**Supplementary Table 4 – Canonical signalling pathways associated with UM**

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| --- | --- | --- | --- | --- |
| **Ingenuity Canonical Signalling Pathways** | **-log(p-value)** | **Ratio** | **z-score** | **Molecules** |
| EIF2 signalling | 2.07E01 | 2.09E-01 | -3.317 | EIF2S1,RPS10,RPL13A,EIF3B,RPS5,EIF3I,RPS20,RPL12,RPS19,RPL5,RPL28,RPS15A,RPS11,RPL3,RPS8,EIF4A1,RPS3A,  RPL30,RPS25,RPL26L1,RPL11,RPS18,RPS7,RPS2,RPS14,RPS3,RPSA,RPS16,EIF2S3,RPL24,RPS9,RPS28,RPS4X,RPS27A,RPL27,RPL10A |
| Regulation of eIF4 and p70S6K signalling | 1.46E01 | 1.9E-01 | NaN | EIF2S1,RPS10,ITGA3,EIF3B,RPS5,EIF3I,RPS20,RPS19,ITGB1,RPS15A,RPS11,RPS8,EIF4A1,RPS3A,RPS25,RPS18,RPS7,  RPS2,RPS14,RPS3,RPSA,RPS16,EIF2S3,RPS9,RPS28,RPS4X,RPS27A |
| Hepatic Fibrosis/Hepatic Stellate Cell activation | 1.27E01 | 1.55E-01 | NaN | IGFBP4,MMP2,COL6A1,CTGF,COL1A1,MYH9,A2M,COL12A1,FN1,MET,COL4A1,LAMA1,COL6A3,COL3A1,COL1A2,IGFBP5,  MYH10,COL6A2,COL18A1,TIMP2,MYL6,COL5A2,COL11A1,COL4A2,TIMP1,SERPINE1,ICAM1,MMP1 |
| Actin cytoskeleton signalling | 1.11E01 | 1.33E-01 | 0.192 | IQGAP1,ACTR2,VCL,ITGA3,ARPC1B,MYH9,FN1,CFL1,PFN1,ACTB,CYFIP1,ITGB1,ARPC4,CRK,ACTN4,TLN1,ARPC3,FLNA,  MYL12B,EZR,MSN,MYH10,ACTN1,ACTR3,CFL2,RDX,MYL6,GSN |
| mTOR signalling | 1.03E01 | 1.37E-01 | NaN | RPS10,FKBP1A,RHOC,EIF3B,RPS5,EIF3I,RPS20,RPS19,RPS15A,RPS11,RPS8,EIF4A1,RPS3A,RPS25,RPS18,RPS7,RPS2,  RPS14,RPS3,RPSA,RPS16,RPS9,RPS28,RPS4X,RPS27A |
| RhoGDI signalling | 1E01 | 1.4E-01 | 0.000 | ACTR2,ARPC3,GNB2L1,ITGA3,MYL12B,EZR,MSN,GDI2,GNB1,RHOC,ARPC1B,ACTR3,CD44,RDX,CFL2,GNB2,MYL6,GNAI2,  CFL1,ACTB,ITGB1,ARPC4,ARHGDIA,CDH1 |
| Leukocyte extravasation signalling | 9.7E00 | 1.3E-01 | -0.209 | CXCL12,VCL,MMP2,ITGA3,GNAI2,ACTB,ITGB1,CRK,ACTN4,CTTN,CTNNB1,VASP,EZR,MSN,ACTN1,EDIL3,CD44,TIMP2,RDX,  MYL6,RAP1B,TIMP1,ICAM1,MMP1,MMP14 |
| Signalling by Rho family GTPases | 9.32E00 | 1.16E-01 | -1.964 | IQGAP1,ACTR2,ITGA3,GNB1,RHOC,ARPC1B,VIM,GNAI2,CFL1,ACTB,CYFIP1,ITGB1,ARPC4,CDH1,ARPC3,GNB2L1,MYL12B,EZR,MSN,ACTR3,SEPT2,STMN1,CFL2,RDX,GNB2,MYL6,SEPT7 |
| Integrin signalling | 8.65E00 | 1.2E-01 | -1.043 | ACTR2,TLN1,ITGAV,ARPC3,VCL,CTTN,ITGA3,CAPN1,MYL12B,VASP,RHOC,ACTN1,ARPC1B,ACTR3,CAPN5,PFN1,ACTB,  GSN,ITGB1,ARPC4,RAP1B,CRK,ACTN4,CAPN2 |
| Remodeling of epithelial adherens junctions | 8.49E00 | 2.12E-01 | -1.897 | IQGAP1,ACTR2,ARPC3,VCL,CTNNB1,ACTN1,ARPC1B,ACTR3,RAB7A,ACTB,ARPC4,MET,CDH1,ACTN4 |
| Protein ubiquitination pathway | 8.49E00 | 1.06E-01 | NaN | PSMB6,HSPA2,UBA1,HSPD1,PSMB5,HSPE1,PSMB1,PSMA7,HSPA8,PSMA2,STUB1,PSMB2,PSMA1,HSP90AA1,TCEB2,  USP14,CRYAB,UCHL1,HSP90B1,PSMA6,HSPB1,HSPA4,HSPA9,HSPA5,HSPH1,HSP90AB1,NEDD4L |
| Epithelial adherens junction signalling | 8.47E00 | 1.4E-01 | NaN | IQGAP1,ACTR2,ARPC3,VCL,CTNNB1,JUP,PVRL2,MYH10,ACTN1,ARPC1B,ACTR3,MYH9,MYL6,ACTB,ARPC4,RAP1B,MET,  CRK,CDH1,ACTN4 |
| Regulation of actin-based motility by Rho | 7.75E00 | 1.72E-01 | -1.387 | ACTR2,ARPC3,ITGA3,MYL12B,RHOC,ARPC1B,ACTR3,MYL6,CFL1,PFN1,ACTB,GSN,ITGB1,ARPC4,ARHGDIA |
| RhoA signalling | 7.37E00 | 1.42E-01 | -2.000 | ACTR2,ARPC3,NRP2,MYL12B,EZR,MSN,ARPC1B,ACTR3,SEPT2,RDX,CFL2,MYL6,CFL1,SEPT7,PFN1,ACTB,ARPC4 |
| Axonal guidance signalling | 6.3E00 | 7.49E-02 | NaN | CXCL12,ACTR2,MMP2,ITGA3,NRP2,PAPPA,GNB1,PLXNC1,ADAM10,ARPC1B,GNAI2,CFL1,PFN1,ITGB1,ARPC4,SEMA3C,  MET,CRK,PRKAR2A,ARPC3,GNB2L1,MYL12B,VASP,SEMA3B,DPYSL2,ACTR3,CFL2,GNB2,MYL6,BMP1,RAP1B,PDIA3 |
| Inhibition of matrix metalloproteases | 6.1E00 | 2.37E-01 | NaN | A2M,MMP2,THBS2,HSPG2,TIMP1,ADAM10,MMP1,TIMP2,MMP14 |
| Clathrin-mediated endocytosis signalling | 5.96E00 | 1.03E-01 | NaN | ACTR2,ARPC3,CTTN,CLTC,AP2B1,ARPC1B,ACTR3,RAB7A,CLTA,ACTB,HSPA8,CLU,ITGB1,ARPC4,MET,APOE,CLTB,  RAB11B,ALB |
| Ephrin receptor signalling | 5.76E00 | 1.05E-01 | -1.732 | CXCL12,ACTR2,ARPC3,GNB2L1,ITGA3,GNB1,ADAM10,ARPC1B,ACTR3,CFL2,GNB2,GNAI2,CFL1,ITGB1,ARPC4,RAP1B,ABI1,  CRK |
| Unfolded protein response | 5.74E00 | 1.89E-01 | NaN | CALR,HSPA2,HSPA4,HSPA9,HSPA8,HSP90B1,HSPA5,HSPH1,VCP,P4HB |
| Regulation of cellular mechanics by calpain protease | 5.58E00 | 1.82E-01 | 0.447 | CAPN5,TLN1,VCL,ITGA3,ITGB1,CAPN1,EZR,ACTN1,ACTN4,CAPN2 |
| IGF-1 signalling | 5.5E00 | 1.34E-01 | NaN | IGFBP4,YWHAQ,CYR61,IGFBP2,CTGF,IGFBP5,YWHAE,NOV,IGFBP7,YWHAZ,YWHAB,IGFBP6,PRKAR2A |
| ILK Signalling | 5.44E00 | 9.94E-02 | -1.000 | FLNB,VCL,FLNA,CTNNB1,DSP,RHOC,MYH10,ACTN1,CFL2,MYH9,VIM,MYL6,FN1,CFL1,ACTB,ITGB1,CDH1,ACTN4 |
| Complement system | 5.26E00 | 2.22E-01 | 1.134 | CD59,C4A/C4B,C2,C3,CFI,C1S,C1R,CFH |
| Ephrin B signalling | 5.25E00 | 1.51E-01 | 0.000 | CXCL12,GNAI2,CFL1,GNB2L1,CTNNB1,HNRNPK,GNB1,ABI1,CAP1,CFL2,GNB2 |
| Germ Cell-Sertoli Cell junction signalling | 5.08E00 | 1.03E-01 | NaN | IQGAP1,VCL,ITGA3,CTNNB1,JUP,PVRL2,RHOC,ACTN1,CFL2,A2M,CFL1,ACTB,GSN,ITGB1,CDH1,ACTN4 |
| Agranulocyte adhesion and diapedesis | 5.04E00 | 9.71E-02 | NaN | CXCL12,MMP2,ITGA3,EZR,MSN,MYH10,RDX,MYH9,MYL6,GLG1,GNAI2,FN1,ACTB,ITGB1,ICAM1,MMP1,MMP14 |

NaN = No activity pattern available, p value determined by Fisher’s exact test