAATCACTTCTGAAGAGTTCTTCATCTCATCACG GGCTACACAGAGGCCACCATCCCATGCCGTGTGACCAACCCAGAGCTG CAGGTGACCCTCTATGAAAAGAAAGTGGAGAATCCATTCCAGCTACT TATGACCCACAACAGGGCTTCAAAGGCTTCTTTGAGGACAAGACCTAC TACTGCCAGGCAATCGTGGATGACCAAGAGGTGGATTGAGACACCTTC TATGTCTACCGGATCCAGGTCTCATCTGTGAACGCTCTCCATCAGCGCAG TGCAGACCGTAGTGCGGCAGGGAGAAAATGTTACCCTGATGTGCACTG TCAGTGGCAATGAGCTGGTCAATTTCAACTGGGATTATCCCCGCAAGC AGGCAGGGAAGGCTGTGGAGCCAGTGACCGATTTCCTGCCTGGATCCA CCCATGACATCCGTTCCATCCTCATCATCCAGAATGCAGAGCTAGAGG ACAGTGGGACCTACGTCTGCAATGTCTCTGAGGGCTACCATGACAGAG CAGACCGGAAAGACATCACGGTCCAAGTGATCGAGCGTGGCTTTGTAC GCTTCCACACCCACCTGGCCAGCACGGTGTATGCTGAGGTCCACAAGA GCCACATCATCCAGGTGGATGTGGAGGCCTACCCACAGCCAAACATTG TGTGGCTGAAGAACAACAAGACATTGACCATGGAGAGCAGCAGCGAG TTCACCATCACCAACAGGAACCTGTGAGAAACCAGGTATCAGACGTCT CTGGTCTGGTGGTGTGAAGCAGGAGGAAGGAGGATATTACCCATC CGAGCTTCCAATGAGGATGATGCACAAGAGCTGTCTTCCATCTGCAG ATAAATGTGCCAGCCAAAGTGGTGGATCTCAAGGAAAACAGCAGTGC CAGCAGCGGGGAGCAGACTGTAACGTGCTCTGCTGAAGGGATGCCCC AGCCAGAGATCAGTTGGTCCACTTGCAGCAACATCAAATGGTGTGGCA GCCAGGGGCAACCCACCCAGCTGCTGGGGAACAACTCTGCAGAGATT GGCCTGCACACTAATGCTACGTACCATGCAGAGCTGCAGGTGTACCGT GTGAACAGCACCTGCAGCTGCACAGGGTGGATGAACCCCTGCTTCTG AGATGCACCGTGCAAACTTCTGGGCTCCAACTCCCAAGACATCACT CTGGTCCCAAATGCCCTTGCCATTCAAAGTGGTCACTCATCTCCGTCATCC TGGCTCTGCTGGTCTCACCGTCATCTCCCTGATCATCCTGATCATCCT GTGGCAGAAGAAACCTCGCTATGAGATCCGCTGGAAGGTGATCGAGTC AGTGAGCTCCGATGGGCACGAGTACATCTACGTGGATCCCATGCAGCT CCCTTATGACTCCAGCTGGGAGGTGCCCAGGGACAAGCTGGTGTAGG ACGCACTCTTGGTCCGGTGCCTTTGGACGCGTGGTGGAGGCAACAGC GCATGGCCTGAGCCATTACAGTCCACCATGAAAGTGGCAGTCAAGAT GCTCAAGTCCACTGCACGGAGCAGTGAGAAGCAAGCCCTCATGTCTGA GCTGAAGATCATGAGCCACCTGGGACCTCACTCAACATCGTCAACTT GCTGGGGGCTGCACCAAGGAGGGGCCATCTATATCATCACCGAGTA CTGCCGTTATGGGGACCTGGTGGACTACCTGCACCGCAACAAGCACAC CTTCTGCACTCTATGGCGAGAAGGCCCGCCGGGAGGCAGAGCTGTA TGGGAATACCATCAAGGAGGACCACGTGCAGAGTCACTCTCCTTGTCT TGTCGAGAGTGATGGGGGCTACATGGACATGAGCAAGGATGAGTCTCT GGATTACGTGCCCATGTCTGACATGAAGGGTGAAGTCAAGTATGTCTGA CATCGAGTCTTCTAACTATGGCACCCCATATGAGCTGGACAGCTATTCC CCATCAGCTCCGGAAGAAGACAGACCGGGTGACACTGATAAATGAATCT CCACTCCTCAGCTACATGGACTTGGTGGGCTTCAGCTTCCAGGTGGCC AATGGGATGGAGTTCCTGGCTTCAAAAAATTGTGTGCATCGTGACCTG

SEQ ID NO:	Description	Sequence
		GCTGCCAGGAACGTCTCATCTGCGAGGGGAAGCTGGTGAAGATCTGT GACTTTGGTCTGGCAAGAGACATCATGAGGGATTCCAACACATCTCC AAAGGCAGTACCTTCTTGCCCCCTTAAGTGGATGGCCCCAGAGAGCATC TTCAACAACCTCTACACCACCCTAAGTGATGTGTGGTCCCTTTGGGATT TTCTCTGGGAGATATTCACTCTAGGAGGGACTCCCTACCCTGAACCTGCC TATGAACGAACAGTTCTACAATGCCATCAAACGTGGCTATCGGATGTC CAAACCTACCCATGCTTCTGATGAAATCTACGATATCATGCAGAAAGTG CTGGGAGGAGAAGTTTGAGATCAGACCGTCTTCTCACAGCTGGTGGT GCTTATGGGAAAACCTCTTGGTGGACTGCTACAGAAAAGAGGTACCAACA GGTAGATGAAGAGTTCATGAAGAGCGACCACCCCGCTGTTGTTTCGCAC AAGACCCACCATCCCCGGGCTGAACAACGCCAGGCTCCCTCCCAGCTC CCCCACCCTCTACACGGCTGTGCACCAGAACGGGGGAGAGAACGACT ACATCATCCCTCTTCTGACCCCAAGCCTGATGCAATCTGTGACCTCCC TCAGGAGGCCTCCGTCAGCCGTGCCAGCTCTATGCTGAATGAAGCCAA CACATCATCTACAATATCCTGTGACAGCCCCCTGGGCCCCCGGCAGGA CGAGGAGCCAGAATGTGACCTGCAGCTGGGCTGCCAGGAGCTGGCCC CGGGTCAACCACGAGGTGGAGGAGAGCTTTCTGTAG
115	(F)-9C3-PDGFRb	ATGGCGGATTACAAGGATGATGATGACAAAAAAGGTGGCATAATCGT CGCGATCCTTCTCCTTATCGTTATGCTTGCTATAGAGATATTGCTTTTG ATAACTCTTATCATTGCTGTAACGTCTGGAGGCAGCGGGCTGCACATC GAACCTGAAGATGCTGAGCTCGTCTTAGGCTCCACAGCACTTTCTCCC TCGTGTGCTATGGGGACGGCACGCTGGTCTGGGAGCGGGATGGTCAGC CTCTCACTGCCGTGCTGGAGCACAGGGACGGGGTCTTCATCAGCAACC TCACCCTCAGGAACGTGACAGGCCGTACACGGGGGAGTATGCTGGTCT TCTACAGCCCTGACCAGGCTCCGGAGCGAGCAGAGAGGAAAGCCCTTT ACATCTATGTTCCAGATCCCTCCTTAGTTTTCTCCCCGCAATCACTTCT GAAGAGTTCTTCATCTTCATCACGGGCTACACAGAGGCCACCATCCCA TGCCGTGTGACCAACCCAGAGCTGCAGGTGACCTCTATGAAAAGAAA GTGGAGAATCCCATTCCAGCTACTTATGACCCACAACAGGGCTTCAAA GGCTTCTTTGAGGACAAGACCTACTACTGCCAGGCAATCGTGGATGAC CAAGAGGTGGATTACAGACACCTTCTATGTCTACCGGATCCAGGTCTCA TCTGTGAACGTCTCCATCAGCGCAGTGCAGACCGTAGTGCGCAGGGA GAAAATGTTACCCTGATGTGCACTGTCACTGGCAATGAGCTGGTCAAT TTCAACTGGGATTATCCCCGCAAGCAGGCAGGGAAGGTGTGGAGCCA GTGACCGATTTCTGCCTGGATCCACCCATGACATCCGTTCCATCTCA TCATCCAGAATGCAGAGCTAGAGGACAGTGGGACCTACGTCTGCAATG TCTCTGAGGGCTACCATGAGAAAGACAGACCGGAAAGACATCACGGTC CAAGTGATCGAGCGTGGCTTTGTACGCTTCCACACCCACCTGGCCAGC ACGGTGTATGCTGAGGTCCACAAGAGCCACATCATCCAGGTGGATGTG GAGGCCTACCCACAGCCAAACATTGTGTGGCTGAAGAACAACAAGAC ATTGACCATGGAGAGCAGCAGCGAGTTCACCATCACCACAGGAACCT GTCAGAAACCAGGTATCAGACGTCTCTGGTCTGGTGCCTGTGAAGCA GGAGGAAGGAGGATATTACACCATCCGAGCTTCCAATGAGGATGATG CACAAGAGCTGTCTTCCATCTGCAGATAAATGTGCCAGCCAAAAGTGG TGGATCTCAAGGAAAACAGCAGTGCCAGCAGCGGGGAGCAGACTGTA ACGTGCTCTGCTGAAGGGATGCCCCAGCCAGAGATCAGTTGGTCCACT TGCAGCAACATCAAATGGTGTGGCAGCCAGGGGCAACCCACCCAGCT GCTGGGGAACAACTCTGCAGAGATTGGCCTGCACACTAATGCTACGTA CCATGCAGAGCTGCAGGTGTACCGTGTGAACAGCACCCTGCAGCTGCA CAGGGTGGATGAACCCCTGCTTCTGAGATGCACCGTGCAAACTTCCT GGGCTCCAACCTCCCAAGACATCACTCTGGTCCCAAATGCCTTGCCATT AAAGTGGTCATCATCTCCGTCATCTGGCTCTGCTGGTCTCACCGTCA TCTCCCTGATCATCTGATCATCTGTGGCAGAAAGAAACCTCGTATGA GATCCGCTGGAAGGTGATCGAGTCACTGAGCTCCGATGGGACAGTA CATCTACGTGGATCCCATGCAGCTCCCTTATGACTCCAGCTGGGAGGT GCCCAGGGACAAGCTGGTGTAGGACGCACTCTGGCTCCGGTGCCTT TGGACGCGTGGTGGAGGCAACAGCGCATGGCCTGAGCCATTACAGTC

SEQ ID NO:	Description	Sequence
		CACCATGAAAAGTGGCAGTCAAGATGCTCAAGTCCACTGCACGGAGCA GTGAGAAGCAAGCCCTCATGTCTGAGCTGAAGATCATGAGCCACCTGG GACCTCACCTCAACATCGTCAACTTGCTGGGGGCCCTGCACCAAAGGAG GGCCCATCTATATCATCACCGAGTACTGCCGTTATGGGGACCTGGTGG ACTACCTGCACCGCAACAAGCACACCTTCCTGCAGTCTATGGCGAGA AGGCCCCGCCGGGAGGCAGAGCTGTATGGGAATACCATCAAGGAGGAC CACGTGCAGAGTCACCTCTCCTTGCTGTGCGAGAGTGATGGGGGCTAC ATGGACATGAGCAAGGATGAGTCTCTGGATTACGTGCCCATGTCTGAC ATGAAGGGTGAAGTCAAGTATGCTGACATCGAGTCTTCTAACTATGGC ACCCCATATGAGCTGGACAGCTATTCCCCATCAGCTCCGGAAGAACA GACCGGGTGACACTGATAAATGAATCTCCACTCCTCAGCTACATGGAC TTGGTGGGCTTCAGCTTCCAGGTGGCCAATGGGATGGAGTTCCTGGCT TCCAAAAATTGTGTGCATCGTGACCTGGCTGCCAGGAACGTCCTCATC TGCGAGGGGAAGCTGGTGAAGATCTGTGACTTTGGTCTGGCAAGAGAC ATCATGAGGGATTCCAACCTACATCTCCAAAGGCAGTACCTTCTTGCCC CTTAAGTGGATGGCCCCAGAGAGCATCTTCAACAACCTCTACACCACC CTAAGTGATGTGTGGTCTTTGGGATTCTTCTCTGGGAGATATTCACTC TAGGAGGGACTCCCTACCTGAACTGCCTATGAACGAACAGTTCTACA ATGCCATCAAACGTGGCTATCGGATGTCCAAACCTACCCATGCTTCTG ATGAAATCTACGATATCATGCAGAAAGTCTGGGAGGAGAAGTTTGAG ATCAGACCGTCTTCTCACAGCTGGTGGTGTATGGGAAACCTCTTG TGGACTGCTACAGAAAGAGGTACCAACAGGTAGATGAAGAGTTCATG AAGAGCGACCAACCCCGCTGTTGTTGCGACAAGACCCACCATCCCCGGG CTGAACAACGCCAGGCTCCCTCCAGCTCCCCACCTCTACACAGGCT GTGCACCAGAACGGGGGAGAGAACGACTACATCATCCCTCTTCTGAC CCCAAGCCTGATGCAATCTGTGACCTCCCTCAGGAGGCCTCCGTCAGC CGTGCCAGCTCTATGCTGAATGAAGCCAACACATCATCAATATCC TGTGACAGCCCCCTGGGCCCCCGGCAGGACGAGGAGCCAGAATGTGA CCTGCACTGGGCTGCCAGGAGCTGGCCCCGGGTACCACGAGGTGGA GGAGAGCTTTCTGTAG
116	PDGF(WT)	ATGTGCCCCGAGCCGGCAAGGCTTGAACCCGGCATGAATTTTCGGCGTG GTCTTCGCCGTCACTCTCTCCCTGCCCTGGCCCCGCCTGGAGGGGGACC CCATACCCGAAGATATTTATGAGATTTTGGGTGGCAGCTCCGTGCGCT CCATCAGTGACCTCCAGCGTGCCCTGCGGATAGACTCCGTAGAGGAGG ACAGCTCTAGCCTGGACCTGAATGCAACTCAGCCCAGCCAAAACCATG TGTCCCTGTCTCGAGAGAGGCGAAGCCTTGATGCTCTGGCAGCAGCAG AGCCAGCTGTCTCGCCGAGTGCAAGACACGGACGGTGGTCTTTGAGA TCTCCCGTGACATGGTGGACAGCACCAATGCCAACTTCGTGGTGTGGC CACCTGCGTGGAGGTGCAGCGGTGCTCCGGCTGCTGCAACAACCGCA ACGTGCAGTGCCGCCCATGCAGATTGCGGTCCGGCATGTCCAGGTGA ACAAGATTGAGTTTTTCCAGAGGAAGCCAATATTCAAAAAAGTCATCG TGCCTTTGGAGGACCACGTGCAGTGCCGGTGCGAAGTGGTGTCCCGGC CGCCACCCAGGAGCAACCGACCGGCATCCCGTGAGCAGAGACGCTTCT CGCCGTATTACACACAGCCGCCATCTCCAGAGGAAGCGGGTACGCC GGCCGCCAGCACAGAAGAGAAAAACACAAGAAATACAAGCATGTCAAC GATAAGAAAGTGCTGAAAGAAATCCTCATAGCATAG
117	PDGF-211*	ATGTGCCCCGAGCCGGCAAGGCTTGAACCCGGCATGAATTTTCGGCGTG GTCTTCGCCGTCACTCTCTCCCTGCCCTGGCCCCGCCTGGAGGGGGACC CCATACCCGAAGATATTTATGAGATTTTGGGTGGCAGCTCCGTGCGCT CCATCAGTGACCTCCAGCGTGCCCTGCGGATAGACTCCGTAGAGGAGG ACAGCTCTAGCCTGGACCTGAATGCAACTCAGCCCAGCCAAAACCATG TGTCCCTGTCTCGAGAGAGGCGAAGCCTTGATGCTCTGGCAGCAGCAG AGCCAGCTGTCTCGCCGAGTGCAAGACACGGACGGTGGTCTTTGAGA TCTCCCGTGACATGGTGGACAGCACCAATGCCAACTTCGTGGTGTGGC CACCTGCGTGGAGGTGCAGCGGTGCTCCGGCTGCTGCAACAACCGCA ACGTGCAGTGCCGCCCATGCAGATTGCGGTCCGGCATGTCCAGGTGA ACAAGATTGAGTTTTTCCAGAGGAAGCCAATATTCAAAAAAGTCATCG

SEQ ID NO:	Description	Sequence
		TGCCCTTTGGAGGACCACGTGCAGTGCCGGTGCGAAGTGGTGTCCCGGC CGCCACCCAGGAGCAACCGACCGGCATCCCGTGAGCAGAGACGCTTCT CGCCGTCAATCACCACAGCCGCCATCTCCAGTAG
118	9C3-SRG	ATGGCGAAAGGTGGCATAATCGTCGCGATCCTTCTCCTTATCGTTATGC TTGCTATAGAGATATTGCTTTTGATAACTCTTATCATTTGCTGTAACGTC TGGAGGCAGCGGGTAG
119	(F)9C3-SRG	ATGGCGGATTACAAGGATGATGATGACAAAAAAGGTGGCATAATCGT CGCGATCCTTCTCCTTATCGTTATGCTTGTATAGAGATATTGCTTTTG ATAACTCTTATCATTTGCTGTAACGTCGAGGCAGCGGGTAG
120	FC551A- empty vector	GCCCCTGCAGCCGAATTATATTATTTTGCCAAATAATTTTAAACAAA GCTCTGAAGTCTTCTTCATTTAAATTCTTAGATGATACTTCATCTGGAA AATTGTCCCAATTAGTAGCATCACGCTGTGAGTAAGTTCTAAACCATTT TTTTATTGTTGATTATCTCTAATCTTACTACTCGATGAGTTTTCGGTAT TATCTCTATTTTAACTTGGAGCAGGTTCCATTTCATTGTTTTTTCATCA TAGTGAATAAAATCAACTGCTTTAAACACTTGTGCCTGAACACCATATC CATCCGGCGTAATACGACTCACTATAGGGAGAGCGGCCGCGTCGACAT GCCCCCGGTGACCGTCGAGAACCCGCTGACGCTGCCCCGCGTATCCGC ACCCGCGGACGCGTCGCACGTCCCGTGCTCACCGTGACCACCGCGCC CAGCGGTTTCGAGGGCGAGGGCTTCCCGGTGCGCCGCGCTTCGCCGG GATCAACTACCGCCACCTCGACCCGTTTCATCATGATGGACCATGAGG TGAGGTGGAGTACGCGCCCGGGAGCCCAAGGGCACGCCCTGGCACC CGCACCGCGGCTTCGAGACCGTGACCTACATCGTCGACGCGGCCCA GATCTTCCGGATGGCTCGAGTTTTTCAGCAAGATATGATAAGATACAT TGATGAGTTTGGACAAACCACAAGTGAATGCAGTGAACCAATGCTT TATTTGTGAAATTTGTGATGCTATTGCTTTATTTGTAACCATATAAGC TGCAATAAACAAGTTTAGTTAACGCATGATACAAAGGCATTAAAGCAG CGTATCCACATAGCGTAAAAGGAGCAACATAGTTAAGAATACCAGTCA ATCTTTCACAAATTTTGTAAATCCAGAGGTTGATTTACAGGCACCGGGCTT GCGGGTCATGCACAGGTGCGCGGTCTTTCGGGCACCTCGACGTCGCG GGTGACGGTGAAGCCGAGCCGCTCGTAGAAGGGGAGGTTGCGGGGCG CGGAGGTCTCCAGGAAGGCGGGCACCCCGCGCGCTCGGCCGCTTCCA CTCCGGGGAGCACGACGCGCTGCCAGACCTTGCCCTGGTGGTTCGG GCGAGACGCCGACGGTGGCCAGGAACACGCGGGCTCCTTGGGCCGG TGCGGCGCCAGGAGGCCTTCCATCTGTTGCTGCGCGGCCAGCCGGGAA CCGCTCAACTCGGCCATGCGCGGGCCGATCTCGCGCAACACCGCCCC GCTTCGACGCTCTCCGGCGTGGTCCAGACCGCCACCGCGGCGCCGTCG TCCGCGACCCACACCTTGCCGATGTGAGCCCGACGCGCGTGAGGAAG AGTTCTTGACGCTCGGTGACCCGCTCGATGTGGCGGTCCGGATCGACG GTGTGGCGCGTGGCGGGTAGTTCGGCGAACGCGGCGCGGAGGGTGCG TACGGCCCTGGGGACGTCGTCGCGGGTGGCGAGGCGCACCGTGGGCTT GTACTCGGTCATAGGGCCGGGATTCTCCTCCACGTCACCGCATGTTAG AAGACTTCTCTGCCCTCGCGAGATCCGGTGGAGCCGGTCCGGCGGT GCCGTCCACGGCAGAATTGGACGACTGAGCGCGGATCTGGCGAAGG CGATGGGGGTCTTGAAGGCGTGCTGGTACTCCACGATGCCAGTCCGG TGTTGCTGTGCAGCTCCTCCACGCGGCGGAAGGCGAACATGGGGCCCC CGTTCTGCAGGATGCTGGGGTGGATGGCGCTCTTGAAGTGCATGTGGC TGTCCACCACGAAGCTGTAGTAGCCGCCGTCGCGCAGGCTGAAGGTGC GGGCGAAGCTGCCACACGACGTTATCGCCATGGGGTGCAGGTGCT CCACGGTGGCGTTGCTGCGGATGATCTTGTGCGGTGAAGATCACGCTGT CCTCGGGGAAGCCGGTGGCCACACCTTGAAGTCGCCGATCACGCGGC CGGCCTCGTAGCGGTAGCTGAAGCTCACGTGCAGCACGCCGCCGCTCCT CGTACTTCTCGATGCGGGTGTGTTGGTGTAGCCGCCGTGTTGATGGCGTG CAGGAAGGGGTTCTCGTAGCCGCTGGGGTAGGTGCCGAAGTGGTAGA AGCCGTAGCCCATCACGTGGCTCAGCAGGTAGGGGCTGAAGGTGAGG GCGCCTTTGGTGTCTTCATCTTGTGGTTCATGCGGCCCTGCTTGGGG TGCCCTCTCCGCCGCCACAGCTCGAACTCCACGCCGTTACAGGTGC CGGTGATGCGGCACTCGATCTCCATGGCGGGCAGGCCGCTCTCGTCGC

SEQ ID NO:	Description	Sequence
		TCTCCATGGTGGCGTCTAGCGTAGGGCGCCGGTCACAGCTTGGATCTGT AACGGCGCAGAACAGAAAAACGAAACAAAGACGTAGAGTTGAGCAAGC AGGGTCAGGCAAAGCGTGGAGAGCCGGCTGAGTCTAGGTAGGCTCCA AGGGAGCGCCGGACAAAGGCCCGGTCTCGACCTGAGCTTTAAACTTAC CTAGACGGCGGACGCAGTTCAGGAGGCACCACAGGCGGGAGGCGGCA GAACGCGACTCAACCGGCGTGGATGGCGGCCCTCAGGTAGGGCGGCGG GCGCGTGAAGGAGAGATGCGAGCCCTCGAAGCTTCAGCTGTGTTCTG GCGGCAAACCCGTTGCGAAAAAGAACGTTACGGCGACTACTGCACTT ATATACGTTTCTCCCCACCCTCGGGAAAAAGGCGGAGCCAGTACACG ACATCACTTTCCAGTTTACCCCGCGCCACCTTCTCTAGGCACCCGTTT AATTGCCGACCCCTCCCCCACTTCTCGGGGACTGTGGGCGATGTGC GCTCTGCCACTGACGGGCACCGGAGCGATCGCAGATCCTTATCTTTCT AGAAATTTACCGGGTAGGGGAGGCGCTTTTCCCAAGGCAGTCTGGAG CATGCGCTTTAGCAGCCCCGCTGGCACTTGGCGCTACACAACTGGCCT CTGGCCTCGCACACATTCCACATCCACCGGTAGCGCCAACCGGCTCCG TTCTTTGGTGGCCCCCTTCGCGCCACCTTCTACTCCTCCCCTAGTCAGGA AGTTCCCCCCCCGCCCCGAGCTCGCGTCGTGCAGGACGTGACAAATGG AAGTAGCACGTCTACTAGTCTCGTGCAGATGGACAGCACCGCTGAGC AATGGAAGCGGGTAGGCCTTTGGGGCAGCGGCCAATAGCAGCTTTGCT CCTTCGCTTTCTGGGCTCAGCAGCTGGGAAGGGTGGGTCCGGGGGCGG GCTCAGGGGCGGGCTCAGGGGCGGGGCGGGCGCCGAAGGTCTCCG GAGGCCCGGCAATTCTGCACGCTTCAAAAGCGCACGTCTGCCGCGTGT TCTCCTCTCTCTCATCTCCGGGCCCTTTGACCTGGATCCGATATCGGTA CCGCTAGCATCGATCAGACATGATAAGATACATTGATGAGTTTGGACA AACCACAAGTAGAATGCAGTGAAAAAATGCTTTATTTGTGAAATTTG TGATGCTATTGCTTTATTTGTAACCATTTATAAGCTGCAATAAACAAGTT AACAAACAACAATTGCATTATTTATGTTTCAGGTTTCAGGGGGAGGTG TGGGAGGTTTTTTGTTTAAACCTCCTGTGTGAAATTTATATCCGCTCAT AATTCCACACATTATACGAGCCGGAAGCATAAAGTGTAAGCCTGGGG TGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCA ATTGCTTTCCAGTCGGGAAACCTGTCTGTGCCAGCTGCATTAATGAATC GGCCAACGCGCGGGGAGAGGCGGTTTGCCTATTGGGCGCTCTTCCGCT TCCTCGCTCACTGACTCGCTGCGCTCGGTCTGCTCGGCTGCGGCGAGCG GTATCAGCTCACTCAAAGGCGGTAATACGTTTATCCACAGAATCAGGG GATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAG GAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCC CCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAA ACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCC TCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGC CTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGG TATCTCAGTTCGGTGTAGGTGCTTCGCTCCAAGCTGGGCTGTGTGCACG AACCCCCCGTTACGCCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCT TGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCAC TGGAACAGGATTAGCAGAGCGAGGTATGTAGCGGTGCTACAGAGTT CTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGAACAGTATTTGG TATCTGCGCTCTGCTGAAGCCAGTTACCTTCGAAAAAGAGTTGGTAG CTCTTGATCCGGCAAAACAAACCACCGCTGGTAGCGGTGGTTTTTTGTT TGCAAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCC TTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTACGT TAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTACCTAGATC CTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGT AAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCT CAGCGATCTGTCTATTTCTGTTTCATCCATAGTTGCCTGACTCCCCGTCGT GTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGTGCG AATGATAACCGGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAAT AAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCTGCAACTT TATCCGCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAA

SEQ ID NO:	Description	Sequence
		GTAGTTCGCCAGTTAATAGTTTGC GCAACGTTGTTGCCATTGCTACAGG CATCGTGGTGTACACGCTCGTCGTTTGGTATGGCTTCATTACAGCTCCGGT TCCCAACGATCAAGGCGAGTTACATGATCCCCATGTTGTGCAAAAAA GCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAAGTAAGTTGGCCG CAGTGTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGT CATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAA GTCATTCTGAGAATAGTGATGCGGCGACCGAGTTGCTCTTGCCCGGC GTCAATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCT CATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACC GCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCT TCAGCATCTTTTACTTTTACCAGCGTTTCTGGGTGAGCAAAAAACAGGA AGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTG AATACTCATACTCTTCTTTTCAATATTATTGAAGCATTTATCAGGGT TATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAA CAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTC TAAGAAACCATTATTATCATGACATTAACCTATAAAAAATAGGCGTATC ACGAGGCC
121	FC550A- empty vector (EVmRuby)	GCCCCTGCAGCCGAATTATATTATTTTGC CAAATAATTTTAAACAAAA GCTCTGAAGTCTTCTTCATTTAAATTCTTAGATGATACTTCATCTGGAA AATTGTCCCAATTAGTAGCATCACGCTGTGAGTAAGTTCTAAACCATTT TTTTATTGTTGTATTATCTCTAATCTTACTACTCGATGAGTTTTCGGTAT TATCTCTATTTTAACTTGAGCAGGTTCCATTTCATTGTTTTTTTCATCA TAGTGAATAAAATCAACTGCTTTAACACTTGTGCCTGAACACCATATC CATCCGGCGTAATACGACTCACTATAGGGAGAGCGGCGCCAGATCTT CCGGATGGCTCGAGTTTTTCAGCAAGATCATGCCTGCTATTGTCTTCCC AATCCTCCCCCTTGCTGTCTGCCCCACCCACCCCAAGAATAGAATG ACACCTACTCAGACAATGCGATGCAATTTCTCTATTTATTAGGAAAG GACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGCACGGGGGAGG GGCAACAACAGATGGCTGGCAACTAGAAGGCACAGTCGCATATGTC AGGCACCGGGCTTGCGGGTCATGCACCAGGTGCGCGGTCTTTCGGGCA CCTCGACGTGCGCGGTGACGGTGAAAGCCGAGCCGCTCGTAGAAGGGG AGGTTGCGGGGCGCGGATGTCTCCAGGAAGGCGGGCACCCCGGCGCG CTCGGCCGCTCCACTCCGGGGAGCACGACGGCGCTGCCAGACCCCTT GCCCTGGTGGTGGGGCGAGACGCCGACGGTGGCCAGGAACACGCGG GCTCCTTGGGCGGTGCGGCGCCAGGAGGCCTTCCATCTGTTGTGCG CGGCCAGCCGGGAACCGCTCAACTCGGCCATGCGCGGGCCGATCTCGG CGAACACCGCCCCCGCTTCGACGCTCTCCGGCGTGGTCCAGACCGCCA CCGCGGCGCGCTCGTCCGCGACCCACACCTTGCCGATGTCGAGCCCCGA CGCGCGTGAGGAAGAGTTCTTGACGCTCGGTGACCCGCTCGATGTGGC GGTCCGGATCGACGGTGTGGCGCGTGGCGGGGTAGTCGGCGAACGCG GCGGCGAGGGTGCGTACGGCCCTGGGGACGTCGTGCGGGGTGGCGAG GCGCACCGTGGGCTTGTACTCGGTTCATAGGACCGGGGTTTTCTTCCAC GTCTCCTGCTTGCTTTAACAGAGAGAAGTTTCGTGGCACCGGATCCTCC AGCGCCTGTGCTATGTCTGCCCTCAGCTCTCTCATATTGTTCCACGATG GTGTAGTCCCCATTATGGCTGATAATGTCGAGTTTAAATATCAGTCATGT AGGCGCCAGGCAGCTGCACTTGTTCCTTGGCCTTGTAAGGTTGTTTTGAC CTCGGCATCGTAGTGCTCCTCCGTCTTTGAGTTTCAGTCTCATTTTAATTT CGCCTTTCAGAGCGCCATCCTCAGGATACATTCTCTCGGTGGAGGCTTC CCATCCCATTGTTTTTTTTTGCATGACAGGGCCATCGGAGGGGAAGTTG GTTCTCTGAGTTTACCTTATAAATAAACTCTCCGTCCTGGAGGGTGC TATCTTGTGTGACTGTCAACACGCCTCCGTCTCGAAGTTCATGAATCT CTCCCACTTGAAAGCCTTCAGGGAAGGAGAGCTTCAGATAGTCAGGGAT GTCGGCAGGGTGTAAACATAGGCTTTGCTTCCGTACTGGAAGTGGAGG GCTCAGAATATCCAGGAGAAGGGGAGGGGTCTCTTTTGTGACCTT GAGCTTAGCGGTTTGTGTGCCCTCGTAAGGCCGGCTTCTCTTCTCCC TCAATCTCGAACTCGTGTCCGTTGACGCTTCCCTCCATCTTGACCTTAA ATCTCATAAACTCTTTGATGACATCCTCGGAGCTGGCCATGGTGGCGA

SEQ ID NO:	Description	Sequence
		TCGATAGGTTCGAAAGGCCCGGAGATGAGGAAGAGGAGAACAGCGCGG CAGACGTGCGCTTTTGAAGCGTGACAGAATGCCGGGCTCCGGAGGACC TTCGGGCGCCCGCCCGCCCTGAGCCCGCCCTGAGCCCGCCCGG ACCCACCCTTCCAGCTGCTGAGCCAGAAAAGCGAAGGAGCAAAGCT GCTATTGGCCGCTGCCCCAAAGGCCTACCCGCTTCCATTGCTCAGCGGT GCTGTCCATCTGCACGAGACTAGTGAGACGTGCTACTTCCATTTGTCAC GTCCTGCACGACGCGAGCTGCGGGGCGGGGGGAACTTCTGACTAG GGGAGGAGTAGAAGGTGGCGCGAAGGGGCCACCAAAGAACGGAGCC GGTTGGCGCTACCGGTGGATGTGGAATGTGTGCGAGGCCAGAGGCCAC TTGTGTAGCGCCAAGTGCCAGCGGGCTGCTAAAGCGCATGCTCCAGA CTGCCTTGGGAAAAGCGCCTCCCCTACCCGGTAGAATTATCTTTCTAGA AAGGATCTGCGATCGCTCCGGTGCCCGTCACTGGGCAGAGCGCACATC GCCCACAGTCCCCGAGAAGTTGGGGGGAGGGGTCGGCAATTGAACGG GTGCCTAGAGAAGGTGGCGCGGGGTAACTGGGAAAAGTGTGCTGTG TACTGGCTCCGCCTTTTTCCCGAGGGTGGGGGAGAACCGTATATAAGT GCAGTAGTCGCCGTGAACGTTCTTTTTCGCAACGGGTTTGCCGCCAGA ACACAGCTGAAGCTTCGAGGGGCTCGCATCTCTCTTACGCGCCCCGC CGCCCTACCTGAGGCCGCCATCCACGCCGTTGAGTCGCGTTCTGCCG CCTCCCGCCTGTGGTGCCTCCTGAAGTGCCTCCCGCTCTAGGTAAGTT TAAAGCTCAGGTCGAGACCGGGCCTTTGTCCGGCGCTCCCTTGGAGCC TACCTAGACTCAGCCGGCTCTCCACGCTTTGCCTGACCCTGCTTGCTCA ACTCTACGTCTTTGTTTCGTTTCTGTTCTGCGCCGTTACAGATCCAAGC TGTGACCGGCGCCTACGAATTCGATATCGGTACCGCTAGCCCTAGGAC GCGTCAGACATGATAAGATACATTGATGAGTTTGGACAAACCAACT AGAATGCAGTGAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATT GCTTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAACAACAAC AATTGCATTCTTTATGTTTCAGGTTTCAGGGGGAGGTGTGGGAGGTTT TTTATCGTTCTTTTATTCTCTCAAGATTTTCAGGCTGTATATTAATA CTTATATTAAGAACTATGCTAACCACCTCATCAGGAACCGTTGTAGGT GGCGTGGGTTTTCTTGGCAATCGACTCTCATGAAAACTACGAGCTAAA TATTCAATATGTTCTCTTGACCAACTTTATTCTGCATTTTTTTTGAACG AGGTTTAGAGCAAGCTTGTGACGATGTAGGTACCGGTCTCGAAGCCG CGGTGCGGGTGCCAGGGCGTGCCCTTGGGCTCCCCGGGCGCGTACTCC ACCTCACCCATCTGGTCCATCATGATGAACGGGTCGAGGTGGCGTAG TTGATCCCGGCGAACGCGCGGCGCACCGGGAAGCCCTCGCCCTCGAAA CCGCTGGGCGCGGTGGTCACGGTGAGCACGGGACGTGCGACGGCGTC GGCGGGTGCGGATACGCGGGGACGCTCAGCGGGTTCTCGACGGTCA CGGCGGGCATGTCGACAAGCTTCAGGAACTGAGACAGGAATTTTATT AAAAATTTAAATTTTGAAGAAAGTTACGGGTTAATAGCATCCATTTTT GCTTTGCAAGTTCCTCAGCATTCTTAACAAAAGACGTCTCTTTTGACAT GTTTAAAGTTTAAACCTCCTGTGTGAAATTATTATCCGCTCATAATCC ACACATTATACGAGCCGGAAGCATAAAGTGTAAGCCTGGGGTGCCTA ATGAGTGAGCTAACTACATTAATTGCGTTGCGCTCACTGCCAATTGCT TTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAA CGCGCGGGGAGAGGCGGTTTGCCTATTGGGCGCTCTTCCGCTTCTCG CTCACTGACTCGCTCGCTCGGTGCTTCCGCTGCGGCGAGCGGTATCA GCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAAC GCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAAC GTAAAAAGGCCCGGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTG ACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCG ACAGGACTATAAAGATACAGGCGTTTCCCCCTGGAAGCTCCCTCGTG CGCTCTCTGTTCGACCTGCCGCTTACCGGATACCTGTCCGCCTTTC TCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCT CAGTTCGGGTGAGGTGCTGCTCCAAGCTGGGCTGTGTGCACGAACC CCCCGTTACGCCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAG TCCAACCCGGTAAGACACGACTATCGCCACTGGCAGCAGCCACTGGT AACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTG

SEQ ID NO:	Description	Sequence
		AAGTGGTGGCCTAACTACGGCTACACTAGAAAGGACAGTATTTGGTATC TGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCT TGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTGCA AGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTG ATCTTTTCTACGGGTCTGACGCTCAGTGGAAACGAAAACTCACGTAA GGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTT TAAATTAAAAATGAAGTTTAAATCAATCTAAAGTATATATGAGTAAA CTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGC GATCTGTCTATTTCGTTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAG ATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATG ATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAAC CAGCCAGCCGGAAGGGCCGAGCGCAGAAAGTGGTCCTGCAACTTTATCC GCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGT TCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCG TGGTGTACGCTCGTCGTTTGGTATGGCTTCATTACGCTCCGGTTCCCA ACGATCAAGGCGAGTTACATGATCCCCATGTTGTGCAAAAAAGCGGT TAGCTCCTTCGGTCTCCGATCGTTGTCAGAAAGTAAGTTGGCCGCGAGTG TTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGC CATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATT CTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAAT ACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCAT TGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGTGT GAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGC ATCTTTTACTTTACAGCGTTTCTGGGTGAGCAAAAAACAGGAAGGCA AAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAATGTTGAATAC TCATACTCTCCTTTTCAATATTATTGAAGCATTATCAGGGTTATTGT CTCATGAGCGGATACATATTGAATGTATTAGAAAAATAACAAATA GGGGTTCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTCTAAGAA ACCATTATTATCATGACATTAACCTATAAAAAATAGGCGTATCACGAGG CC
122	FC550A-eBFP2 empty vector (EVeBFP2)	GCCCCTGCAGCCGAATTATATTATTTTTGCCAAATAATTTTAAACAAAA GCTCTGAAGTCTTCTTCATTTAAATTCTTAGATGATACTTCATCTGGAA AATTGTCCCAATTAGTAGCATCACGCTGTGAGTAAGTTCTAAACCATTT TTTTATTGTTGTATTATCTCTAATCTTACTACTCGATGAGTTTTCGGTAT TATCTCTATTTTAACTTGGAGCAGGTTCCATTCAATTGTTTTTTCATCA TAGTGAATAAAATCAACTGCTTTAACACTTGTGCCTGAACACCATATC CATCCGGCGTAATACGACTCACTATAGGGAGAGCGGCCGCCAGATCTT CCGGATGGCTCGAGTTTTTCAGCAAGATCATGCCTGCTATTGTCTTCCC AATCCTCCCCCTGTCTGCTGCCCCACCCACCCCGAGAAATAGAATG ACACCTACTCAGACAATGCGATGCAATTTCTCATTTTATTAGGAAAG GACAGTGGGAGTGGCACCTTCCAGGGTCAAGGAAGGCACGGGGGAGG GGCAAAACAAGATGGCTGGCAACTAGAAGGCACAGTCGCATATGTC AGGCACCGGGCTTGGGGTTCATGCACAGGTGCGCGGTCTTCGGGCA CCTCGACGTGCGCGGTGACGGTGAAGCCGAGCCGCTCGTAGAAGGGG AGGTTGCGGGGCGCGGATGTCTCCAGGAAGGCGGGCACCCCGGCGCG CTCGGCCGCTCCACTCCGGGGAGCACGACGGCGCTGCCAGACCCTT GCCCTGGTGGTGGGGCGAGACGCGGACGGTGCCAGGAACACGCGG GCTCCTTGGGCCGGTGCGGCGCCAGGAGGCCCTTCCATCTGTGTGCG CGGCCAGCCGGAACCGCTCAACTCGGCCATGCGCGGGCCGATCTCGG CGAACACCGCCCCCGCTTCGACGCTCTCCGGCGTGGTCCAGACCGCCA CCGCGGCGCCGCTCGTCCGCGACCCACACCTTGCCGATGTGAGCCCGA CGCGCGTGAGGAAGAGTTCTTGACGCTCGGTGACCCGCTCGATGTGGC GGTCCGATCGACGGTGTGGCGCGTGGCGGGGTAGTCGGCGGAACGCG GCGGCGAGGGTGCATACGGCCCTGGGGACGTCGTCGCGGGTGGCGAG GCGCACCGTGGGCTTGTACTCGGTTCATAGGACCGGGGTTTTCTTCCAC GTCTCCTGCTTGTCTTAACAGAGAGAAGTTCTGTGGCACCGGATCCCTTG TACAGCTCGTCCATGCCGAGAGTGATCCCGGCGGGCGGTGCGGAACCTC

SEQ ID NO:	Description	Sequence
		AGCAGGACCATGTGATCGCGCTTCTCGTTGGGGTCTTTGCTCAGCACG GACTGGGTGCTCAGGTAGTGGCTGTCGGGCAGCAGCACGGGGCCGTCG CCGATGGGGGTGTTCTGCTGGTAGTGGTCGGCGAGCTGCACGCTGCCG TCCTCCACGTTGTGGCGGATCTTGAAGTTCACCTTGATGCCGTTCTCT GCTTGACGGCCATGATATAGATGTTGTGGCTGTTGAAGTTGTACTCCA GCTTGTGCCCCAGGATGTTGCCGTCCTCCTTGAAGTCGACGCCCTTCAG CTCGATGCGGTTCACTAGGGTGTGCGCCCTCGAACTTCACCTCGGGCGG GGTCTTGTAGGTGCCGTCGTCCTTGAAGAAGATGGTGCGCTCCTGGAC GTAGCCTTCGGGCATGGCGGACTTGAAGAAGTCGTGCTGCTTCATGTG GTCGGGGTAGCGGGCGAAGCACTGCACGCCGTGGCTCAGGGTGGTCA CGAGGGTGGGCCAGGGCACGGGCAGCTTGCCGGTGGTGCAGATGAAC TTCAGGGTCAGCTTGCCGTTGGTGGCATCGCCCTCGCCCTCGCCCTCA CGCTGAACCTTGTGGCCGTTTACGTCGCCGTCCAGCTCGACCAGGATGG GCACCACCCCGGTGAACAGCTCCTCGCCCTTGCTACCATGGTGCGGA TCGATAGGTGAAAGGCCCGGAGATGAGGAAGAGGAGAACAGCGCGG CAGACGTGCGCTTTTGAAGCGTGCAGAATGCCGGGCCTCCGAGGACC TTCGGGCGCCCGCCCGCCCTGAGCCCGCCCTGAGCCCGCCCGCCG ACCCACCTTCCCAGCTGCTGAGCCAGAAAGCGAAGGAGCAAAGCT GCTATTGGCCGCTGCCCAAAGGCCTACCCGCTTCCATTGCTCAGCGGT GCTGTCCATCTGCACGAGACTAGTGAGACGTGCTACTTCCATTTGTCAC GTCCTGCACGACGCGAGCTGCGGGGCGGGGGGAACTTCTGACTAG GGGAGGAGTAGAAGGTGGCGCGAAGGGGCCACCAAAGAACGGAGCC GGTTGGCGCTACCGGTGGATGTGGAATGTGTGCGAGGCCAGAGGCCAC TTGTGTAGCGCCAAGTGCCAGCGGGGCTGCTAAAGCGCATCTGGTCAGA CTGCCTTGGGAAAAGCGCCTCCCTACCCGGTAGAATTATCTTTCTAGA AAGGATCTGCGATCGCTCCGGTGCCCGTCAGTGGGCAGAGCGCACATC GCCCACAGTCCCCGAGAAGTTGGGGGGAGGGGTGCGCAATTGAACGG GTGCCTAGAGAAGGTGGCGCGGGGTAACTGGGAAAGTGATGTCGTG TACTGGCTCCGCTTTTTCCTGAGGGTGGGGGAGAACCTATATAAGT GCAGTAGTCGCCGTGAACGTTCTTTTCGCAACGGGTTTGCCGCCAGA ACACAGCTGAAGCTTCGAGGGGCTCGCATCTCTCCTTACGCGCCCGC CGCCCTACCTGAGGCCGCCATCCACGCCGGTTGAGTCGCGTTCTGCCG CCTCCCGCCTGTGGTGCCTCCTGAACTGCGTCCGCGCTTAGGTAAAGTT TAAAGCTCAGGTCGAGACCGGGCCTTTGTCCGGCGCTCCCTTGGAGCC TACCTAGACTCAGCCGGCTCTCCACGCTTTGCCTGACCCTGCTTGCTCA ACTCTACGTCTTTGTTTCGTTTCTGTTCTGCGCCGTTACAGATCCAAGC TGTGACCGGCGCCTACGAATTCGATATCGGTACCGCTAGCCCTAGGAC GCGTCAGACATGATAAGATACATTGATGAGTTTGGACAAACCACAAC AGAATGCAGTGAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATT GCTTTATTTGTAACCATTAAGCTGCAATAAAACAAGTTAACAACAAC AATTGCATTCAATTTATGTTTCAGGTTACGGGGGAGGTGTGGGAGGTTT TTTATCGTCTTTCTTTTATTCTCTCAAGATTTTCAGGCTGTATATTAAAA CTTATATTAAGAACTATGCTAACCACCTCATCAGGAACCGTTGTAGGT GGCGTGGGTTTTCTTGGCAATCGACTCTCATGAAACTACGAGCTAAA TATTCAATATGTTCTCTTGACCAACTTTATTCTGCATTTTTTTTGAACG AGGTTTAGAGCAAGCTTGTGACGATGTAGGTACGGTCTCGAAGCCG CGGTGCGGGTGCCAGGGCGTGCCCTTGGGCTCCCGGGGCGCGTACTCC ACCTCACCATCTGGTCCATCATGATGAACGGGTGAGGTGGCGGTAG TTGATCCCGGCGAACGCGCGGCGCACCGGGAAGCCCTCGCCCTCGAAA CCGCTGGGCGCGGTGGTCACGGTGAGCACGGGACGTGCGACGGCGTC GGCGGGTGCGGATACGCGGGGCAGCGTCAGCGGGTTCTCGACGGTCA CGGCGGGCATGTGACAAGCTTCAGGAACTGAGACAGGAATTTTATT AAAAATTTAAATTTTGAAGAAAGTTACGGGTTAATAGCATCCATTTTTT GCTTTGCAAGTTCCCTCAGCATTCTTAACAAAAGACGCTCTTTTGACAT GTTTAAAGTTTAAACCTCCTGTGTGAAATTATTATCCGCTCATAATTCC ACACATTATACGAGCCGGAAGCATAAAGTGTAAGCCTGGGGTGCCTA ATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCAATTGCT

SEQ ID NO:	Description	Sequence
		TTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAA CGCGCGGGGAGAGGCGGTTTGCCTATTGGGCGCTCTTCCGCTTCCTCG CTCACTGACTCGCTGCGCTCGGTCTGTTCCGCTGCGGCGAGCGGTATCA GCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAAC GCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACC GTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTG ACGAGCATCACAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCG ACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTG CGCTCTCCTGTCCGACCTGCCGCTTACCGGATACCTGTCGCGCTTTC TCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCT CAGTTCGGTGTAGGTCGTTTCGCTCCAAGCTGGGCTGTGTGCACGAACC CCCCGTTACAGCCGACCGCTGCGCCTTATCCGGTAACCTATCGTCTTGAG TCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGT AACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTG AAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATC TGCGCTCTGCTGAAGCCAGTTACCTTCGGAAGAGTTGGTAGCTCT TGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTGTTGCA AGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTG ATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTAA GGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTT TAAATTAATAATGAAGTTTAAATCAATCTAAAGTATATAGAGTAAA CTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGC GATCTGTCTATTTGTTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAG ATAACTACGATACGGGAGGGCTTACCCTTGCCCCAGTGCGCAATG ATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAAC CAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCACTTTATCC GCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGT TCGCCAGTTAATAGTTTGGCACAACGTTGTTGCCATTGCTACAGGCATCG TGGTGTACGCTCGTGTGTTGGTATGGCTTCATTACGCTCCGTTCCCA ACGATCAAGGCGAGTTACATGATCCCCATGTTGTGCAAAAAAGCGGT TAGCTCCTTCGGTCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCGAGTG TTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGC CATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATT CTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAAT ACGGGATAATACCGCGCCACATAGCAGAACTTTAAAGTGCTCATCAT TGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTT GAGATCCAGTTCGATGTAACCCACTCGTGACCCAACTGATCTTCAGC ATCTTTTACTTTCAACAGCGTTTCTGGGTGAGCAAAAAACAGGAAGGCA AAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAATGTTGAATAC TCATACTCTTCCTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGT CTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAACAATA GGGGTTCGCGCACATTTCCCCGAAAAAGTGCCACCTGACGCTAAGAA ACCATTATTATCATGACATTAACCTATAAAAAATAGGCGTATCACGAGG CC
123	Consensus FGF2	MAAMAAGSITTLPALPEDGGSGAFPPGHFKDPKRLYCKNGGFFLRHPDG RVDGVREKSDPHIKLQLQAEERG VVSIKGVCANRYLAMKEDGRLLASKC ATDECFFFERLESNNYNTYRSRKYSSWYVALKRTGQYKLGPKTGPGQKAI LFLPMSAKS*
124	human FGF2	MAAGSITTLPALPEDGGSGAFPPGHFKDPKRLYCKNGGFFLRHPDGRVD GVREKSDPHIKLQLQAEERG VVSIKGVCANRYLAMKEDGRLLASKCVTD ECFFFERLESNNYNTYRSRKYTSWYVALKRTGQYKLGSKTGPGQKAILFL PMSAKS*
125	Consensus IGF1	GPETLCGAELVDALQFVCGDRGFYFSKPTGYGSSSRRLHHKGIVDECCFQ SCDLRRLEMYCAPIKPPKSA
126	Bovine IGF1	GPETLCGAELVDALQFVCGDRGFYFSKPTGYGSSSRRLHHKGIVDECCFQ SCDLRRLEMYCAPIKPPKSA

SEQ ID NO:	Description	Sequence
127	Porcine IGF1	GPETLCGAELVDALQFVCGDRGFYFSKPTGYGSSSRRLHHKGIVDECCFQ SCDLRRLEMYCAPIKPPKSA
128	Human IGF	GPETLCGAELVDALQFVCGPRGFYFSKPTGYGSSIRRLHHKGIVDECCFQS CDLRRLEMYCAPIKPTKAA
129	Consensus PDGFb	MCPQPARLEMNRCWALFLSLCCYLRLVSAEGDPIPEELYEMLSDHSIRSFDDLQRLHGD SVEDGAELDLNTRSHSGGELESLSRGRSLGSXTIAEPAVIAECKTRTEVFEISRRLIDRTNANFLVWPPC VEVQRCSGCCNNRNVQCRPTQVQXRXVQVXKIEIVRKKPIFKKATVTLEDHLACRCETVXAXRPVTRXPG SSQEQRXAXTPQTRVTIRTVRVRRPPKGKHKFKHTHDKTALKETLGA
130	Bovine PDGFb	MNRCWALFLSLCCYLRLVSAEGDPIPEELYKMLSDHSIRSFDDLQRLHGD DSVDEDGAELDLNTRSHSGGELESLSRGRSLGSPTVAAEPAVIAECKTRTEVFEISRRLIDRTNANFLVWPPC VEVQRCSGCCNNRNVQCRPTQVQDRKVQVKKIEIVRKKKIFKKATVTLDHLACRCETVVARAVTRTPGSSQEQRA RTPQTRVTIRTVRVRRPPKGKHKFKHTHDKTALKETLGA
131	Human PDGFb	MNRCWALFLSLCCYLRLVSAEGDPIPEELYEMLSDHSIRSFDDLQRLHGD DPGEEDGAELDLNMTSRSHSGGELESLSRGRSLGSLTIAEPAMIAECKTRTEVFEISRRLIDRTNANFLVWPPC VEVQRCSGCCNNRNVQCRPTQVQLRPVQVRKIEIVRKKPIFKKATVTLEDHLACKCETVAAARPVTRSPGGSQEQRA KTPQTRVTIRTVRVRRPPKGKHKFKHTHDKTALKETLGA

* Indicates a stop codon

9. EQUIVALENTS AND INCORPORATION BY REFERENCE

[0428] All references cited herein are incorporated by reference to the same extent as if each individual publication, database entry (e.g., Genbank sequences or GeneID entries), patent application, or patent, was specifically and individually indicated incorporated by reference in its entirety, for all purposes. This statement of incorporation by reference is intended by Applicants, pursuant to 37 C.F.R. §1.57(b)(1), to relate to each and every individual publication, database entry (e.g., Genbank sequences or GeneID entries), patent application, or patent, each of which is clearly identified in compliance with 37 C.F.R. §1.57(b)(2), even if such citation is not immediately adjacent to a dedicated statement of incorporation by reference. The inclusion of dedicated statements of incorporation by reference, if any, within the specification does not in any way weaken this general statement of incorporation by reference. Citation of the references herein is not intended as an admission that the reference is pertinent prior art, nor does it constitute any admission as to the contents or date of these publications or documents.

[0429] While the invention has been particularly shown and described with reference to a preferred embodiment and various alternate embodiments, it is understood by persons skilled in the relevant art that various changes in form and details can be made therein without departing from the spirit and scope of the invention

WHAT IS CLAIMED IS:

1. A method of engineering a cell line for reduced dependence on exogenous growth factors, comprising:
 - (a) introducing into the cell line one or more of:
 - (i) a polynucleotide comprising a coding sequence of a growth factor ligand;
 - (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or
 - (iii) a polynucleotide comprising a coding sequence of an activated downstream growth factor target; and
 - (b) culturing the cell line in a cultivation infrastructure.
2. A method of increasing a concentration of a growth factor ligand in culture medium of cells in culture, comprising:
 - (a) introducing into a cell line one or more of:
 - (i) a polynucleotide comprising a coding sequence of a growth factor ligand;
 - and
 - (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or
 - (iii) a polynucleotide comprising a coding sequence of an activated downstream growth factor target; and
 - (b) culturing the cell line in a cultivation infrastructure.
3. A method for improving anchorage independent growth in a cell line, comprising:
 - (a) introducing into the cell line one or more of:
 - (i) a polynucleotide comprising a coding sequence of a growth factor ligand;
 - and
 - (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or
 - (iii) a polynucleotide comprising a coding sequence of an activated downstream growth factor target; and
 - (b) culturing the cell line in a cultivation infrastructure.
4. A method for increasing a cell density of a culture comprising a cell line, comprising:
 - (a) introducing into the cell line one or more of:

- (i) a polynucleotide comprising a coding sequence of a growth factor ligand;
and
 - (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or
 - (iii) a polynucleotide comprising a coding sequence of an activated growth factor receptor; and
- (b) culturing the cell line in a cultivation infrastructure.
5. The method of any one of claims 1-4, wherein the growth factor ligand is selected from basic fibroblast growth factor (FGF2), insulin-like growth factor 1 (IGF1), and platelet-derived growth factor subunit B (PDGFb).
 6. The method of any one of claims 1-5, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises an additional two or more growth factor ligands, wherein each of the additional growth factor ligands is selected from FGF2, IGF1, and PDGFb.
 7. The method of claim 5 or 6, wherein the growth factor ligands is FGF2.
 8. The method of claim 7, wherein the FGF2 comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 1-15.
 9. The method of claim 5, wherein the growth factor ligands is IGF1.
 10. The method of claim 9, wherein the IGF1 comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 16-17.
 11. The method of claim 5 or 6, wherein the growth factor ligands is PDGFb.
 12. The method of claim 11, wherein the PDGFb comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 18-21.
 13. The method of any one of claims 1-12, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of a signal peptide located 5' to the coding sequence of the growth factor ligand, and wherein the signal sequence and the growth factor ligand are a fusion protein.

14. The method of claim 13, wherein the signal sequence comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 22-31.
15. The method of any one of claims 1-14, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a regulatory sequence operably linked to the coding sequence of the growth factor ligand and/or additional growth factor ligands.
16. The method of claim 15, wherein the regulatory sequence comprises a promoter selected from: an inducible promoter, a tissue specific promoter, and a constitutively active promoter.
17. The method of claim 15 or 16, wherein the promoter is selected from EF1alpha, PGK, CMV, RSV, and β -actin.
18. The method of any one of claims 1-17, wherein the polynucleotide comprising a coding sequence of a growth factor ligand comprises a sequence encoding a polycistronic mRNA, wherein the polycistronic mRNA comprises the coding sequence of the growth factor ligand and the coding sequence one or more additional growth factor ligands.
19. The method of claim 18, wherein the polynucleotide comprising a coding sequence of a growth factor ligand comprises one or more sequences encoding a self-cleaving peptide, one or more internal ribosome entry sites (IRES), or a combination thereof.
20. The method of any one of claim 1-19, wherein activity and/or expression of the growth factor ligand is controllable.
21. The method of claim 20, where activity and/or expression of the growth factor ligand is controlled using an inducible promoter, an inducible tag, or a degradation tag.
22. The method of claim 21, wherein expression of the growth factor ligands is controlled using an inducible promoter.
23. The method of claim 22, wherein the coding sequence of the growth factor ligand is operably linked to the inducible promoter.
24. The method of claim 22 or 23, further comprising:
 - maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible promoter, thereby enabling expression of the growth factor ligand.

25. The method of claim 21, wherein activity of the growth factor ligand is controlled using an inducible tag.
26. The method of claim 25, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of an inducible tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the inducible tag and the growth factor ligand are a fusion protein.
27. The method of claim 25 or 26, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible tag, thereby inducing activity of the growth factor ligand/fusion protein.
28. The method of claim 21, wherein activity of the one or more growth factor ligands is controlled using a degradation tag.
29. The method of any one of claims 28, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of a degradation tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the degradation tag and the growth factor ligand are a fusion protein.
30. The method of claim 28 or 29, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the degradation tag, thereby targeting the growth factor ligand/fusion protein for degradation.
31. The method of any one of claims 1-30, wherein
- (a) the concentration of FGF2 in the culture medium is increased by at least 0.001 ng/mL as compared to cell lines not engineered to include a polynucleotide encoding FGF2;
 - (b) the concentration of IGF-1 in the culture medium is increased by at least 0.001 ng/mL as compared to cell lines not engineered to include a polynucleotide encoding IGF1; and/or
 - (c) the concentration of PDGFb in the culture medium is increased by at least 0.001 ng/mL as compared to cell lines not engineered to include a polynucleotide encoding PDGFb.

32. The method of any one of claims 1-30, wherein
- (a) the concentration of FGF2 in the culture medium is increased by at least 2.5% as compared to cell lines not engineered to include a polynucleotide encoding FGF2;
 - (b) the concentration of IGF-1 in the culture medium is increased by at least 2.5% as compared to cell lines not engineered to include a polynucleotide encoding IGF1; and/or
 - (c) the concentration of PDGFb in the culture medium is increased by at least 2.5% as compared to cell lines not engineered to include a polynucleotide encoding PDGFb.
33. The method of any one of claims 1-32, wherein the growth factor receptor is selected from fibroblast growth factor receptor (FGFR), insulin growth factor 1 receptor (IGF1R), and platelet-derived growth factor receptor (PDGFR).
34. The method of claim 33, wherein the polynucleotide comprising a coding sequence of a growth factor receptor further comprises an additional two or more growth factor receptors, wherein each additional growth factor receptor is selected from FGFR, IGF1R, and PDGFR.
35. The method of claim 33 or 34, wherein the growth factor receptor is an FGFR selected from FGFR1, FGFR2, FGFR3, and FGFR4.
36. The method of claim 35, wherein the FGFR comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 32-49.
37. The method of claim 33 or 34, wherein the growth factor receptor is IGF1R.
38. The method of claim 37, wherein the IGF1R comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 50-51.
39. The method of claim 33 or 34, wherein the growth factor receptor is PDGFR.
40. The method of claim 39, wherein the PDGFR comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 52-58.
41. The method of any one of claims 1-40, wherein the polynucleotide comprising a coding sequence of an activated downstream growth factor target comprises a growth factor receptor comprising one or more amino acid insertions, deletions, or substitutions that result in the receptor being constitutively activated.

42. The method of any one of claims 33-41, wherein the polynucleotide comprising a coding sequence of a growth factor receptor comprises a regulatory sequence operably linked to the coding sequence of the growth factor receptor and/or the coding sequence of the additional growth factor receptors.
43. The method of claim 42, wherein the regulatory sequence comprises a promoter selected from: an inducible promoter, a tissue specific promoter, and a constitutively active promoter.
44. The method of claim 42 or 43, wherein the promoter is selected from EF1alpha, PGK, CMV, RSV, and β -actin.
45. The method of any one of claims 1-44, wherein the polynucleotide comprising a coding sequence of a growth factor receptor comprises a sequence encoding a polycistronic mRNA, wherein the polycistronic mRNA comprises the coding sequence of the growth factor receptor and the coding sequence of the two or more additional growth factor receptors.
46. The method of claim 45, wherein the polynucleotide comprising a coding sequence of a growth factor receptor comprises one or more sequences encoding a self-cleaving peptide, one or more internal ribosome entry sites (IRES), or a combination thereof.
47. The method of any one of claim 1-46, wherein activity and/or expression of the growth factor receptors is controllable.
48. The method of claim 47, wherein expression of the growth factor receptor is controlled using an inducible promoter, an inducible tag, and a degradation tag.
49. The method of claim 48, wherein expression of the growth factor receptor is controlled using an inducible promoter.
50. The method of claim 49, wherein the coding sequence of the growth factor receptor is operably linked to the inducible promoter.
51. The method of claim 49 or 50, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible promoter, thereby enabling expression of the growth factor receptor.

52. The method of claim 48, wherein activity of the growth factor receptor is controlled using an inducible tag.
53. The method of claim 52, wherein the polynucleotide comprising a coding sequence of a growth factor receptor further comprises a coding sequence of an inducible tag located 5' or 3' to the coding sequence of the growth factor receptor, and wherein the inducible tag and the growth factor receptor are a fusion protein.
54. The method of claim 52 or 53, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible tag, thereby inducing activity of the growth factor receptor/fusion protein.
55. The method of claim 48, wherein activity of the one or more growth factor ligands is controlled using a degradation tag.
56. The method of claim 55, wherein the polynucleotide comprising a coding sequence of a growth factor receptor further comprises a coding sequence of a degradation tag located 5' or 3' to the coding sequence of the growth factor receptor, and wherein the degradation tag and the growth factor receptor are a fusion protein.
57. The method of claim 55 or 56, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the degradation tag, thereby targeting the growth factor receptor/fusion protein for degradation.
58. The method of any one of claims 1-57, further comprising introducing a polynucleotide sequence encoding an accessory protein.
59. The method of any one of claim 1-58, wherein the polynucleotide comprising a coding sequence of a growth factor ligand and/or the polynucleotide comprising a coding sequence of a growth factor receptor further comprises a coding sequence of an accessory protein.
60. The method of claim 58 or 59, wherein the accessory protein is fibroblast growth factor binding protein (FGFBP).

61. The method of claim 60, wherein the FGFBP comprises an amino acid sequence having at least 80% sequence identity to a sequence of SEQ ID NO: 59.
62. The method of claim 58 or 59, wherein the accessory protein is RASV12.
63. The method of claim 62, wherein the RASV12 comprises an amino acid sequence having at least 80% sequence identity to a sequence of SEQ ID NO: 60.
64. The method of any one of claims 1-63, wherein the method comprises introducing into the cell:
- (i) a polynucleotide comprising a coding sequence of FGF2, and a polynucleotide comprising a FGFR;
 - (ii) a polynucleotide comprising a coding sequence of IGF1, and a polynucleotide comprising an IGF1R;
 - (iii) a polynucleotide comprising a coding sequence of PDGF, and a polynucleotide comprising a PDGFR, or
 - (iv) a combination selected from: (i) and (ii), (ii) and (iii), (ii) and iii), and (i), (ii), and (iii).
65. The method of any one of claims 1-64, wherein the cell line is from a livestock, poultry, game or aquatic animal species.
66. The method of claim 65, wherein the cell line is from a chicken, duck, or turkey.
67. The method of claim 65, wherein the cell line is from a fish.
68. The method of claim 65, wherein the cell line is from a livestock species.
69. The method of claim 65, wherein the livestock species is porcine or bovine.
70. The method of any one of claims 1-64, wherein the cells are from any animal species intended for human or non-human dietary consumption.
71. The method of any one of claims 1-70, wherein the cells are myogenic cells.
72. The method of claim 71, wherein the myogenic cells are myoblasts, myocytes, satellite cells, side population cells, muscle derived stem cells, mesenchymal stem cells, myogenic pericytes, or mesoangioblasts.

73. The method of any one of claims 1-72, wherein the cells are non-myogenic cells.
74. An in vitro method for producing cell-based meat suitable for consumption, comprising:
- (a) introducing into a cell one or more of:
 - (i) a polynucleotide comprising a coding sequence of a growth factor;
 - (ii) a polynucleotide comprising a coding sequence of a growth factor receptor; or
 - (iii) a polynucleotide comprising a coding sequence of an activated downstream growth factor target; and
 - (b) inducing myogenic specific differentiation, wherein the differentiated cells form myocytes and multinucleated myotubes;
 - (c) culturing the myocytes and myotubes to generate skeletal muscle fibers, thereby producing a cell-based meat suitable for consumption.
75. The method of claim 74, wherein the cell line is from a livestock, poultry, game or aquatic animal species.
76. The method of claim 75, wherein the cell line is from a chicken, duck, or turkey.
77. The method of claim 75, wherein the cell line is from a fish.
78. The method of claim 75, wherein the cell line is from a livestock species.
79. The method of claim 75, wherein the livestock species is porcine or bovine.
80. The method of claim 74, wherein the cells are from any animal species intended for human or non-human dietary consumption.
81. The method of any one of claims 74-80, wherein the cells are myogenic cells.
82. The method of claim 81, wherein the myogenic cells are myoblasts, myocytes, satellite cells, side population cells, muscle derived stem cells, mesenchymal stem cells, myogenic pericytes, or mesoangioblasts.
83. The method of any one of claims 74-82, wherein the cells are non-myogenic cells.

84. The method of any one of claims 74-83, wherein the growth factor ligand is selected from basic fibroblast growth factor (FGF2), insulin-like growth factor 1 (IGF1), and platelet-derived growth factor subunit B (PDGFb).
85. The method of claim 84, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises an additional two or more growth factor ligands, wherein each of the additional growth factor ligands is selected from FGF2, IGF1, and PDGFb.
86. The method of claim 84 or 85, wherein the growth factor ligands is FGF2.
87. The method of claim 86, wherein the FGF2 comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 1-15.
88. The method of claim 84 or 85, wherein the growth factor ligands is IGF1.
89. The method of claim 88, wherein the IGF1 comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 16-17.
90. The method of claim 84 or 85, wherein the growth factor ligands is PDGFb.
91. The method of claim 90, wherein the PDGFb comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 18-21.
92. The method of any one of claims 74-91, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of a signal peptide located 5' to the coding sequence of the growth factor ligand, and wherein the signal sequence and the growth factor ligand are a fusion protein.
93. The method of claim 92, wherein the signal sequence comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 22-31.
94. The method of any one of claims 74-93, wherein the polynucleotide comprising a coding sequence of a growth factor ligand comprises a regulatory sequence operably linked to the coding sequence of the growth factor ligand and/or additional growth factor ligands.
95. The method of claim 94, wherein the regulatory sequence comprises a promoter selected from: an inducible promoter, a tissue specific promoter, and a constitutively active promoter.

96. The method of claim 94 or 95, wherein the promoter is selected from EF1alpha, PGK, CMV, RSV, and β -actin.
97. The method of any one of claims 74-96, wherein the polynucleotide comprising a coding sequence of a growth factor ligand comprises a sequence encoding a polycistronic mRNA, wherein the polycistronic mRNA comprises the coding sequence of the growth factor ligand and the coding sequence one or more additional growth factor ligands.
98. The method of claim 97, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises one or more sequences encoding a self-cleaving peptide, one or more internal ribosome entry sites (IRES), or a combination thereof.
99. The method of any one of claim 74-98, wherein activity and/or expression of the growth factor ligand is controllable.
100. The method of claim 99, wherein activity and/or expression of the growth factor ligand is controlled using an inducible promoter, an inducible tag, or a degradation tag.
101. The method of claim 100, wherein expression of the growth factor ligands is controlled using an inducible promoter.
102. The method of claim 101, wherein the coding sequence of the growth factor ligand is operably linked to the inducible promoter.
103. The method of claim 101 or 102, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible promoter, thereby enabling expression of the growth factor ligand.
104. The method of claim 100, wherein activity of the growth factor ligand is controlled using an inducible tag.
105. The method of claim 104, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of an inducible tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the inducible tag and the growth factor ligand are a fusion protein.

106. The method of claim 104 or 105, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible tag, thereby inducing activity of the growth factor ligand/fusion protein.
107. The method of claim 100, wherein activity of the one or more growth factor ligands is controlled using a degradation tag.
108. The method of any one of claims 107, wherein the polynucleotide comprising a coding sequence of a growth factor ligand further comprises a coding sequence of a degradation tag located 5' or 3' to the coding sequence of the growth factor ligand, and wherein the degradation tag and the growth factor ligand are a fusion protein.
109. The method of claim 107 or 108, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the degradation tag, thereby targeting the growth factor ligand/fusion protein for degradation.
110. The method of any one of claims 74-109, wherein the growth factor receptor is selected from fibroblast growth factor receptor (FGFR), insulin growth factor 1 receptor (IGF1R), and platelet-derived growth factor receptor (PDGFR).
111. The method of claim 110, wherein the polynucleotide comprising a coding sequence of a growth factor receptor further comprises an additional two or more growth factor receptors, wherein each additional growth factor receptor is selected from FGFR, IGF1R, and PDGFR.
112. The method of claim 110 or 111, wherein the growth factor receptor is an FGFR selected from FGFR1, FGFR2, FGFR3, and FGFR4.
113. The method of claim 112, wherein the FGFR comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 32-49.
114. The method of claim 110 or 111, wherein the growth factor receptor is IGF1R.
115. The method of claim 114, wherein the IGF1R comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 50-51.
116. The method of claim 110 or 111, wherein the growth factor receptor is PDGFR.

117. The method of claim 116, wherein the PDGFR comprises an amino acid sequence having at least 80% sequence identity to a sequence selected from SEQ ID NO: 52-58.
118. The method of any one of claims 74-117, wherein the polynucleotide comprising a coding sequence of an activated downstream growth factor target comprises a growth factor receptor comprising one or more amino acid insertions, deletions, or substitutions that result in the receptor being constitutively activated.
119. The method of any one of claims 110-118, wherein the polynucleotide comprising a coding sequence of a growth factor receptor comprises a regulatory sequence operably linked to the coding sequence of the growth factor receptor and/or the coding sequence of the additional growth factor receptors.
120. The method of claim 119, wherein the regulatory sequence comprises a promoter selected from: an inducible promoter, a tissue specific promoter, and a constitutively active promoter.
121. The method of claim 119 or 120, wherein the promoter is selected from EF1alpha, PGK, CMV, RSV, and β -actin.
122. The method of any one of claims 74-121, wherein the polynucleotide comprising a coding sequence of a growth factor receptor comprises a sequence encoding a polycistronic mRNA, wherein the polycistronic mRNA comprises the coding sequence of the growth factor receptor and the coding sequence of the two or more additional growth factor receptors.
123. The method of claim 122, wherein the polynucleotide comprising a coding sequence of a growth factor receptor comprises one or more sequences encoding a self-cleaving peptide, one or more internal ribosome entry sites (IRES), or both.
124. The method of any one of claim 74-123, wherein activity and/or expression of the growth factor receptors is controllable.
125. The method of claim 124, where expression of the growth factor receptor is controlled using an inducible promoter, an inducible tag, and a degradation tag.
126. The method of claim 125, wherein expression of the growth factor receptor is controlled using an inducible promoter.

127. The method of claim 126, wherein the coding sequence of the growth factor receptor is operably linked to the inducible promoter.
128. The method of claim 126 or 127, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible promoter, thereby enabling expression of the growth factor receptor.
129. The method of claim 125, wherein activity of the growth factor receptor is controlled using an inducible tag.
130. The method of claim 129, wherein the polynucleotide comprising a coding sequence of a growth factor receptor further comprises a coding sequence of an inducible tag located 5' or 3' to the coding sequence of the growth factor receptor, and wherein the inducible tag and the growth factor receptor are a fusion protein.
131. The method of claim 129 or 130, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the inducible tag, thereby inducing activity of the growth factor receptor/fusion protein.
132. The method of claim 125, wherein activity of the one or more growth factor ligands is controlled using a degradation tag.
133. The method of claim 132, wherein the polynucleotide comprising a coding sequence of a growth factor receptor further comprises a coding sequence of a degradation tag located 5' or 3' to the coding sequence of the growth factor receptor, and wherein the degradation tag and the growth factor receptor are a fusion protein.
134. The method of claim 132 or 133, further comprising:
maintaining the engineered cell line in a culture medium comprising a molecule capable of controlling the degradation tag, thereby targeting the growth factor receptor/fusion protein for degradation.
135. The method of any one of claims 74-134, further comprising introducing a polynucleotide sequence encoding an accessory protein.

136. The method of any one of claim 74-134, wherein the polynucleotide comprising a coding sequence of a growth factor ligand, the polynucleotide comprising a coding sequence of a growth factor receptor, or both, further comprises a coding sequence of an accessory protein.
137. The method of claim 135 or 136, wherein the accessory protein is fibroblast growth factor binding protein (FGFBP).
138. The method of claim 137, wherein the FGFBP comprises an amino acid sequence having at least 80% sequence identity to a sequence of SEQ ID NO: 59.
139. The method of claim 135 or 136, wherein the accessory protein is RASV12.
140. The method of claim 139, wherein the RASV12 comprises an amino acid sequence having at least 80% sequence identity to a sequence of SEQ ID NO: 60.
141. The method of any one of claims 74-140, wherein the method comprises introducing into the cell:
- (i) a polynucleotide comprising a coding sequence of FGF2, and a polynucleotide comprising a coding sequence of FGFR;
 - (ii) a polynucleotide comprising a coding sequence of IGF1, and a polynucleotide comprising a coding sequence of IGF1R;
 - (iii) a polynucleotide comprising a coding sequence of PDGF, and a polynucleotide comprising a coding sequence of PDGFR, or
 - (iv) a combination selected from: (i) and (ii), (ii) and (iii), (ii) and iii), and (i), (ii), and (iii).
142. A myogenic cell suitable for consumption comprising cells having increased expression of FGF2, IGF1, PDGFb, FGFR, IGF1R, or PDGFR, or a combination thereof.
143. A population of cells suitable for consumption comprising cells having increased expression of FGF2, IGF1, PDGFb, FGFR, IGF1R, or PDGFR, or a combination thereof.
144. A vector comprising a polynucleotide encoding a fusion protein comprising a coding sequence of a signaling sequence and a coding sequence of a growth factor ligand, and optionally a coding sequence of an inducible tag or a degradation tag.

145. A cell comprising a polynucleotide encoding a fusion protein comprising a coding sequence of a signaling sequence and a coding sequence of a growth factor ligand, and optionally a coding sequence of an inducible tag or a degradation tag.
146. A vector comprising a polynucleotide comprising a first coding sequence of a growth factor ligand or a fragment thereof, and a second coding sequence of growth factor receptor or a fragment thereof.
147. A cell comprising a polynucleotide comprising a coding sequence of a growth factor ligand or a fragment thereof, and a polynucleotide comprising a coding sequence of a growth factor receptor or a fragment thereof.
148. A cell-based meat suitable for consumption produced using the methods of any one of claims 74-141.