**Supplemental Table S12.** Pathway analysis of DE genes for cells in subpopulation three

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Reactome Pathway | Total genes in pathway | Genes in geneset | P-value | FDR | HitGenes |
| SubPop 3 vs. 1 (top 10 most enriched) | Signaling by TGF-beta Receptor Complex | 73 | 11 | 0.000 | 0.16 | *TGFBR1, FURIN, PMEPA1, RNF111, F11R, NCOR2, CCNK, PARD3, SKIL, PRKCZ, USP9X* |
| Chromatin modifying enzymes | 190 | 18 | 0.001 | 0.28 | *EPC1, IKBKAP, CCND1, USP22, WHSC1, KMT2A, KMT2B, CHD4, MRGBP, SMYD2, NCOR2, RBBP4, MBD3, TRRAP, MSL2, MSL1, HCFC1, ATXN7L3* |
| TGF-beta receptor signaling in EMT (epithelial to mesenchymal transition) | 16 | 4 | 0.004 | 0.39 | *TGFBR1, F11R, PARD3, PRKCZ* |
| Signaling by NODAL | 19 | 4 | 0.007 | 0.39 | *NODAL, FURIN, LEFTY1, ACVR2B* |
| Regulation of signaling by NODAL | 10 | 3 | 0.008 | 0.39 | *NODAL, LEFTY1, ACVR2B* |
| SubPop 3 vs. 2 | Chromatin modifying enzymes | 190 | 17 | 0.001 | 0.04 | *EPC1, TAF12, USP22, KDM2A, EP400, WHSC1, KDM5B, KMT2A, MRGBP, TBL1X, SAP30L, NCOR2, MBD3, SETDB1, HCFC1, DR1, SETD2* |
| Signaling by NODAL | 19 | 5 | 0.001 | 0.04 | *NODAL, FOXH1, LEFTY1, SMAD4, ACVR2B* |
| Pre-NOTCH Processing in the Endoplasmic Reticulum | 6 | 3 | 0.001 | 0.04 | *NOTCH3, NOTCH2, NOTCH1* |
| Signaling by Activin | 13 | 4 | 0.001 | 0.04 | *FOXH1, FST, SMAD4, ACVR2B* |
| Regulation of signaling by NODAL | 10 | 3 | 0.006 | 0.09 | *NODAL, LEFTY1, ACVR2B* |
| Notch-HLH transcription pathway | 11 | 3 | 0.008 | 0.10 | *NOTCH3, NOTCH2, NOTCH1* |
| PI-3K cascade:FGFR1; FGFR2; FGFR3;FGFR4; ERBB2 | 95 | 9 | 0.008 | 0.10 | *ERBB3, GSK3A, AGO1, FGF19, PDGFA, FGFR1, FGFR4, MTOR, CHUK* |
| PI3K Cascade | 79 | 8 | 0.008 | 0.10 | *STK11, FGF19, FGFR1, FGFR4, RRAGD, EIF4B, MTOR, AKT2* |
| Transcriptional regulation of pluripotent stem cells | 35 | 5 | 0.009 | 0.10 | *FOXD3, SMAD4, POLR2B, SALL4, NR6A1* |
| POU5F1 (OCT4), SOX2, NANOG activate genes related to proliferation | 13 | 3 | 0.012 | 0.11 | *FOXD3, SALL4, NR6A1* |
| Signaling by EGFR | 296 | 16 | 0.071 | 0.28 | *CUL3, ERBB3, GSK3A, LRIG1, JAK1, ADCY2, PXN, AGO1, FGF19, PDGFA, FGFR1, FGFR4, PAQR3, MTOR, CHUK, SPTAN1* |
|  | Signaling by VEGF; FGFR3; FGFR4 | 274 | 15 | 0.073 | 0.29 | *CUL3, JUP, ERBB3, MAPKAPK2, JAK1, PXN, NRP2, FGF19, PDGFA, FGFR1, FGFR4, PAQR3, MTOR, CRK, SPTAN1* |
| SubPop 3 vs. 4 | Signaling by NGF | 390 | 91 | 0.000 | 0.00 | *not listed herea* |
| Signaling by EGFR | 296 | 69 | 0.000 | 0.00 | *not listed here* |
| Signaling by PDGF | 302 | 70 | 0.000 | 0.00 | *not listed here* |
| Chromatin modifying enzymes | 190 | 46 | 0.000 | 0.00 | *not listed here* |
| GAB1 signalosome | 99 | 29 | 0.000 | 0.00 | *not listed here* |
| Signaling by ERBB2 | 278 | 60 | 0.000 | 0.00 | *not listed here* |
| Signaling by FGFR1;FGFR2;FGFR3;FGFR4 | 275 | 59 | 0.000 | 0.00 | *not listed here* |
| PI-3K cascade: FGFR1;FGFR2;FGFR3;FGFR4 | 95 | 27 | 0.000 | 0.00 | *THEM4, GSK3A, PHLPP1, PDPK1, FYN, PDGFA, FOXO1, FOXO3, FGFR2, FGFR4, TRIB3, RICTOR, TSC2, LCK, PDGFRA, MOV10, AGO1, AGO2, AGO3, FGF19, AKT1, FGF8, MTOR, CHUK, ERBB3, ERBB2, IRS2* |

aGene lists contain too many genes to be displayed in this table.