|  |  |  |
| --- | --- | --- |
| **Medication** | **HbA1c < 7.0%** | **HbA1c ≥ 7.0%** |
| Metformin | 6/8 | 7/8 |
| Sulfonylurea | 1/8 | 2/8 |
| Dipeptidyl peptidase-4 (DPP-4) inhibitor  | 2/8 | 4/8 |
| Glucagon-like peptide-1 (GLP-1) agonist | 0/8 | 3/8 |
| Long acting insulin | 0/8 | 1/8 |
| Short acting insulin | 1/8 | 3/8 |

Supplemental Table 1. List of diabetic medications.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Canonical Pathway** | **-log (p-value)** | **Ratio** | **z-score** | **molecules** |
| Antigen Presentation Pathway | 8.93 | 0.368 |  | PSMB9, CALR, HLA-A, HLA-B, PSMB8, CD74, HLA-DQB1, TAP1, HLA-G, HLA-DRB4, HLA-C, HLA-F, HLA-DPB1, HLA-DPA1 |
| Huntington's Disease Signaling | 5.2 | 0.12 | 2.324 | GNA11, GNB1, CTSD, ARFIP2, POLR2C, IGF1, SP1, HDAC11, MAPK3, CREB1, CASP1, PIK3R2, GOSR1, NAPA, FRS2, PRKD3, CAPN10, EGFR, HDAC9, AKT2, PIK3C2A, FGFR1, TAF9B, DNAJC5, CLTA, CLTCL1, DCTN1, STX16, NCOR2 |
| Protein Ubiquitination Pathway | 4.73 | 0.114 |  | PSMA7, USP5, HLA-A, USP53, HLA-B, PSMB8, DNAJB2, TAP1, USP48, PAN2, SACS, HSP90B1, UBE2B, STUB1, USP42, PSMB9, USP15, UBE2R2, DNAJC1, MDM2, HSPD1, XIAP, DNAJC5, USP32, HLA-C, ANAPC5, USP34, UBE2E1, VHL |
| Telomerase Signaling | 4.61 | 0.153 | 2.887 | HDAC9, AKT2, PIK3C2A, PPP2R2A, FGFR1, ELF1, TERF2, HSP90B1, MAP2K2, SP1, MAPK3, HDAC11, PIK3R2, PPP2R1B, TERF1, FRS2, EGFR |
| mTOR Signaling | 4.43 | 0.121 | 2.138 | RPS6KB1, RPS19, ULK1, AKT2, PIK3C2A, PPP2R2A, FGFR1, RPS10, RPS7, EIF3B, RHOT1, RPS26, MAPK3, EIF4A1, RPS27L, RHOU, EIF3A, PRKAA1, RPS27A, VEGFD, PIK3R2, PPP2R1B, FRS2, PRKD3 |
| p70S6K Signaling | 4.2 | 0.137 | 3 | RPS6KB1, AKT2, PIK3C2A, YWHAE, YWHAB, PPP2R2A, FGFR1, PLCL2, MAP2K2, MAPK3, MAPT, EEF2K, PIK3R2, PPP2R1B, PRKD3, FRS2, AGTR1, EGFR |
| Neuroprotective Role of THOP1 in Alzheimer's Disease | 4 | 0.225 |  | HLA-G, YWHAE, HLA-C, HLA-A, MAPT, HLA-B, CREB1, PRKAR2A, HLA-F |
| AMPK Signaling | 3.88 | 0.116 | 2.668 | PBRM1, RPS6KB1, ULK1, AKT2, ARID1A, ACACB, GNAS, CPT1A, PIK3C2A, PPP2R2A, FGFR1, PRKAR2A, SMARCA4, CRTC2, CREB1, PRKAA1, SMARCC2, PIK3R2, EEF2K, MLYCD, PPP2R1B, FRS2 |
| Ovarian Cancer Signaling | 3.67 | 0.125 |  | RPS6KB1, TCF4, AKT2, PA2G4 ,PIK3C2A, FGFR1, DVL1, PRKAR2A, PTEN, MAP2K2, MAPK3, MSH6, VEGFD, PIK3R2, FRS2, TCF7L2, EGFR, WNT5A |
| Regulation of eIF4 and p70S6K Signaling | 3.65 | 0.121 | 2.53 | RPS6KB1, RPS19, AKT2, PIK3C2A, PPP2R2A, FGFR1, RPS10, RPS7, MAP2K2, EIF3B, RPS26, MAPK3, EIF4A1, RPS27L, EIF3A, RPS27A, PIK3R2, PPP2R1B, FRS2 |

Supplemental Table 2. Top 10 canonical pathways associated with HbA1c from the NCBI GEO dataset GSE18732 (21). Z-score was calculated where possible.