Appendix - ROCK signaling promotes collagen remodeling to facilitate invasive pancreatic ductal adenocarcinoma tumor cell growth.

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References

Appendix Supplementary Methods

Primary pancreatic exocrine cultures

Pancreatic exocrine cells were isolated as previously described(Pinho et al, 2011). Pancreata were injected with 2.5 ml of a 1.25 mg/ml Collagenase P (Roche)/HBSS (Gibco) solution and after removal from the mouse, placed into 5 ml of Collagenase P/HBSS solution. The tissue was cut into small pieces and digested in a shaking water bath at 37°C for 20 min. The reaction was stopped by placing the solution on ice. 10 ml cold HBSS + 5% FBS was added and after sedimentation of the cellular fraction, the supernatant was aspirated. Cell pellets were washed three times with 10 ml HBSS + 5% FBS. The cell suspension was centrifuged twice for 2 min at 1000 rpm and then the cell suspension was filtered sequentially through a 500 µm polypropylene mesh (Spectrum laboratories) and a 100 µm nylon filter (BD Falcon). Next, the cell suspension was layered on top of a 20 ml HBSS + 30% FBS solution and viable acinar cells pelleted by centrifugation for 2 min at 1000 rpm. Cells were cultured in defined media: DMEM/F12 supplemented with 3% FBS (Sigma), 1 mM Pyruvate (Gibco), 1x Non-essential amino acids (Gibco), 1x N2 supplement (Gibco), 0.5x B27 supplement (Gibco), 0.1% β-mercaptoethanol (Gibco), 20 ng/ml EGF (R&D systems), 10³ U/mL Esgro mLIF (Millipore), 25 μg/ml G418 (10131-027, Gibco), 0.1 mg/ml Soybean Trypsin Inhibitor (T6522, Sigma), and antibiotics (Penicillin-Streptomycin, 15070-063, Gibco)(Pinho et al, 2011). As indicated, EtOH vehicle, 2 μ M 4HT or 10 μ M Y27632 were added to the medium.

Attachment assay

Primary exocrine cells were seeded into 24-well plates and allowed to attach over a period of 48 h. Attachment of primary acinar cells was measured using the

Sulforhodamine B (SRB) assay. Cells were fixed to tissue culture plates with 1% trichloroacetic acid, stained with 0.4% SRB/1% glacial acetic acid for 45 min, and then washed 4 times with 1% acetic acid. Plates were left to dry overnight. Next day, 500 μ l of 10 mM Tris Base was added to each well and plates were left on a shaker for 15 min. For *Pdx1-Cre; LSL-KRas^{G12D/+}* primary cultures 75 μ l and for *Pdx1-Cre* and *Pdx1-Cre; LSL-ROCK2:ER* primary cultures 100 μ l were transferred to a 96-well-plate and absorbance was measured at 570 nm in triplicate.

Appendix Figure S1 - ROCK2 expression in mouse pancreata (related to Fig 1).

A Validation of ROCK2 antibody specificity using serial sections of pancreatic tissue from *Pdx1-Cre; Rosa26-LSL-RFP; ROCK2*^{fl/fl} mice. Serial tissue sections were immunohistochemically stained for RFP or ROCK2. Images reveal mosaic activity of the Pdx1-Cre recombinase as indicated by RFP expression. The ROCK2 antibody stained RFP negative cells that had not recombined the *ROCK2*^{fl/fl} locus. Scale bar = 100 μ m.

B Pdx1-Cre; Rosa26-LSL- $RFP; ROCK2^{fl/fl}$ cohorts were aged for 25 weeks. No significant effect of Pdx1-Cre mediated ROCK2 deletion was observed by comparing ROCK2^{+/+}, ROCK2^{+/fl} and ROCK2^{fl/fl} mice for body weight or pancreas/body weight, for males or females. Scatter plots show means \pm SD (n=6-15), p-values determined by Kruskal-Wallis test.



В



Appendix Figure S2 - Tissue selective expression of conditionally-regulated ROCK2 (related to Fig 1).

A, B Immunoblot of ROCK2:ER fusion protein in pancreata of 2 *LSL-ROCK2:ER*; *Pdx1-Cre* mice induced by Cre-mediated recombination but not in 2 *LSL-ROCK2:ER* mice (A) and uncropped immunoblot (B).

C Primary acinar cells from *Pdx1-Cre* or *Pdx1-Cre; LSL-ROCK2:ER* mice were cultured with vehicle or 2 μ M 4HT, and imaged after 5 days (left, scale bar = 200 μ m), or assessed for attachment after 48 h (right). Means ± SEM (n=4), p value by ratio paired t test.

D Primary acinar cells from *Pdx1-Cre; LSL-KRas*^{G12D/+} mice were cultured with vehicle or 10 μ M Y27632, and imaged after 48 h (left, scale bar = 200 μ m), or assessed for attachment after 48 h (right). Means ± SEM (n=9), p value by ratio paired t test.

E Primary acinar cells from Pdx1-Cre mice were cultured with vehicle or 10 μ M Y27632, and assessed for attachment after 48 h. Means ± SEM (n=4), p value by ratio paired t test.



Appendix Figure S3 - Conditional ROCK activation in KC mice does not alter PanIN numbers (related to Fig 1).

Pdx1-Cre; LSL-KRas^{G12D/+} (KC) or *Pdx1-Cre; LSL-KRas*^{G12D/+}; *LSL-ROCK2:ER* (RKC) mice were treated with 1% EtOH vehicle or tamoxifen citrate (100 mg/L) for conditional ROCK activation for 14 days starting at 6 weeks of age. No differences in the incidence of PanINs were observed in 8 week old mice (n=7). Box plots with p-value determined by Kruskal-Wallis test.



Appendix Figure S4 - Invasion of KPC or KPfIC cells into fibroblast conditioned collagen (related to Fig 2).

H&E stained sections of cell invasion into collagen matrix after 8 days, in the presence (top) or absence of matrix-embedded fibroblasts (bottom). Scale bar = 100 μ m. Invasion index of KPC and KPfIC cells. Means ± SEM (n=6), p value by unpaired t test.





Appendix Figure S5 - ROCK-induced substrate phosphorylation and changes in cell morphology (related to Fig 2).

A Ratio of phosphorylated MLC (pMLC) to total MLC for KPfIC cells expressing indicated ER-fusion proteins as shown in Fig 2C. Cells were left untreated or treated with 4HT in the absence or presence of 1 μ M or 10 μ M H1152 as indicated. Means ± SEM (n=3).

B KPfIC cells expressing indicated ER-fusion proteins, grown as adherent cells and treated with vehicle or 1 μ M 4HT for 24 h (scale bar = 50 μ m).





Appendix Figure S6 - Average RNA sequence reads for indicated collagens

with >10 copies detected. (related to Fig 4).

Means \pm SEM (n=3) * adjusted p-value <0.05.



Collagens >10 copies

Appendix Figure S7 - Analysis of KPC mouse tumors with Fasudil ROCK inhibitor treatment (related to Fig 8).

A-E PDAC endpoint tumors were examined for percentages of SMA positive area, Ki67 positive cells, necrotic area, CD3 positive cells and CD31 positive cells as indicated. Box plots with exact p value by Mann-Whitney test.



Appendix Table S1 - ROCK induced changes in gene expression associated

with Metacore[™] gene process networks.

| | Networks | Total in network | p-value | FDR | In Data | Network Objects from Active Data |
|---|--|---------------------|---------------|---------------|---------|---|
| 1 | Cell adhesion_Cell-matrix interactions | 211 | 3.551E- 08 | 5.398E- 06 | 37 | MMP-12, Galectin-3, ADAM33, ADAM-TS1, COL4A2, ADAM23, Fibulin-2, ITGA6, COL6A1, MMP-13, CD44 (ICD), LAMC2, TIMP3, Stromelysin-2, Aggrecanase-1, LAMB3, Collagen IV, CD44, ITGA3, ADAM-TS15, CD38, Tenascin-C, LAMB1, ITIH2, COL16A1, A1M, ITGB6, CD44 soluble, Aggrecan, ADAM-TS14, LAMR1, TIMP1, Connexin 43, CD44 (EXT), Aggrecanase-2, Versican, TINAG |
| 2 | Proteolysis_Connective tissue degradation | 119 | 2.664E- 06 | 2.025E- 04 | 23 | MMP-12, Meprin, ADAM33, ADAM- TS1, ADAM23, Meprin A, alpha, MMP-13, TIMP3, ADAM8, Stromelysin-2, Aggrecanase-1, Collagen IV, PLAT (TPA), ADAM- TS15, Tenascin-C, COL16A1, PAI1, PLAU (UPA), Aggrecan, ADAM- TS14, TIMP1, Aggrecanase-2, TINAG |
| 3 | Cell adhesion_Integrin-mediated cell-matrix adhesion | 214 | 2.845E- 05 | 1.135E- 03 | 31 | Tubulin beta, Talin, Cyclin D1, Pl3K cat class IA, Tubulin beta 3, Fibulin- 2, ITGA6, Tubulin alpha, Beta- parvin, Filamin A, Caveolin-1, Collagen IV, Tubulin alpha 1A, Lpd, ITGA3, LIMK1, CD53, Tenascin-C, ERM proteins, MyHC, Tcf(Lef), Filamin B (TABP), ITGB6, Zyxin, Tubulin beta 2, Pl3K cat class IA (p110-delta), Filamin C, Cyr61, TINAG, Tubulin alpha-4A, Tubulin (in microtubules) |
| 4 | Development_Ossification and bone remodeling | 157 | 3.477E- 05 | 1.135E- 03 | 25 | ATF-4, GDF11(BMP11), TGF-beta, TIEG, SHH, Filamin A, Ihh, TWIST1, Hedgehog, FGFR2, CSF1, TIEG1, SLC26A2, Spp24, WNT7A, ETS, WNT, BMP4, Annexin II, p38 MAPK, Galpha(s)-specific calcitonin GPCRs, p90Rsk, IBP, Frizzled, Activin |
| 5 | Signal transduction_WNT signaling | 177 | 3.732E- 05 | 1.135E- 03 | 27 | COX-2 (PTGS2), WNT4, TGF-beta 2, WNT10A, PP2A regulatory, TGF- beta, Cyclin D1, DLX2, Adenylate cyclase type I, ERK3, E2F2, p38beta (MAPK11), ESR1 (nuclear), CD44, WNT7B, Fra-1, DAAM1, Tcf(Lef), WNT7A, Cyclin E, WNT, SLUG, p38 MAPK, Adenylate cyclase, TCF7L2 (TCF4), Frizzled, IP3 receptor |
| 6 | Cytoskeleton_Regulation of cytoskeleton rearrangement | 183 | 6.772E- 05 | 1.716E- 03 | 27 | Ankyrin-G, Plectin 1, Tubulin beta, Talin, SPTBN(spectrin1-4), Advillin (p92), Tubulin beta 3, Galpha(i)- specific amine GPCRs, RhoF (Rif), Tubulin alpha, Filamin A, VAV-3, RHO6, Tubulin alpha 1A, CD43, CD44, LIMK1, ERM proteins, MyHC, Filamin B (TABP), Beta-fodrin, Zyxin, Tubulin beta 2, Filamin C, WaspIP, Protein kinase G, Tubulin (in microtubules) |
| 7 | Proliferation_Negative regulation of cell proliferation | 184 | 1.897E- 04 | 4.120E- 03 | 26 | COX-2 (PTGS2), GDF11(BMP11), GAB2, Galpha(i)-specific peptide GPCRs, FGFR3, ADAM-TS1, TGF- |

| 8 | Blood coagulation | 94 | 4.137E- | 7.860E- | 16 | beta, Cyclin D1, PI3K cat class IA, Amphiregulin, Calgizzarin, VEGFR- 2, GRO-1, OSMR, BTG2, p21, IBP5, PI3K reg class IB (p101), ETS1, Cyclin E, Sestrin 1, IBP, MAD4, IL6RA, C/EBPalpha, IBP3 Galpha(q)-specific nucleotide-like GPCRs, MSP, Thrombomodulin |
|----|--|-----|---------------|---------------|----|--|
| | | | | | | AR1, Caveolin-1, Collagen IV, Protein C receptor (endothelial), Tissue factor, PLAT (TPA), Protein S, Protein C, PAR2, PAI1, Adenosine A2a receptor, SERPINF2, PLAU (UPA) |
| 9 | Development_Blood vessel morphogenesis | 228 | 5.137E- 04 | 8.675E- 03 | 29 | Neuropilin-2, Galpha(i)-specific peptide GPCRs, Galpha(q)-specific nucleotide-like GPCRs, Pl3K cat class IA, Galpha(i)-specific amine GPCRs, Amphiregulin, VEGFR-2, PAR1, Galpha(q)-specific peptide GPCRs, ALDOA, Transferrin, Galpha(s)-specific nucleotide-like GPCRs, LDHA, Alpha-1B adrenergic receptor, PGAR, PLGF, PDE3B, PDE, PLAT (TPA), Neuregulin 1, Epiregulin, BMP4, Galpha(q)- specific amine GPCRs, Adenosine A2a receptor, PGK1, Neuropilin-1, Protein kinase G, Cyr61, FGF1 |
| 10 | Cell adhesion_Platelet aggregation | 158 | 7.154E- 04 | 1.087E- 02 | 22 | COX-2 (PTGS2), GAB2, Talin, PI3K cat class IA, PAR1, Adenylate cyclase type I, PLA2G7, Filamin A, VAV-3, Alpha-2A adrenergic receptor, Collagen IV, PLA2, MyHC, Ca-ATPase3, THAS, P-selectin, ENTPD2-alpha, Gab, Adenylate cyclase, PI3K cat class IA (p110- delta), IP3 receptor, Adenylate cyclase type VII |
| 11 | Proteolysis_ECM remodeling | 85 | 1.306E- 03 | 1.678E- 02 | 14 | MMP-12, ADAM33, MMP-13, TIMP3, Stromelysin-2, Aggrecanase-1, Collagen IV, PLAT (TPA), Tenascin-C, PAI1, PLAU (UPA), Aggrecan, ADAM-TS14, TIMP1 |
| 12 | Cytoskeleton_Actin filaments | 176 | 1.324E- 03 | 1.678E- 02 | 23 | Ankyrin-G, Plectin 1, Talin, SPTBN(spectrin1-4), MYH10, Filamin A, CD44, Myosin I, Troponin T, cardiac, LIMK1, DAAM1, ERM proteins, MyHC, Filamin B (TABP), Annexin II, NEBL, Beta-fodrin, Zyxin, Tropomyosin-4, Filamin C, Tropomyosin, WaspIP, Protein kinase G |
| 13 | Cell adhesion_Cell junctions | 162 | 2.340E- 03 | 2.735E- 02 | 21 | GJC1, Tubulin beta, Nectin-2, JAM2, ZO-3, PI3K cat class IA, ATP1B1, Tubulin alpha, Desmocollin 3, WNK4, Plakophilin 1, Connexin 45, Caveolin-1, Tcf(Lef), DSC2, Beta- fodrin, Connexin 31, Claudin-7, Connexin 43, SIP1 (ZFHX1B), Tubulin (in microtubules) |
| 14 | Development_EMT_Regulation of epithelial-to-mesenchymal transition | 225 | 3.882E- 03 | 4.215E- 02 | 26 | COX-2 (PTGS2), PDGF-A, GAB2, 4E-BP1, TGF-beta 2, Nestin, TGF- beta, PI3K cat class IA, HMGA2, PDGF-B, TWIST1, FGFR2, ESR1 (nuclear), Keratin 14, ETS1, Cyclin E, WNT, BMP4, SLUG, p38 MAPK, PAI1, SOX9, p90Rsk, Frizzled, SIP1 (ZFHX1B), FGF1 |
| 15 | Development_Neurogenesis_Ax onal guidance | 230 | 5.208E- 03 | 5.277E- 02 | 26 | Neuropilin-2, Ephrin-A receptor 7, MYH10, ADAM23, PI3K cat class IA, Ephrin-A receptors, APOE, FMR2, DCAMKL1, Adenylate cyclase type I, CRMP4, RH06, DARPP-32, |

| | | | | | | Semaphorin 7A, LIMK1, APOER2, ERM proteins, MyHC, BDNF, Ephrin-A receptor 2, Selenoprotein P, Neuropilin-1, IP3 receptor, MIR (Idol), Tubulin (in microtubules), Plexin A4 |
|----|--|-----|---------------|---------------|----|--|
| 16 | Cell adhesion_Cadherins | 180 | 8.076E- 03 | 7.672E- 02 | 21 | WNT4, Galectin-3, PTP-2, PTPRF (LAR), Nectin-2, WNT10A, PTPR- mu, PI3K cat class IA, FXYD5, Desmocollin 3, Plakophilin 1, ITGA3, PDZK3, VLDLR, Tcf(Lef), WNT7A, WNT, DSC2, LI-cadherin, Frizzled, Tubulin (in microtubules) |
| 17 | Reproduction_FSH-beta signaling pathway | 160 | 9.538E- 03 | 8.528E- 02 | 19 | 4E-BP1, TGF-beta 2, FSRP, PP2A regulatory, PI3K cat class IA, p90RSK3(RPS6KA2), Activin beta A, DUSP5, Adenylate cyclase type I, PEA3, Epiregulin, BMP4, p38 MAPK, Adenylate cyclase, p90Rsk, IBP, IP3 receptor, Cyclin D, IBP3 |
| 18 | Cardiac development_Wnt_beta-catenin, Notch, VEGF, IP3 and integrin signaling | 150 | 1.033E- 02 | 8.727E- 02 | 18 | Neuropilin-2, ID1, GLI-3R, CRLR, VEGFR-2, GLI-3, Connexin 45, Alpha-1B adrenergic receptor, Troponin T, cardiac, MyHC, Tcf(Lef), HHEX (PRH), WNT, Galpha(s)- specific calcitonin GPCRs, Frizzled, Connexin 43, IP3 receptor, Versican |
| 19 | Development_Neurogenesis_Sy naptogenesis | 180 | 1.592E- 02 | 1.274E- 01 | 20 | Homer, Synaptotagmin, X11, Neuregulin 4, Synapsin I, Semaphorin 4F, APOE, nAChR alpha, FGFR2, Synaptotagmin XI, Neuregulin 2, APOER2, Neuregulin 1, WNT7A, FGFR4, WNT, BDNF, DLGAP1 (GKAP), Semaphorin 4G, Frizzled |
| 20 | Cytoskeleton_Intermediate filaments | 81 | 1.762E- 02 | 1.339E- 01 | 11 | Plectin 1, Tubulin beta, Nestin, Tubulin alpha, Plakophilin 1, Desmuslin, Keratin 14, ZNF239, Tubulin beta 2, Lamin A/C, Tubulin (in microtubules) |
| 21 | Chemotaxis | 137 | 1.916E- 02 | 1.387E- 01 | 16 | GRO-2, Galpha(i)-specific peptide GPCRs, PI3K cat class IA, CXCL16, GRO-1, Galpha(q)-specific peptide GPCRs, CCL13, CD43, CD44, Fra- 1, CCL2, GRO-3, p38 MAPK, C3aR, PLAU (UPA), Cyr61 |
| 22 | Proliferation_Positive regulation cell proliferation | 221 | 2.097E- 02 | 1.442E- 01 | 23 | COX-2 (PTGS2), GAB2, Galpha(i)- specific peptide GPCRs, Glypican-1, Cyclin D1, PI3K cat class IA, Galpha(i)-specific amine GPCRs, SHH, FGFR2, Alpha-2A adrenergic receptor, CSF1, p21, Fra-1, PLGF, Alpha-1D adrenergic receptor, Cyclin E, GM-CSF, N-Myc, Neuropilin-1, PI3K cat class IA (p110-delta), TIMP1, LIF, LIFR |
| 23 | Cell adhesion_Platelet- endothelium-leucocyte interactions | 174 | 2.182E- 02 | 1.442E- 01 | 19 | PDGF-A, TGF-beta 2, JAM2, TGF- beta, Thrombomodulin, VEGFR-2, MMP-13, PDGF-B, Collagen IV, CD44, CCL2, PLAT (TPA), VLDLR, Protein S, Protein C, P-selectin, PAI1, PLAU (UPA), Cyr61 |
| 24 | Immune response_Th17-derived cytokines | 98 | 2.850E- 02 | 1.787E- 01 | 12 | COX-2 (PTGS2), C/EBP, PI3K cat class IA, PGES, GRO-1, MMP-13, Calgranulin A, CCL2, Calgranulin B, p38 MAPK, GM-CSF, TIMP1 |
| 25 | Development_Cartilage development | 66 | 2.955E- 02 | 1.787E- 01 | 9 | TR-alpha, Activin beta A, MMP-13, p38beta (MAPK11), Ihh, Aggrecanase-1, BMP4, SOX9, Aggrecan |
| 26 | Development_Hedgehog signaling | 254 | 3.057E- 02 | 1.787E- 01 | 25 | ID1, LRP2 (Megalin), Cyclin D1, GLI-3R, Activin beta A, DLX2, DHH, SHH, Adenylate cyclase type I, Filamin A, p38beta (MAPK11), Ihh, Hedgehog, FGFR2, GLI-3, p21, |

| 27 Apoptosis, Anti-apoptosis mediated by external signals via NF-&B 111 3.208E- 02 1.806E- 02 10 13 ODx-2 (PG-R), P2A regulatory, P3X cat lass IA, VEGFR-2, PDG-R, Bot-3, APATIL, PINSTS, FLANGES, PDG-RA, Bot-3, PARIL, PINSTS, PLANGES, PLANGES, PDG-RA, Bot-3, PLANGES, PLANGES, | | | | | | | ROR-alpha, PI3K reg class IB |
|--|-----|----------------------------------|-----|---------------|---------------|----|--|
| Image: constraint of the second sec | | | | | | | (p101), BMP4, N-Myc, Adenylate |
| 27 Apoptosis ME-k8 111 3.209E 1.806E 13 CD28_L/REGIM points (PCFS2, PDGF-8, Bc3, APRRI, (PFS51), PDK reg class IB (p101), CM-CSF, Bc3, APRRI, (PFSF13), PDK reg class IB (p101), CM-CSF, Adenylate cyclase, p90RsK, FN14(TNFSF12A) 28 Cell adhesion_Amyloid proteins 195 3.433E 1.864E- 02 20 PAR3, WN14, Adenylate cyclase, p90RsK, FN14(TNFSF12A) 29 Inflammation_L1-13 signaling pathway 91 3.808E- 02 1.953E- 01 11 II, IFR, Adenylate cyclase type I, II, 19RA1, DCOR, CL2, Tenasch- G, G 101 1.953E- SOCS1 30 Reproduction_Feeding and Neurohormone signaling 211 4.058E- 02 1.953E- 01 21 4.674E- 02 1.953E- 01 21 4.674E- SOCS1 23 Adenylate cyclase type I, CG 101 4.674E- 01 1.953E- 01 23 PDGF-A, WN14, 4E-BPT, TGF-beta 2, CalphaQ)- specific petide GPCRs, LRP2, (Megalin), PP2A regulatory, TGF- beta, MSP, P13K citass IA, Mather cyclass SN, CG 101 3.006E- 01 1.953E- 01 23 PDGF-A, WN14, 4E-BPT, TGF-beta 2, CalphaQ)- specific petide GPCRs, CRP3, Adenylate cyclase type I, FCGR7, Neuropather physical calss IA, Mather type I, 197A, CGR7, SNR, BP3, SOCS1 31 Signali | | | | | | | cyclase, SOX9, TCF7L2 (TCF4), |
| 21 Applicities dy external signals via NF-k6 111 3.208E 100 10 10 100 10 10 | 07 | Apontonia Anti apontonia | 111 | 2 2005 | 1 9065 | 10 | Frizzied, Adenylate cyclase type VII |
| NF-KB VEGEP2.PDCP.EB.BG.3. 28 Cell adhesion_Amyloid proteins 195 3.433E- 1.864E- 20 PAR3. WNT4, BACE, ADAM33, TGL, FARAER, FM14(TINFSF12A) 28 Cell adhesion_Amyloid proteins 195 3.433E- 1.864E- 20 PAR3. WNT4, BACE, ADAM33, TGL, Fabra Z, X11, WNTTA, Filamin A, Caveolin T, Collagen IV, WNT7A, Filamin B (TABP), WNT, Filzzled, Connexin, A3, Tubulin (in microtubules) 29 Inflammation_IL-13 signaling pathway 91 3.808E- 1.953E- 11 ILTRA, Adenylate cyclase type I, IL13RA1, DCCR, CL2, Tenascin-C, HSDB1, FOXJI, PI3K cat class IA, (p110-delta), PI37 cceptor, SOC51 30 Reproduction_Feeding and Neurohome signaling 211 4.058E- 1.953E- 21 4E-BP1, TGF-beta Z, Clai, Field C, RA, Galphal()-specific peptide CPCR, ILP2 (Megalin), PP2A, Clai, Class IA, BP3, CCL, Tenascin-C, HSDB1, FOXJI, PI3K cat class IA, BP3, CCL, Tenascin-C, HSDB1, FOXJI, PI3K cat class IA, GP3A, MP4, Field C, Class IA, BP3, CCL, Tenascin-C, HSDB1, FOXJI, PI3K cat class IA, BP3, CCL, Tenascin-C, HSDB1, FOXJI, PI3K cat class IA, BP3, CCL, Tenascin-C, HSDB1, FOXJI, PI3K cat class IA, BP3, CCL, Tenascin-C, CH, MNTA, BP3K C, CL2, Tenascin-C, C, HSDB1, FOXJI, PI3K cat class IA, BP3, CCL, Teolaga, IV, MITA, LEP3, TGF-beta Z, MI1, PIAK, BP3, CCL, Teolaga, IV, MITA, SOVB, BP3, SCL, CL4, COCR, TISAA, CCL2, CD4, WNTA, SOVB, BP3, SCL, CL4, CCL4, WNTA, SOVB, BP3, SCL, CL4, CCL4, WNTA, SOVB, BP3, SCL, CL4, CL4, SCL, CL4, WNTA, SOVB, BP3, SCL, CL4, CCL4, WNTA, SOVB, BP3, SCL, CL4, CCL4, WNTA, SCL4, SCL4, CCL4, WNTA, SCL4, SCL4, CL43, SCL4, CL43, SCL4, CCL44, WNTA, SCL43, SCL44, SCL44, SCL44, SCL44, SCL44, SCL44, SCL44, SCL44, SCL44, | 21 | mediated by external signals via | 111 | 3.209E- 02 | 1.000E- 01 | 15 | regulatory PI3K cat class IA |
| 28 Cell adhesion_Amyloid proteins 195 3.433E: 1.884E: 20 PARX_(TINESF12A) 28 Cell adhesion_Amyloid proteins 195 3.433E: 1.884E: 20 PARX_NIT4_BACE2, ADM33 28 Cell adhesion_Amyloid proteins 195 3.433E: 1.884E: 20 PARX_NIT4_BACE2, ADM33 29 Inflammation_IL-13 signaling 91 3.608E: 1.953E: 11 I.ITRN, Adenylate cyclase type I, Introdubules) 29 Inflammation_IL-13 signaling 91 3.608E: 1.953E: 11 I.ITRN, Adenylate cyclase type I, Introdubules) 30 Reproduction_Feeding and Neurohormone signaling 211 4.058E: 1.953E: 21 4.EEP1, TGF-beta 2, Galpha()- specific petited CPCRs, LRP2 (MagRin, PP2A, regulatory, TGF-beta, SOCS1 31 Signal transduction_NOTCH 236 4.074E: 1.953E: 23 PDGF-A, WNT4, 4EBPT, TGF-beta 2, Calpha()- specific petited CPCRs, LRP2 (MagRin, PP2A, regulatory, TGF-beta 2, Calpha()- specific petited CPCRs, CP3A, response type I, FCGRT, Neuropatite cyclase type I, FCGRT, Neuropatite cyclase LRP2 (MagRin, PP2A, regulatory, TGF-beta 2, WNT10A, TGF-beta 2, CUT1, Cyclin 17, PI3K Kai class IA, PDGF-B, ADSN, PB3, SOCS1 31 Signal transduction_NOTCH 236 4.074E: 1.953E: 23 | | NF-kB | | 02 | 01 | | VEGER-2 PDGE-B Bcl-3 |
| 28 Cell adhesion_Amyloid proteins 195 3.433E 1.864E- 02 20 PAK3, WN14, BACE2, ADAM33, TGF-beta 2, X11, WN170A, Flamin A, Caveolin-1, Collagen IV, WNT7A, Flamin B (TABP), WNT7A, SOOBH, FOX1H, PI3K cat class IA (p110-deta), IP3 receptor, SOC54 30 Reproduction_Feeding and Neurohormone signaling 211 4.058E- 02 1.953E- 01 21 4.874, DCOR, CL2, Tenascin- SOC54 SOC54 31 Signal transduction_NOTCH signaling 236 4.074E- 02 1.953E- 01 23 20GFA, WNT4, KE-BP1, TGF-beta 2, WMT7A, TGF-beta, CL44, WNT7A, SOR9, IBP3, SOR1, EP3, SOR4, IBP3, SOR1, EP3, SOR4, IBP3, SOR1, EP3, SOR4, IBP3, SOR1, EP3, SOR1, EP3, SOR4, IBP3, SOR4, EP3, SOR4, IBP3, SOR4, EP3, SOR4, IBP3, SOR4, Flazel, CL44, WNT7A, SOR4, IBP3, SOR4, IBP3, | | | | | | | APRIL(TNFSF13), PI3K reg class IB |
| 28 Cell adhesion_Amyloid proteins 195 3.433E 1.864E 20 PARS, WNT4, BACE2, ADAM33, TGF-beta 2, ADAM33, TGF-beta 2, ATI, WNT10A, Filamin A, Caveolin-1, Collagent V, WNT7A, Filamin B, TABP), WNT7A, Filamin B, TABP, TAP, TAP, TAP, TAP, TAP, TAP, TAP, TA | | | | | | | (p101), GM-CSF, Adenylate cyclase, |
| 28 Cell adhesion_Amyloid proteins 195 3.433E- 02 1.864E- 02 20 PAK3_WTR_BACE2_ADAM33, Caveolin-1, Collagen IV, WNT7B, PZCX3, LIMK1, Tc(Le), WNT7A, Filamin B (TABP), WNT7, Frizzled, Connexin 43, Tubulin (in microtubules) 29 Inflammation_IL-13 signaling pathway 91 3.808E- 02 1.953E- 02 11 ILTRN, Adenylate, cyclase type I, LINR, Adenylate, cyclase type I, SOCS1 30 Reproduction_Feeding and Neurohormone signaling 211 4.058E- 02 1.953E- 01 21 4.658E- 2.002 1.953E- 01 21 4.658E- SOCS1 24 4.674E- 2.002 1.953E- 01 23 24 4.074E- 2.002 1.953E- 01 23 24 4.074E- 2.002 1.953E- 01 23 24 4.074E- 02 1.953E- 01 23 24< | | | | | | | p90Rsk, FN14(TNFRSF12A) |
| 1 02 01 TG-beta 2, X1, WNT10A, Filamin Acaveolin-1, Collagent V, WNT7A, Filamin B (TABP), Tabin, Filamin B (TABP), Tabin, Filamin B (TABP), Tabin, Filamin B (TABP), Tabin, Filamin B (TABP), Filamin B (TABP), Filamin B (TAB | 28 | Cell adhesion_Amyloid proteins | 195 | 3.433E- | 1.864E- | 20 | PAK3, WNT4, BACE2, ADAM33, |
| A. Caveoin-Y. Collagen IV, WNT7B, Pathway A. Caveoin-Y. Collagen IV, WNT7B, Pathway 29 Inflammation_IL-13 signaling pathway 91 3.808E- 1.953E- 11 ILITRN, Adenylate cyclase type I, ILITSN, Adenylate cyclase type I, ILITSN, Adenylate cyclase type I, ILITSN, Adenylate cyclase type I, ILITSN, ADDR, FOXI, PISK cat class IA (p110-delta), P3 receptor, SCCS1 30 Reproduction_Feeding and Neurohormone signaling 211 4.058E- 1.953E- 21 4E-BP1, TGF-beta 2, Galpha(I)- secific peptide GPCRs, IRP2 (Megalin, P2A regulatory, TGF- beta, MSP, PI3K cat class IA, Galpha(a)-Specific peptide GPCRs, Adelpha(a)-Specific catas IA, Amphiregulin, PGF-B, p38beta (MAR-K11), p21, CD44, WNT78, Neuregulin 1, PGF-B, p38beta (MAR-K11), p21, CD44, WNT78, Neuregulin 1, p24, CD44, WNT78, Neuregulin 1, PGF-B, p38beta (MAR-K11), p21, CD44, WNT78, Neuregulin 1, p24, CD44, MNT78, Neuregulin 1, p24, CD44, MNT78, Neuregulin 1, p24, CD44, MNT78, Neuregulin 1, p24, CD44, PDE3, Galpha(a)- specific peptide GPCRs, Adenylate cyclase k, Frizzled, IP3 < | | | | 02 | 01 | | TGF-beta 2, X11, WNT10A, Filamin |
| 29 Inflammation_IL-13 signaling pathway 91 3.808E- 02 1.953E- 01 11 ILTRN, Advalute cyclase type I, ILTRN, Advalute cyclase type I, ICGRT, Balance Cyclase type I, ICGRT, ICGRT, PEA3, CD44, DCOR, ITGA3, Cyclin E, PA1, PH3, Cat class IA, Galpha(c)-specific peptide GPCRs, Adenylate cyclase type I, ICGRT, ICGRT, PEA3, CD44, DCOR, ITGA3, Cyclin E, PA1, PH3, Cat class IA, Galpha(c)-specific peptide GPCRs, Adenylate cyclase type I, ICGRT, PI3, CD44, WNT7, AE, EPP2, ICGRT, PI3, CD44, WNT7, AE, EPP3, ICGF- Balance I, ILTRN, Advalute Cyclase I, PA1, PT3, Eprequin, P217, WNT4, AE-BP1, ICGF-Beta 3, Cyclin E, PA1, PT3, Eprequin, P217, WNT, AE Corcequin, P217, WNT, AE Corcequin, P217, WNT, AE Corcequin, P217, WNT, AE Corcequin, P217, WNT, AE Corcequin, P218, Cat class IA, P117, AE Corcequin, P218, Cat class IA, P117, AE, D128, Tubulin apha 1A, MAPRE2(RP1), Tubulin apha 1A, MAPRE2(RP1), Tubulin apha 1A, MAPRE2(RP1), Tubulin apha, IA, MAPRE2(RP1), Tubulin apha, IA, MAPRE2(R | | | | | | | A, Caveolin-1, Collagen IV, WNT7B, |
| 29 Inflammation_IL-13 signaling pathway 91 3.808E- 02 1.953E- 01 11 ILTRN, Adenyiate cyclase type I, ILTRN, Adenyiate cyclase type I, CHEMID SC 1, P3X cat class IA, Galpha(a)-specific peptide GPCRs, LRP2 (Megalin), P2A regulatory, TGF- beta, MSP, PI3K cat class IA, Galpha(a)-specific peptide GPCRs, LRP2 (Megalin), P2A regulatory, TGF- beta, MSP, PI3K cat class IA, Galpha(a)-specific peptide GPCRs, Advise cyclase type I, FCGRT, PEAS. OD4A DCOR, ITGA3. Cyclin E, PA1I, PIN, A 4E-BP1, TGF-beta SOCS1 31 Signal transduction_NOTCH signaling 236 4.074E- 02 1.953E- 02 23 PDGFA, WINT 4, 4E-BP1, TGF-beta Guipta(c)-specific peptide GPCRs, Amphireguin, PDSC-B, p38beta (MAPK1), p21, CD44, WINT78, Meureguin1, TDTA, Epireguin, F2D7, WINT, AB MAPK, Frizzled, INTTA, Epireguin, MAPK, Tubulin alpha, MAPK, Tubulin alpha, TA, MAPRE, Tubulin alpha, TGF-beta_S, Galpha(a)- specific peptide GPCRs, Adenyiate cyclase type I, JDTS, ESRT (membrash, PASY, Chains, Tubulin beta 3, RHOF (R), TUbulin (in microtubules) 33 Reproduction_Progesterone signaling 117 4.626E- 02 2068E- 01 13 Tubulin ba, MAPK, Frizzled, JR3 (TGL-P), MVT, Adenyiate cyclase, Galpha(a)-specific calcionin GPCRs, | | | | | | | PDZK3, LIMK1, 1 ct(Let), WN1/A, Filomin B (TABD) W/NT, Frizzlad |
| 29 Inflammation_IL-13 signaling pathway 91 3.808E- 02 1.953E- 01 11 ILTRA Alexiyate cyclase type I, ILTRA Alexiyate cyclase type I, ICF-beta J, Galpha(I)- specific peptide GPCRs, IRP2 (Megalin), P2A regulatory, TGF- beta, MSP, PIX cat class IA, Galpha(c)-specific peptide GPCRs, Adenylate cyclase type I, FCGRT, PEA3, CD44, DCOR, ITGA3, Cyclin E, PA1, PH3, Cat class IA, Galpha(c)-specific peptide GPCRs, Adenylate cyclase type I, FCGRT, PEA3, CD44, DCOR, ITGA3, Cyclin E, PA1, PH3, Cat class IA, Galpha(C)-specific peptide GPCRs, Adenylate cyclase type I, FCGRT, PEA3, CD44, DCOR, ITGA3, Cyclin E, PA1, PH3, Cat class IA, Galpha(C)-specific peptide GPCRs, Adenylate cyclase type I, TGF-beta, GLUTH, Cyclin D, PIX cat class IA, Amphireguin, PDCF-B, p38beta (MAPK1), p21, CD44, WNT78, Neuroguin1, WNT7A, Epireguin, PZD7, WNT, ASB MAPK, Frizzled, PI3K cat class IA, (P110-detta) 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 01 1.953E- 01 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin abrea, Al-NDFG (Ri), Tubulin abrea, MAPK1, PDCR, CH3, Specific cyclase type I, JDP2, ESR1 (microtubules) 33 Reproduction_Progesterone signaling 214 4.811E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(Q)- specific peptide GPCR9, HOR2, Tubulin development_BMP_TGF_beta_s ignaling 117 4.826E- 01 | | | | | | | Connevin 43 Tubulin (in |
| 29 Inflammation_LL-13 signaling pathway 91 3.808E. 1.953E. 01 11 ILTRN Atienylate cyclase type I, C, HSD381, FOXJ, PI3K cat class IA (p110-delta), IP3 receptor, SOCS1 30 Reproduction_Feeding and Neurohormone signaling 211 4.058E- 1.953E- 21 4E-BP1, TGF-beta 2, Galpha(I)- specific peptide GPCRs, LRP2 (Megalin), PP2A regulatory, TGF-beta, MSP, PI3K cat class IA, Galpha(I)-specific peptide GPCRs, LRP2 (Megalin), PP2A regulatory, TGF-beta, SCD4, DCOR, ITGA3, Cyclin DF, PI3K cat class IA, Galpha(I)-specific peptide GPCRs, LRP2 (Megalin), PP3K cat class IA, Galpha(I)-specific peptide GPCRs, LRP2 (Megalin), PD3K cat class IA, Adenylate cyclase type I, TGF-beta, GLUT1, Cyclin D1, P13K cat class IA, MCHARA (MAPK11), p21, CD44, WNT78, SOCS1 31 Signaling 236 4.074E- 1.953E- 23 ODGFA, WNT4, 4E-BP1, TGF-beta, GLUT1, Cyclin D1, P13K cat class IA, Amphregulin, PD3F-B, p38beta (MAPK11), p21, CD44, WNT78, PI3K (MAPK11), p21, P21, P21, P21, P21, P21, P21, P21, P | | | | | | | microtubules) |
| pathway Dot O2 O1 L13RA1, DCOR, C12, Teńascin-, CH3D3B1, DCOR, C12, Teńascin-, C14D3B1, DCOR, TCAS, L72B1, DCOR, TCAS, C12B1, DCOR, TCAS, DC | 29 | Inflammation IL-13 signaling | 91 | 3.808E- | 1.953E- | 11 | IL1RN, Adenylate cyclase type I, |
| 30 Reproduction_Feeding and Neurohormone signaling 211 4.058E- 02 1.953E- 01 21 4.058E- 01 21 4.058E- 01 21 4.053E- 01 21 4.054E- 01 21 4.054E- 01 21 4.054E- 01 21 4.054E- 01 21 4.054E- 01 21 4.054E- 01 21 4.054E- 02 21 4.054E- 01 21 4.054E- 01 21 4.054E- 01 21 4.054E- 01 21 4.054E- 02 21 4.054E- 01 21 4.054E- 02 21 4.054E- 02 21 90GF-A.WNT4, 4E-BP1, TGF-beta 2. GoCS1 90GF-A.WNT4, 4E-BP1, TGF-beta 3. SOCS1 31 Signal transduction_NOTCH 236 4.074E- 02 1.953E- 01 23 PDGF-A.WNT4, 4E-BP1, TGF-beta 3. SOCS1 20 PDGF-A.WNT4, 4E-BP1, TGF-beta 3. SOCS1 20 101 24 24 24.074E- 01 20 21 PDGF-A.WNT4, 4E-BP1, TGF-beta 3. SOCS1 20 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 | | pathway | | 02 | 01 | | IL13RA1, DCOR, CCL2, Tenascin- |
| 30 Reproduction_Feeding and Neurohormone signaling 211 4.058E- 02 1.953E- 01 21 4.611P, TGF-beta 2, Galpha(), specific peptide GPCRs, Adenylate cyclase type 1, FCGRT, PEA3, CD44, DCOR, TGF- beta, MSP, P13K cat class 1A, Galpha(), specific peptide GPCRs, Adenylate cyclase type 1, FCGRT, PEA3, CD44, DCOR, TGF- beta, MSP, P13K cat class 1A, Galpha(), specific peptide GPCRs, Adenylate cyclase type 1, FCGRT, PEA3, CD44, DCOR, TGF- beta, MSP, P13K cat class 1A, Galpha(), specific peptide GPCRs, Adenylate cyclase type 1, FCGRT, PEA3, CD44, DCOR, TGF-beta 2, WNT10A, TGF-beta (GLUT), Cyclin D1, P13K cat class 1A, Amphiregulin, PDGF-B, p3Bbeta (MAPK11), p21, CD44, WNT7B, Neurgulin 1, WNT7A, Epiregulin, PZD7, WNT, p38 MAPK, Frizzled, P37K cat class 1A, (p110-detla) 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 01 13 Tubulin hapta, AMPKF, Trizzled, P10FGR1, TUbulin alpha, MAPR, Tubulin alpha 1A, MAPRE (PRI), TUBGCP2, DLGAPI (GKAP), HOCK2, Tubulin (in microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (nuclear), PLA2, DHB4, PDE3B, Tuftleft, WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p0Rsk, Frizzled, P3 Teopolers, Lapted, P3 34 Cardiac development_BMP_TGF_beta_s 117 4.626E- 02 2.068E- 01 13 TGF-beta 2, D1M, WHO, GL-3R, GL3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MH4, SLUG, Signaling 35 Inflammation_Amphoterin signaling 118 | | | | | | | C, HSD3B1, FOXJ1, PI3K cat class |
| 30 Reproduction_Feeding and Neurohormone signaling 211 4.058E- 02 1953E- 01 21 4E-BP1, TGF-beta 2, Galpha()- specific peptide GPCRs, LRP2 (Megalin), PP2A regulatory, TGF- beta, MSP, PI3K cat class IA, Galpha(q), specific peptide GPCRs, Adenylate cyclase type I, FCGRT, PEA3, CD44, DCOR, ITGA3, Cyclin E, PA11, Pm-1, SOX9, IBP3, Signaling 31 Signal transduction_NOTCH signaling 236 4.074E- 02 1.953E- 01 23 PDGF-A, WNT4, 4E-BP1, TGF-beta, GLUT1, Cyclin D1, PI3K cat class IA, Amphireguin, PDGF-B, p38beta (MAPK11), p21, CD44, WNT7B, Neureguin, PDGF-B, p38beta (MAPK11), D21, CD44, WNT7B, Neureguin, PDGF-B, p38beta (MAPK11), CD43, WNT7B, Neureguin, PDGF-B, p38beta (MAPK11), CD43, WNT7B, Neureguin, PDGF-B, p38beta (MAPK11), CAPA, D44, P34, CD44, P3 (Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 01 | | | | | | | IA (p110-delta), IP3 receptor, |
| 30 Reproduction_Peeding and Neurohormone signaling 211 4.098E- 02 1.934E- 02 21 4EPT, 1GF-beta 2, Galpha(1)- specific peptide GPCRs, Adenylate cyclase type I, FCGRT, PEA3, CD44, DCOR, ITGA3, Cyclin E, PA11, Pim-1, SOX9, IBP3, SOCS1 31 Signal transduction_NOTCH signaling 236 4.074E- 02 1.953E- 01 23 PDGF-A, WNT4, 4E-BP1, TGF-beta 2, WNT10, ATGF-beta GLUT1, Cyclin D1, PI3K cat class IA, Maphregulin, PDGF-B, p38beta (MAPK11), p21, CD44, WNT7B, FZD7, WNT7A, Epiregulin, FZD7, WNT7A, Epiregulin, FZD7, WNT7A, Epiregulin, FZD7, WNT7A, Epiregulin, Socs1 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 01 1.953E- 01 13 Tubulin beta X11, Dynein, axonemal, heavy chains, Tubulin beta X11, Dynein, axonemal, heavy chains, Tubulin aba, MAPE, Tubulin alpha A, MAPE, Tubulin alpha, MAPE, Tubulin alpha, MAPE, Tubulin alpha, MAPE, Tubulin alpha, TA, MAPE, Tubulin alpha, MAPE, Tubulin alpha, TA, MAPE, Tubulin alpha, MAPE, Tubulin alp | | | | 10505 | 10505 | | SOCS1 |
| Neuronomione signaling 02 01 Specific peptide GFCRs, LRP2 (Megaliatory, TGF- beta, MSP, P13K cat class IA, Galphar(Q)-specific peptide GFCRs, Adenylate cyclase type I, FCGRT, PEA3, CO44, DCCR, TIGA3, Cyclin E, PA11, Pim-1, SOX9, IBP3, Signaling 31 Signal transduction_NOTCH signaling 236 4.074E- 02 1.953E- 02 23 PDGF-A, WNT4, 4E-BP1, TGF-beta SUMT0A, TGF-beta, GLUT1, Cyclin DI, P13K cat class IA, Amphiregulin, PDGF-B, p38beta (MAPK1), p21, CD44, WNT7B, Neuregulin 1, WNT7A, Epiregulin, FZD7, WNT, p38 MAPK, Frizzled, P13K cat class IA, (p110-delta) 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 01 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin (in microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, P13K cat class IA, PDE3, Galpha(q)- specific caticitorin GPCRs, 90RsK, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 <td< td=""><td>30</td><td>Reproduction_Feeding and</td><td>211</td><td>4.058E-</td><td>1.953E-</td><td>21</td><td>4E-BP1, I GF-beta 2, Galpha(I)-</td></td<> | 30 | Reproduction_Feeding and | 211 | 4.058E- | 1.953E- | 21 | 4E-BP1, I GF-beta 2, Galpha(I)- |
| 31 Signal transduction_NOTCH 236 4.074E- 02 1.953E- 02 23 PDGF-A, WNT4, 4E-BP1, TGF-beta Signaling 31 Signal transduction_NOTCH 236 4.074E- 02 1.953E- 02 23 PDGF-A, WNT4, 4E-BP1, TGF-beta 2, WNT0A, TGF-beta, GLUT1, Cyclin D1, P13K cat class IA, Amphireguin, PDGF-B, p38beta (MAPK11), p21, CD44, WNT7B, Epireguin, FZD7, WNT, p38 MAPK, Frizzled, P13K cat class IA (p110-delta) 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 02 13 Tubulin beta, X1, Dynein, axonemal, heavy chains, Tubulin beta, X1, Dubuin alpha, MAPRE2(RP1), TUBGCP2, DLGAP1 (GKAP), HOOK2, Tubulin alpha, MAPRE2(RP1), TUBGCP2, DLGAP1 (GKAP), HOOK2, Tubulin (n microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K (rat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (ructear), Activin A, Troponin T, cardiac, MHC, TI, Adenylate cyclase, Galpha(g)-specific calcitonin GPCRs, p09Rsk, Frizzled, IP3 (racidars, MHP4, SLUG, SOX9 34 Cardiac development_BMP_TGF_beta_s ignaling 118 4.898E- 02 13 PI3K cat class IA, MMP-13, IL1RN, P3 | | Neuronormone signaling | | 02 | 01 | | (Megalin) PP2A regulatory TGE |
| 31 Signal transduction_NOTCH 236 4.074E- 02 1.953E- 02 23 PDGF-A, WNT4, 4E-BP1, TGF-beta SOCS1 31 Signal transduction_NOTCH 236 4.074E- 02 01 23 PDGF-A, WNT4, 4E-BP1, TGF-beta SOCS1 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 02 23 PDGF-A, WNT4, 4E-BP1, TGF-beta SOCS1 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 01 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta 3, RhoF (Rif), Tubulin alpha, MAP6, Tubulin alpha 1A, MAP6, Tubulin alpha 1A, MAP6, Tubulin alpha 1A, MAP6, Tubulin alpha 1A, MAP6, Tubulin alpha, 1A, MAP6, Tubulin, 1BGCP2, DLGAP1 (GKAP), HOCK2, Tubulin (In microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 01 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 01 13 TGF-beta 2, ID1, MYH10, CLI-3R, Galpha(s)-specific calcitorin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 35 Inflammation_Amphoterin signaling 118 4.898E- 0 | | | | | | | heta MSP PI3K cat class IA |
| 31 Signal transduction_NOTCH signaling 236 4.074E- 02 1.953E- 02 23 PDCF-A, WNT4, 4E-BP1, TGF-beta SOCS1 SOX9, IBP3, SOX9, IIP3, SOX9, IBP3, SOX9, IIP3, SOX9, IIP3, SOX9, SOX9, IIP3, SOX9, IIP3, | | | | | | | Galpha(g)-specific peptide GPCRs. |
| Signal transduction_NOTCH 236 4.074E- 02 1.953E- 01 23 PEA3_CD44, DCOR, ITGA3, Cyclin E, PAI1, Pim-1, SOX9, IBP3, SOCS1 31 Signal transduction_NOTCH signaling 236 4.074E- 02 1.953E- 01 23 PDGF-A, WNT4, 4E-BP1, TGF-beta 2, WNT40A, TGF-beta, GLUT1, Cyclin D1, PI3K cat class IA, Amphiregulin, PDGF-B, p38beta (MAPK11), p21, CD44, WNT7B, Neuregulin 1, WNT7A, Epiregulin, FZD7, WNT, 93 MAPK, Frizzled, PI3K cat class IA (p110-delta) 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 01 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta 3, Rhof (Rf), Tubulin alpha, MAPRF, Tubulin alpha 1A, MAPRE2(RP1), TUBGCP2, DLCAP1 (GKAP), HOOK2, Tubulin (in microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, DP2, ESR1 (nuclear), PLA2, DH84, PDE38, TcftLef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 01 2.068E- 01 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MJHC, Troponin T, cardiac, MJHC, Troponin T, cardiac, MJHC, Troponin T, cardiac, MJHC, SOX9 35 Inflammation_Amphoterin signaling 118 | | | | | | | Adenylate cyclase type I, FCGRT, |
| Signal transduction_NOTCH signaling Signal transduction_NOTCH signaling 236 4.074E- 02 1.953E- 02 23 PDGF-A, WNT4, 4E-BP1, TGF-beta 2, WNT10A, TGF-beta, GLUT1, Cyclin D1, PI3K cat class IA, Amphiregulin, PDGF-B, p38beta (MAPK11), p21, CD44, WNT7B, Neuregulin 1, WNT7A, Epiregulin, FZD7, WNT, p38 MAPK, Frizzled, PI3K cat class IA (p110-delta) 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 02 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta 3, RhoF (Rif), Tubulin alpha, MAP6, Tubulin alpha 1A, MAP6, Tubulin alpha, MAP6, Tubulin alpha, MAP6, Tubulin alpha, MAP6, Tubulin alpha, MAP6, Tubulin alpha, MAP6, Tubulin alpha, MAP6, Tubulin alpha, AL, MAPREZ(RP1), TUBGCP2, DLGAP1 (KAP), HOOK2, Tubulin (in microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type 1, JDP2, ESR1 (nuclear), RLA2, DHB4, PDE3B, Tic/Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 01 2.068E- 01 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, MyHC, Troponin T, cardiac, MyH4, SLUG, SOX9 SOX9 < | | | | | | | PEA3, CD44, DCOR, ITGA3, Cyclin |
| Signal transduction_NOTCH 236 4.074E- 1.953E- 23 PDGF-A, WNT4, 4E-BP1, TGF-beta 31 Signaling 236 4.074E- 0 01 23 PDGF-A, WNT4, 4E-BP1, TGF-beta, GLUT1, Cyclin D1, PI3K cat class IA, Amphiregulin, PDGF-B, p3beta (MAPK11), p21, CD44, WN17B, Neuregulin, FZD7, WNT, p38 MAPK, Frizzled, PI3K cat class IA (p110-delta) 32 Cytoskeleton_Cytoplasmic 115 4.112E- 1.953E- 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin alpha, MAP6, Tubulin alph | | | | | | | E, PAI1, Pim-1, SOX9, IBP3, |
| 31 Signal transduction_NOTCH 236 4.074E- 1.953E- 23 PDGF-A, WNT4, 4E-BP1, TGF-beta, GLUT1, Cyclin D1, PI3K cat class IA, Amphiregulin, PDGF-B, p38beta (MAPK11), p21, CD44, WNT7B, Neuregulin 1, WNT7A, Epiregulin, PZD7, WNT, AEBbeta (MAPK11), p21, CD44, WNT7B, Stat class IA (p110-delta) 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 1.953E- 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin alpha, MAP6, Tubulin, Alpha | | | | | | | SOCS1 |
| signaling 02 01 2. WN110A. FIG-beta, GLU11, Cyclin D1, PI3K cat class IA, Amphiregulin, PDGF-B, p38beta (MAPK11), p21, CD44, WN17B, Neuregulin 1, WN17A, Epiregulin, FZD7, WNT, p38 MAPK, Frizzled, PI3K cat class IA (p110-delta) 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 02 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta 3, RhoF (Rif), Tubulin alpha, MAP6; Tubulin alpha 1A, MAPRE2(RP1), TUBGCP2, DLGAP1 (GKAP), HOOK2, Tubulin (in microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(0)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Tcf(Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 01 13 TGF-beta 2, ID1, MYH10, GL1-3R, GL1-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, MyHC, Calgranulin B, p38 MAPK, PA11, PI3K cat class IA (N10-delta) | 31 | Signal transduction_NOTCH | 236 | 4.074E- | 1.953E- | 23 | PDGF-A, WNT4, 4E-BP1, TGF-beta |
| 32 Cytoskeleton_Cytoplasmic 115 4.112E- 1.953E- 13 Tubulin J, P1A, Cat Class IA, Amphiregulin, PDCF-B, p38beta (MAPK11), p21, CD44, WNT7B, Neuregulin 1, WNT7A, Epiregulin, PZDT, WNT, p38 MAPK, Frizzled, P13K cat class IA (p110-delta) 32 Cytoskeleton_Cytoplasmic 115 4.112E- 1.953E- 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta 3, RhoF (Rif), Tubulin alpha, IA, MAPRE2(RP1), TUBGCP2, DLGAP1 (GKAP), HOOK2, Tubulin (im microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 2.068E- 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, P13K cat class IA, PDE3, Galpha(a)- specific peptide GPCRs, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p30Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 2.068E- 13 TGF-beta 2, ID1, MYH10, GLI-3R, GUP3, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 2.127E- 13 P13K cat class IA, MMP-13, IL1RN, P38 MAPK, PA11, P13K cat class IA, PDE3, IC110-delta) | | signaling | | 02 | 01 | | 2, WNT10A, TGF-beta, GLUT1, |
| 32 Cytoskeleton_Cytoplasmic 115 4.112E- microtubules 1.953E- 02 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta 3, RhoF (Rf), Tubulin alpha, MAPRE2(RP1), TUBGCP2, DLGAP1 (GKAP), HOOK2, Tubulin (in microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 02 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Tcf(Lef), WNT, Adenylate cyclase, galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 Troponin T, cardiac, MyHC, Troponin T, cardiac, MMP-13, IL1RN, signaling 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 01 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MHP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, PI3K cat class IA, I010-deita) | | | | | | | Cyclin DT, PI3K cat class IA, Amphirogulia, PDCE R, p38hota |
| 32 Cytoskeleton_Cytoplasmic 115 4.112E- microtubules 1.953E- 02 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta 3, RhoF (Rif), Tubulin alpha, MAPRE2(RP1), TUBGCP2, DLGAP1 (GKAP), HOOK2, Tubulin in microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Tcf(Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MHP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PA11, PI3K cat class IA (n110-deita) | | | | | | | (MAPK11) n21 CD44 WNT7B |
| 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 02 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta 3, RhoF (Rif), Tubulin alpha, MAP6, Tubulin alpha 1A, MAPRE2(RP1), TUBGCP2, DLGAP1 (GKAP), HOOK2, Tubulin (in microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 02 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Teff(Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 01 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MHP4, SLUG, Troponin T, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK 11), Calgranulin A, CL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PA11, PI3K cat class IA (n110-de1a) | | | | | | | Neuregulin 1 WNT7A Epiregulin |
| Second Stress Second S | | | | | | | FZD7. WNT. p38 MAPK. Frizzled. |
| 32 Cytoskeleton_Cytoplasmic microtubules 115 4.112E- 02 1.953E- 01 13 Tubulin beta, X11, Dynein, axonemal, heavy chains, Tubulin beta 3, RhoF (Rif), Tubulin alpha, MAP6, Tubulin alpha, MAP6, Tubulin alpha, MAP6, Tubulin alph | | | | | | | PI3K cat class IA (p110-delta) |
| microtubules 02 01 axonemal, heavy chains, Tubulin beta 3, RhoF (Rif), Tubulin alpha, MAP6, Tubulin alpha 1A, MAPRE2(RP1), TUBGCP2, DLGAP1 (GKAP), HOOK2, Tubulin (in microtubules) 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 01 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (MOLear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, MyHC, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PA11, PI3K cat class IA (n110-delta) | 32 | Cytoskeleton_Cytoplasmic | 115 | 4.112E- | 1.953E- | 13 | Tubulin beta, X11, Dynein, |
| 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Tcf(Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, MyHC, Troponin T, cardiac, MyHC, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (o110-delta) | | microtubules | | 02 | 01 | | axonemal, heavy chains, Tubulin |
| 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Tcf(Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (n010-delta) | | | | | | | beta 3, RhoF (Rif), Tubulin alpha, |
| 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Tcf(Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (o110-delta) | | | | | | | MAP6, Lubulin alpha 1A, |
| 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Tcf(Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 01 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (o110-delta) | | | | | | | MAPRE2(RPT), TUBGCP2, DLCAP1(CKAP) HOOK2 Tubulin |
| 33 Reproduction_Progesterone signaling 214 4.611E- 02 2.068E- 01 21 COX-2 (PTGS2), ESR1 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)- specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Tcf(Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 01 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (n110-delta) | | | | | | | (in microtubules) |
| signaling 02 01 (membrane), MIF, ADAM-TS1, PI3K cat class IA, PDE3, Galpha(q)-specific peptide GPCRs, Adenylate cyclase type I, JDP2, ESR1 (nuclear), PLA2, DHB4, PDE3B, Tcf(Lef), WNT, Adenylate cyclase, Galpha(s)-specific calcitonin GPCRs, p90Rsk, Frizzled, IP3 receptor, Tubulin (in microtubules) 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (M10-delta) | 33 | Reproduction Progesterone | 214 | 4.611E- | 2.068E- | 21 | COX-2 (PTGS2), ESR1 |
| 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (n110-delta) | | signaling | | 02 | 01 | | (membrane), MIF, ADAM-TS1, PI3K |
| AdditionSubscription< | | | | | | | cat class IA, PDE3, Galpha(q)- |
| 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (o110-delta) | | | | | | | specific peptide GPCRs, Adenylate |
| 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (o110-delta) | | | | | | | cyclase type I, JDP2, ESR1 |
| 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (o110-delta) | | | | | | | (nuclear), PLA2, DHB4, PDE3B, |
| 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (o110-delta) | | | | | | | Calpha(c) specific calcitonin |
| 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 02 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (o110-delta) | | | | | | | GPCRs ngnRsk Frizzlad IP3 |
| 34 Cardiac development_BMP_TGF_beta_s ignaling 117 4.626E- 02 2.068E- 01 13 TGF-beta 2, ID1, MYH10, GLI-3R, GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (p110-delta) | | | | | | | receptor. Tubulin (in microtubules) |
| development_BMP_TGF_beta_s 02 01 GLI-3, ESR1 (nuclear), Activin A, Troponin T, cardiac, MyHC, Troponin T, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (o110-delta) | 34 | Cardiac | 117 | 4.626E- | 2.068E- | 13 | TGF-beta 2, ID1, MYH10, GLI-3R. |
| ignaling ignaling Troponin T, cardiac, MyHC, Troponin C, cardiac, BMP4, SLUG, SOX9 35 Inflammation_Amphoterin signaling 118 4.898E- 02 2.127E- 01 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (p110-delta) | | development_BMP_TGF_beta_s | | 02 | 01 | - | GLI-3, ESR1 (nuclear), Activin A, |
| 35 Inflammation_Amphoterin 118 4.898E- 2.127E- 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (p110-delta) | | ignaling | | | | | Troponin T, cardiac, MyHC, |
| 35 Inflammation_Amphoterin 118 4.898E- 2.127E- 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (p110-delta) | | | | | | | Troponin C, cardiac, BMP4, SLUG, |
| 35 Inflammation_Ampnoterin 118 4.898E- 2.127E- 13 PI3K cat class IA, MMP-13, IL1RN, p38beta (MAPK11), Calgranulin A, CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (p110-delta) | 0.5 | | 110 | 4.0005 | 0.4075 | 40 | SUX9 |
| CCL2, LIMK1, PLAT (TPA), MyHC, Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (p110-delta) | 35 | initammation_Amphoterin | 118 | 4.898E- | 2.12/E- 01 | 13 | PI3K CAT CLASS IA, MMP-13, IL1RN, |
| Calgranulin B, p38 MAPK, PAI1, PI3K cat class IA (p110-delta) | | Signaling | | 02 | 01 | | CCI 2 LIMK1 PLAT (TPA) MUHC |
| PI3K cat class IA (p110-delta) | | | | | | | Calgranulin B n38 MAPK PAI1 |
| | | | | | | | PI3K cat class IA (p110-delta) |

Appendix Table S2 - RNA sequencing reads for Mmp and Timp transcripts.

| | | | | | | | | | | | RNA | sequence i | reads | | | |
|----------------|--------|---|---|---|---|---|---|--------------|--------------|--------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| | symbol | D2_log2F oldChang e(ROCK1_ 4HT_vs_G FP_4HT) | D2_pvalu e(ROCK1_ 4HT_vs_G FP_4HT) | D2_padj(ROCK1_4 HT_vs_GF P 4HT) | D2_log2F oldChang e(ROCK2_ 4HT_vs_G FP_4HT) | D2_pvalu e(ROCK2_ 4HT_vs_G FP 4HT) | D2_padj(ROCK2_4 HT_vs_GF P 4HT) | GFP_4HT 1 | GFP_4HT 2 | GFP_4HT 3 | ROCK1_4 HT 1 | ROCK1_4 HT 2 | ROCK1_4 HT 3 | ROCK2_4 HT 1 | ROCK2_4 HT_2 | ROCK2_4 HT 3 |
| | Mmp1a | NA , | NA | NA | NA | NA | NA | - 0 | - 0 | - 0 | - 0 | - 0 | - 0 | - 0 | - 0 | - 0 |
| C | Mmp1b | NA | NA | NA | NA | NA | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Collagenases | Mmp8 | NA | NA | NA | NA | NA | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Mmp13 | 3.405297 | 2.55E-28 | 6.06E-26 | 3.70139 | 2.94E-33 | 6.37E-31 | 50 | 46 | 49 | 476 | 679 | 363 | 530 | 959 | 591 |
| Colatinação | Mmp2 | 0.003215 | 0.993782 | NA | 0.359147 | 0.397855 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Gelatinases | Mmp9 | 0.03459 | 0.967397 | NA | 1.39613 | 0.106042 | NA | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 5 | 1 |
| | Mmp3 | 2.321984 | 0.002659 | NA | 2.130918 | 0.005915 | NA | 0 | 2 | 0 | 4 | 11 | 4 | 4 | 9 | 5 |
| Stromelysins | Mmp10 | 4.456138 | 2.11E-22 | 2.95E-20 | 4.952517 | 1.52E-27 | 2.19E-25 | 3 | 6 | 2 | 75 | 146 | 69 | 123 | 227 | 108 |
| | Mmp11 | -0.06396 | 0.65525 | 0.774096 | -0.17104 | 0.232381 | 0.386352 | 542 | 541 | 649 | 386 | 494 | 653 | 408 | 592 | 544 |
| | Mmp14 | 0.19228 | 0.052914 | 0.130848 | 0.091522 | 0.356834 | 0.525506 | 3236 | 2977 | 3810 | 3214 | 3245 | 4117 | 3354 | 3633 | 3668 |
| | Mmp15 | -0.32209 | 0.001578 | 0.007868 | -0.34341 | 0.000745 | 0.003808 | 2716 | 2475 | 2811 | 1981 | 1702 | 2214 | 2211 | 1976 | 2070 |
| | Mmp16 | -0.38359 | 0.379612 | NA | -0.38704 | 0.379023 | NA | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1011-101101195 | Mmp17 | -0.23058 | 0.624187 | NA | -0.57807 | 0.227735 | 0.381344 | 11 | 10 | 19 | 6 | 14 | 11 | 7 | 12 | 7 |
| | Mmp24 | 3.831482 | 2.25E-08 | NA | 3.769133 | 3.68E-08 | 5.74E-07 | 0 | 1 | 0 | 17 | 24 | 10 | 13 | 28 | 13 |
| | Mmp25 | 0.003561 | 0.993347 | NA | 0.388659 | 0.377848 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Matrilysin | Mmp7 | NA | NA | NA | NA | NA | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Mmp12 | 0.003803 | 0.993036 | NA | 0.000106 | 0.999807 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Mmp19 | 0.75619 | 0.053251 | 0.131397 | 0.938257 | 0.014749 | 0.045962 | 14 | 13 | 13 | 12 | 32 | 20 | 19 | 35 | 26 |
| | Mmp20 | NA | NA | NA | NA | NA | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Others | Mmp21 | -0.37722 | 0.383874 | NA | -0.38059 | 0.383298 | NA | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Mmp23 | -1.08272 | 8.24E-05 | 0.000657 | -0.60269 | 0.021261 | 0.061806 | 62 | 64 | 80 | 38 | 13 | 37 | 36 | 55 | 44 |
| | Mmp27 | -0.74639 | 0.309149 | NA | -0.02728 | 0.971456 | NA | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 2 | 0 |
| | Mmp28 | 0.077473 | 0.489099 | 0.641417 | -0.06304 | 0.573828 | 0.718039 | 623 | 519 | 551 | 534 | 488 | 625 | 485 | 531 | 600 |
| | Timp1 | 0.753121 | 1.04E-09 | 2.54E-08 | 1.006326 | 1.37E-16 | 7.25E-15 | 247 | 220 | 252 | 318 | 429 | 370 | 476 | 506 | 464 |
| Inhibitors | Timp2 | -0.11704 | 0.017681 | 0.05635 | -0.10203 | 0.038417 | 0.099637 | 13329 | 12456 | 13380 | 10343 | 10826 | 12100 | 11168 | 12965 | 12334 |
| minutors | Timp3 | 0.736928 | 3.72E-13 | 1.66E-11 | 0.646805 | 1.78E-10 | 4.18E-09 | 1345 | 1118 | 1004 | 1719 | 1672 | 1939 | 1538 | 1984 | 1921 |
| | Timp4 | -2.79873 | 7.79E-05 | NA | -2.03629 | 0.001699 | NA | 10 | 9 | 13 | 0 | 1 | 1 | 2 | 4 | 0 |

Appendix Table S3 - RNA sequencing reads for collagen transcripts.

| | | | | | | | | | | RNA | sequence i | reads | | | |
|----------|----------|----------|----------------|----------------|----------|----------|---------|---------|---------|---------|------------|---------|---------|---------|---------|
| | | | | | | | | | | | | | | | |
| | D2 log2F | | | D2 log2F | | | | | | | | | | | |
| | oldChang | D2 pvalu | D2 padi(| oldChang | D2 pvalu | D2 padi(| | | | | | | | | |
| | e(ROCK1 | e(ROCK1 | ROCK1 4 | e(ROCK2 | e(ROCK2 | ROCK2 4 | | | | | | | | | |
| | AHT_vs_G | 4HT_vs_G | HT_vs_GF | 4HT_vs_G | 4HT_vs_G | HT_vs_GF | GFP_4HT | GFP_4HT | GFP_4HT | ROCK1_4 | ROCK1_4 | ROCK1_4 | ROCK2_4 | ROCK2_4 | ROCK2_4 |
| symbol | FP_4HT) | FP_4HT) | P_4HT) | FP_4HT) | FP_4HT) | P_4HT) | _1 | _2 | _3 | HT_1 | HT_2 | нт_з | HT_1 | HT_2 | нт_з |
| Col1a1 | 0.312066 | 0.15701 | 0.291354 | 0.465923 | 0.030863 | 0.083734 | - 53 | - 45 | - 45 | - 51 | - 55 | - 58 | - 70 | - 68 | - 60 |
| Col1a2 | 0.018414 | 0.979364 | NA | 1.512879 | 0.04886 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 1 |
| Col2a1 | 0.415513 | 0.630897 | NA | -0.01121 | 0.989603 | NA | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 |
| Col3a1 | 0.415347 | 0.482824 | NA | 0.406062 | 0.495073 | NA | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| Col4a1 | 0.478588 | 2.31E-13 | 1.06E-11 | 0.45232 | 4.20E-12 | 1.25E-10 | 8556 | 8992 | 8357 | 10570 | 10714 | 11991 | 10231 | 12914 | 12375 |
| Col4a2 | 0.663892 | 3.44E-23 | 5.02E-21 | 0.667922 | 1.66E-23 | 1.70E-21 | 3380 | 3562 | 3392 | 4756 | 4852 | 5492 | 4765 | 5881 | 5800 |
| Col4a3 | -0.15392 | 0.809322 | NA | 0.082687 | 0.894652 | NA | 5 | 7 | 4 | 4 | 4 | 5 | 7 | 5 | 5 |
| Col4a3bp | 0.147223 | 0.10393 | 0.217937 | 0.076039 | 0.40079 | 0.567474 | 3131 | 2736 | 2886 | 2834 | 2767 | 3336 | 2480 | 3322 | 3443 |
| Col4a4 | -0.18678 | 0.82894 | NA | -0.85667 | 0.317038 | NA | 0 | 3 | 1 | 0 | 1 | 2 | 0 | 1 | 0 |
| Col4a5 | -0.08187 | 0.509388 | 0.658514 | -0.30197 | 0.015111 | 0.04692 | 1202 | 1154 | 1228 | 866 | 1003 | 1259 | 726 | 1088 | 1103 |
| Col4a6 | 0.335089 | 0.701462 | NA | 0.004966 | 0.995471 | NA | 1 | 1 | 0 | 1 | 0 | 2 | 0 | 0 | 2 |
| Col5a1 | 0.222949 | 0.132179 | 0.257836 | 0.067658 | 0.647867 | 0.776333 | 995 | 1094 | 1228 | 1035 | 1083 | 1467 | 892 | 1173 | 1417 |
| Col5a2 | 0.005609 | 0.990904 | NA | 0.00014 | 0.999775 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Col5a3 | -1.12081 | 0.117833 | NA | -0.48486 | 0.476544 | NA | 5 | 7 | 3 | 0 | 2 | 3 | 3 | 4 | 3 |
| Col6a1 | 0.568581 | 2.02E-08 | 3.97E-07 | 0.609569 | 1.66E-09 | 3.36E-08 | 1113 | 1027 | 1270 | 1324 | 1546 | 1803 | 1553 | 1875 | 1784 |
| Col6a2 | 0.921556 | 5.28E-10 | 1.35E-08 | 1.055604 | 7.92E-13 | 2.63E-11 | 206 | 176 | 236 | 348 | 300 | 438 | 395 | 441 | 453 |
| Col6a3 | 1.340891 | 0.098938 | NA | 1.415439 | 0.080235 | NA | 0 | 0 | 3 | 4 | 5 | 2 | 1 | 6 | 6 |
| Col6a4 | NA | NA | NA | NA | NA | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Col6a5 | NA | NA | NA | NA | NA | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Col6a6 | 0.421594 | 0.351879 | NA | 0.000109 | 0.999804 | NA | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Col7a1 | 0.829486 | 0.004379 | 0.018278 | 0.682067 | 0.019145 | 0.056802 | 336 | 223 | 384 | 562 | 430 | 577 | 447 | 415 | 659 |
| Col8a1 | 0.968036 | 0.000102 | 0.000786 | 0.936309 | 0.000159 | 0.001017 | 39 | 38 | 30 | 65 | 70 | 60 | 59 | 63 | 85 |
| Col8a2 | -0.36364 | 0.675884 | NA | -0.41646 | 0.631878 | NA | 2 | 1 | 2 | 2 | 1 | 0 | 2 | 0 | 1 |
| Col9a1 | NA | NA | NA | NA | NA | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Col9a2 | 0.672602 | 0.384395 | NA | -0.4569 | 0.537239 | NA | 0 | 0 | 1 | 0 | 2 | 1 | 0 | 0 | 0 |
| Col9a3 | 0.200064 | 0.74867 | NA | 0.50452 | 0.406033 | NA | 4 | 3 | 5 | 3 | 6 | 4 | 6 | 6 | 6 |
| Col10a1 | 0.745259 | 0.270492 | NA | 0.413016 | 0.537771 | NA | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 |
| Col11a1 | 1.132016 | 0.071311 | NA | 1.424773 | 0.020579 | NA | 2 | 3 | 3 | 5 | 7 | 7 | 6 | 12 | 8 |
| Col11a2 | -0.27371 | 0.408348 | 0.569186 | -0.46562 | 0.162588 | 0.297879 | 25 | 27 | 26 | 22 | 16 | 21 | 17 | 25 | 14 |
| Col12a1 | -0.05517 | 0.850216 | 0.907857 | -0.0724 | 0.803088 | 0.881337 | 49 | 48 | 37 | 35 | 34 | 50 | 22 | 47 | 59 |
| Col13a1 | 0.003215 | 0.993782 | NA | 0.359147 | 0.397855 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Col14a1 | -0.12439 | 0.878328 | NA | -0.20902 | 0.79673 | NA | 1 | 2 | 2 | 1 | 2 | 1 | 0 | 1 | 3 |
| Col15a1 | 1.297059 | 0.000283 | 0.001857 | 1.521421 | 1.61E-05 | 0.000138 | 28 | 5 | 16 | 40 | 43 | 32 | 39 | 60 | 49 |
| Col16a1 | 1.38897 | 7.29E-07 | 1.03E-05 | 1.620727 | 4.94E-09 | 9.22E-08 | 21 | 38 | 30 | 5/ | /9 | 85 | 50 | 120 | 109 |
| | -0.09078 | 0.91304 | NA 0.026226 | -0.51593 | 0.01427 | | 11740 | 11 / 01 | 12154 | 11205 | 11440 | 12627 | 12204 | 14244 | 12000 |
| Col18a1 | U.100285 | 0.010108 | 0.030330 | 0.152742 NA | 0.01427 | 0.044695 | 11749 | 11481 | 12154 | 11385 | 11448 | 13037 | 12204 | 14244 | 12890 |
| Col20a1 | -0 22052 | 0 2718/1 | 0 / 2 1 8 1 8 | -0 65015 | 0.002715 | 0.011386 | 65 | 66 | 62 | 54 | 17 | 50 | 38 | 12 | 12 |
| Col22a1 | NA | NA | NA | NA | NA | NA | 05 | 0 | 02 | 0 | 47 0 | 0 | 0 | -72 | -72 |
| Col23a1 | 0.034988 | 0.967894 | NA | 0.005451 | 0.995001 | NA | 1 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 2 |
| Col24a1 | 0.67632 | 0.219197 | NA | 0.68377 | 0.210801 | 0.360879 | 3 | 7 | 6 | 11 | 7 | 7 | 12 | 5 | 10 |
| Col25a1 | 0.003215 | 0.993782 | NA | 0.359147 | 0.397855 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Col26a1 | 0.947476 | 0.277441 | NA | 0.876831 | 0.314868 | NA | 1 | 0 | 0 | 1 | 2 | 1 | 2 | 2 | 0 |
| Col27a1 | -0.05436 | 0.570746 | 0.707291 | -0.08741 | 0.36151 | 0.530112 | 2974 | 2630 | 2634 | 2654 | 2109 | 2534 | 2561 | 2517 | 2635 |
| Col28a1 | -0.78436 | 0.260309 | NA | -0.3594 | 0.617 | NA | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 |

Appendix Table S4 - Clinical information data provided by US Biomax for Pancreas cancer tissue array (PA961c).

| catalognum | position | sex | age | organ | pathology | grade | stage | tnm | type |
|------------|----------|-----|-----|----------|-----------------------------------|-------|-------|---------|-----------|
| PA961c | A1 | F | 67 | Pancreas | Duct adenocarcinoma | 1 | | T3N1bM0 | Malignant |
| PA961c | A2 | F | 48 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | A3 | F | 47 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | A4 | Μ | 59 | Pancreas | Duct adenocarcinoma | 1 | IIB | T2N1M0 | Malignant |
| PA961c | A5 | F | 44 | Pancreas | Adenocarcinoma (sparse) | - | IIB | T3N1M0 | Malignant |
| PA961c | A6 | М | 34 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | A7 | М | 49 | Pancreas | Duct adenocarcinoma | 1 | IB | T2N0M0 | Malignant |
| PA961c | A8 | М | 56 | Pancreas | Duct adenocarcinoma | 1 | IB | T2N0M0 | Malignant |
| PA961c | A9 | М | 49 | Pancreas | Duct adenocarcinoma | 1 | IB | T2N0M0 | Malignant |
| PA961c | A10 | М | 67 | Pancreas | Duct adenocarcinoma | 1 | IB | T2N0M0 | Malignant |
| PA961c | A11 | М | 48 | Pancreas | Duct adenocarcinoma | 1 | IB | T2N0M0 | Malignant |
| PA961c | A12 | F | 56 | Pancreas | Duct adenocarcinoma | - | IB | T2N0M0 | Malignant |
| PA961c | B1 | F | 58 | Pancreas | Duct adenocarcinoma | 1 | IIB | T2N1M0 | Malignant |
| PA961c | B2 | М | 52 | Pancreas | Duct adenocarcinoma | 1 | IIB | T3N1M0 | Malignant |
| PA961c | B3 | F | 51 | Pancreas | Duct adenocarcinoma | - | IIA | T3N0M0 | Malignant |
| PA961c | B4 | М | 55 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | B5 | F | 62 | Pancreas | Duct adenocarcinoma with necrosis | 2 | | T4N0M0 | Malignant |
| PA961c | B6 | М | 56 | Pancreas | Duct adenocarcinoma | 2 | IB | T2N0M0 | Malignant |
| PA961c | B7 | М | 60 | Pancreas | Duct adenocarcinoma | 2 | IA | T2N0M0 | Malignant |
| PA961c | B8 | М | 52 | Pancreas | Duct adenocarcinoma | - | IIA | T3N0M0 | Malignant |
| PA961c | В9 | М | 42 | Pancreas | Hyperplasia of duct epithelium | - | IB | T2N0M0 | Malignant |
| PA961c | B10 | М | 54 | Pancreas | Duct adenocarcinoma | - | IIA | T3N0M0 | Malignant |
| PA961c | B11 | F | 51 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | B12 | F | 54 | Pancreas | Duct adenocarcinoma | 2 | IB | T2N0M0 | Malignant |
| PA961c | C1 | М | 54 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | C2 | Μ | 39 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | C3 | F | 41 | Pancreas | Duct adenocarcinoma | - | IIA | T3N0M0 | Malignant |
| PA961c | C4 | F | 68 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | C5 | F | 44 | Pancreas | Duct adenocarcinoma | 2 | IIB | T3N1M0 | Malignant |
| PA961c | C6 | М | 42 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | C7 | М | 53 | Pancreas | Duct adenocarcinoma | 2 | IB | T2N0M0 | Malignant |
| PA961c | C8 | М | 51 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |

| PA961c | C9 | М | 48 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
|--------|-----|---|----|----------|---|---|-----|---------|-----------|
| PA961c | C10 | М | 57 | Pancreas | Duct adenocarcinoma | - | IIA | T3N0M0 | Malignant |
| PA961c | C11 | F | 64 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | C12 | М | 49 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | D1 | М | 72 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | D2 | F | 72 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | D3 | М | 59 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | D4 | F | 45 | Pancreas | Duct adenocarcinoma | 2 | III | T3N2M0 | Malignant |
| PA961c | D5 | F | 60 | Pancreas | Duct adenocarcinoma | 2 | IV | T2N1M1 | Malignant |
| PA961c | D6 | М | 52 | Pancreas | Chronic inflammation of pancreas tissue | - | IA | T1N0M0 | Malignant |
| PA961c | D7 | F | 44 | Pancreas | Duct adenocarcinoma with necrosis | 2 | IB | T2N0M0 | Malignant |
| PA961c | D8 | F | 46 | Pancreas | Duct adenocarcinoma | 2 | IB | T2N0M0 | Malignant |
| PA961c | D9 | М | 52 | Pancreas | Duct adenocarcinoma | 2 | IB | T2N0M0 | Malignant |
| PA961c | D10 | М | 52 | Pancreas | Duct adenocarcinoma | 2 | IB | T2N0M0 | Malignant |
| PA961c | D11 | F | 53 | Pancreas | Duct adenocarcinoma | 2 | IIB | T2N1M0 | Malignant |
| PA961c | D12 | М | 40 | Pancreas | Duct adenocarcinoma | 1 | IIB | T3N1bM0 | Malignant |
| PA961c | E1 | М | 57 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | E2 | М | 31 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | E3 | М | 44 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | E4 | М | 61 | Pancreas | Adenocarcinoma | 3 | IV | T3N0M1 | Malignant |
| PA961c | E5 | М | 51 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | E6 | М | 59 | Pancreas | Duct adenocarcinoma | 2 | IA | T1N0M0 | Malignant |
| PA961c | E7 | М | 44 | Pancreas | Adenocarcinoma | 3 | IIA | T3N0M0 | Malignant |
| PA961c | E8 | М | 45 | Pancreas | Adenocarcinoma | 3 | IIB | T2N1M0 | Malignant |
| PA961c | E9 | М | 41 | Pancreas | Duct adenocarcinoma | 2 | IB | T2N0M0 | Malignant |
| PA961c | E10 | F | 72 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | E11 | F | 51 | Pancreas | Duct adenocarcinoma | - | IIA | T3N0M0 | Malignant |
| PA961c | E12 | F | 42 | Pancreas | Duct adenocarcinoma | 2 | IB | T2N0M0 | Malignant |
| PA961c | F1 | F | 39 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | F2 | F | 51 | Pancreas | Duct adenocarcinoma with necrosis | 2 | IIA | T3N0M0 | Malignant |
| PA961c | F3 | М | 62 | Pancreas | Duct adenocarcinoma | 1 | IIA | T3N0M0 | Malignant |
| PA961c | F4 | Μ | 60 | Pancreas | Duct adenocarcinoma | 2 | IB | T2N0M0 | Malignant |
| PA961c | F5 | F | 53 | Pancreas | Duct adenocarcinoma | 2 | IIA | T3N0M0 | Malignant |

| PA961c | F6 | Μ | 77 | Pancreas | Duct adenocarcinoma | 2 | IA | T1N0M0 | Malignant |
|--------|-----|---|----|----------|--|---|-----|---------|-----------|
| PA961c | F7 | М | 47 | Pancreas | Adenocarcinoma | 3 | IIA | T3N0M0 | Malignant |
| PA961c | F8 | М | 67 | Pancreas | Adenocarcinoma | 3 | IIA | T3N0M0 | Malignant |
| PA961c | F9 | М | 78 | Pancreas | Adenocarcinoma | 3 | IB | T2N0M0 | Malignant |
| PA961c | F10 | М | 62 | Pancreas | Adenocarcinoma | 3 | IIA | T3N0M0 | Malignant |
| PA961c | F11 | М | 50 | Pancreas | Adenocarcinoma | 3 | IB | T2N0M0 | Malignant |
| PA961c | F12 | М | 55 | Pancreas | Adenocarcinoma | 3 | IIB | T3N1M0 | Malignant |
| PA961c | G1 | F | 48 | Pancreas | Adenocarcinoma | 3 | IIA | T3N0M0 | Malignant |
| PA961c | G2 | М | 50 | Pancreas | Adenocarcinoma | 3 | IIB | T3N1M0 | Malignant |
| PA961c | G3 | F | 53 | Pancreas | Adenocarcinoma with necrosis | 3 | IB | T2N0M0 | Malignant |
| PA961c | G4 | М | 50 | Pancreas | Adenocarcinoma | 3 | IB | T2N0M0 | Malignant |
| PA961c | G5 | F | 23 | Pancreas | Adenocarcinoma | 3 | IB | T2N0M0 | Malignant |
| PA961c | G6 | М | 56 | Pancreas | Adenocarcinoma | - | IIB | T2N1bM0 | Malignant |
| PA961c | G7 | F | 56 | Pancreas | Undifferentiated carcinoma | • | IIA | T3N0M0 | Malignant |
| PA961c | G8 | F | 54 | Pancreas | Mixed acinar-neuroendocrine carcinoma | - | IB | T2N0M0 | Malignant |
| PA961c | G9 | М | 52 | Pancreas | Adenosquamous carcinoma | - | IIA | T3N0M0 | Malignant |
| PA961c | G10 | F | 49 | Pancreas | Adenosquamous carcinoma | - | IIB | T3N1M0 | Malignant |
| PA961c | G11 | М | 50 | Pancreas | Adenosquamous carcinoma | • | IIA | T3N0M0 | Malignant |
| PA961c | G12 | М | 62 | Pancreas | Squamous cell carcinoma | 2 | IIA | T3N0M0 | Malignant |
| PA961c | H1 | F | 52 | Pancreas | Carcinoid | - | IIA | T3N0M0 | Malignant |
| PA961c | H2 | F | 50 | Pancreas | Carcinoid | - | IIA | T3N0M0 | Malignant |
| PA961c | H3 | М | 51 | Pancreas | Atypical carcinoid | • | III | T4N0M0 | Malignant |
| PA961c | H4 | М | 42 | Pancreas | Neuroendocrine carcinoma | • | IIA | T3N0M0 | Malignant |
| PA961c | H5 | М | 53 | Pancreas | Acinic cell carcinoma | - | IB | T2N0M0 | Malignant |
| PA961c | H6 | F | 33 | Pancreas | Solid pseudo-papillary carcinoma (chronic inflammation of pancreas tissue) | - | IIA | T3N0M0 | Malignant |
| PA961c | H7 | Μ | 42 | Pancreas | Solid pseudo-papillary carcinoma | - | IB | T2N0M0 | Malignant |
| PA961c | H8 | F | 21 | Pancreas | Pancreatic tissue | - | - | - | Normal |
| PA961c | H9 | М | 47 | Pancreas | Pancreatic tissue | - | - | - | Normal |
| PA961c | H10 | М | 38 | Pancreas | Pancreatic tissue | - | - | - | Normal |
| PA961c | H11 | М | 40 | Pancreas | Pancreatic tissue | - | - | - | Normal |
| PA961c | H12 | F | 38 | Pancreas | Pancreatic tissue | - | - | - | Normal |

Appendix References

Pinho AV, Rooman I, Reichert M, De Medts N, Bouwens L, Rustgi AK, Real FX (2011) Adult pancreatic acinar cells dedifferentiate to an embryonic progenitor phenotype with concomitant activation of a senescence programme that is present in chronic pancreatitis. *Gut* **60**: 958-966