

S3 Table. Top 10 Canonical Pathways Used by the Target Genes of the Smoking Cessation Persistent miRNAs

Ingenuity canonical pathways¹	p value²	Ratio³ (%)	Target genes of the smoking cessation persistent miRNAs in the given pathway⁴
Wnt/ β -catenin signaling	10^{-9}	24	TCF4,SFRP2,TGFBR1,WNT10B,CSNK1G1,PPP2CA,PPP2R2A,TGFBR3,MARK2,LRP6,SOX12,BCL9,CCND1,TCF7,CSNK1E,RARA,RARB,TGFB2,WNT4,GSK3B,CSNK2B,SOX5,SOX4,AXIN2,APPL2,CSNK1G3,PPP2R5D,WNT2B,CREBBP,ACVR1B,PPP2R5A,FZD8,PPP2CB,CDH2,FZD4,WNT3A,SOX6,PPP2R4,BTRC,DVL3,PPP2R5E
Cardiac β -adrenergic signaling	10^{-8}	21	AKAP12,PPP1CC,PDE7A,PPP2R2A,PPP2CA,PDE3A,PDE12,PPP1CB,ATP2A2,AKAP11,GNB1,GNB4,ADRB1,ADCY5,ADCY9,CACNA1D,PDE10A,ADRBK2,PPP2R5D,ADCY6,AKAP6,PPP1R11,GNG3,PPP2R5A,PDE8A,PPP2CB,AKAP2/PALM2,AKAP2,PRKAR2B,PPP2R4,PRKACA,PDE8B,PPP2R5E,AKAP9
Protein kinase A signaling	10^{-7}	16	TGFBR1,MAPK1,NFATC3,PDE12,PDE3A,CREB5,TCF7,GNB1,GNB4,PTPRO,ADCY5,DUSP7,GSK3B,ADCY9,YWHAG,YWHAZ,PDE10A,PTCH1,CREBBP,YWHAZ,PPP1R11,PLCL2,GNG3,PTPN3,PTP4A1,PTPRM,PDE8A,PTPN11,PRKACA,PTPRA,CAMK2G,AKAP12,PPP1CC,TCF4,PDE7A,PPP1CB,AKAP11,DUSP5,NFAT5,CREB1,TGFB2,PRKCE,PRKCA,PXN,PTPRK,MAP3K1,ADCY6,PLCG1,AKAP6,NFATC1,GNAI2,GNAI3,CALM1,AKAP2/PALM2- AKAP2,PTPRU,PRKAR2B,FLNC,CDC14B,PDE8B,SFN,ELK1,EYA1,AKAP9,PTPRT,DUSP16
IGF-1 signaling	10^{-7}	25	SOCS3,CTGF,MAPK1,PIK3R1,SOCS6,PDPK1,PIK3CG,IGF1R,CSNK2B,RPS6KB1,PXN,NRAS,YWHAG,PIK3C2A,YWHAZ,GRB2,YWHAZ,SOCS4,PRKAR2B,PTPN11,IRS1,PRKACA,ELK1,SOCS7,SFN,SOCS5
ERK5 signaling	10^{-7}	31	RPS6KB1,YWHAG,NRAS,YWHAZ,SGK1,CREBBP,RPS6KA3,YWHAZ,CREB5,RPS6KA6,GAB1,PTPN11,MEF2D,CREB1,MEF2C,SFN,MAP3K3,ELK4,MAP3K2,EGFR
Axonal guidance signaling	10^{-6}	15	WNT10B,MAPK1,ITSN1,NFATC3,PIK3R1,UNC5B,ARPC5,SEMA6B,SEMA4F,BRCC3,GNB1,GNB4,SUFU,PIK3CG,WNT4,PLXNB2,SRGAP2,GSK3B,EPHA7,KALRN,CRKL,SEMA5A,PTCH1,GNG3,PLCL2,SRGAP3,PTPN11,PRKACA,GNAL,NRP1,ADAM17,RGS3,ARPC1B,SEMA6A,CRK,PLXNA2,ROBO1,EIF4E,EFNB2,NFAT5,MYSM1,PLXNA1,SDC2,EFNB1,MKNK1,PRKCE,PFN2,RASSF5,SHANK2,PRKCA,TUBB1,EPHB4,PXN,NRAS,PLXNC1,ARHGEF12,NRP2,PIK3C2A,GRB2,WNT2B,PLCG1,NFATC1,GNAI2,GNAI3,SEMA3A,FZD8,PRKAR2B,FZD4,WNT3A

S3 Table. Top 10 Canonical Pathways Enriched in the Target Genes of the Smoking Cessation Persistent miRNAs (cont., page 2)

Ingenuity canonical pathways¹	p value²	Ratio³ (%)	Target genes of the smoking cessation persistent miRNAs in the given pathway⁴
ERK/MAPK signaling	10 ⁻⁶	18	PPP1CC,MAPK1,PPP2R2A,PPP2CA,PIK3R1,ETS2,PPP1CB,CRK,CREB5,EIF4E,ELF3,PIK3CG,MKNK1,CREB1,PRKCE,PRKCA,ETS1,PXN,YWHAG,NRAS,PIK3C2A,GRB2,PPP2R5D,CRKL,CREBBP,YWHAZ,PLCG1,NFATC1,PPP1R11,PPP2R5A,PPP2CB,ELF2,PRKAR2B,ARAF,PPP2R4,PRKACA,PPP2R5E,ELK1
Insulin receptor signaling	10 ⁻⁶	21	SOCS3,PPP1CC,MAPK1,SGK1,PIK3R1,PDPK1,PPP1CB,CRK,STXBP4,EIF4E,PIK3CG,GSK3B,SCNN1B,RPS6KB1,NRAS,PIK3C2A,GRB2,CRKL,PPP1R11,VAMP2,PRKAR2B,RHOQ,CBL,PTPN11,SYNJ1,GAB1,IRS1,ASIC1,PRKACA,INSR
B cell receptor signaling	10 ⁻⁶	19	MAP2K4,GAB2,MAPK1,NFATC3,POU2F2,PIK3R1,PDPK1,CREB5,NFAT5,PIK3CG,CREB1,GSK3B,MAP3K2,ETS1,RPS6KB1,NRAS,PIK3C2A,GRB2,MAP3K13,CREBBP,MAP3K1,NFATC1,BCL2L1,CALM1 (includes others),PTPN11,SYNJ1,GAB1,VAV3,PAG1,PIK3AP1,ELK1,MAP3K3,CAMK2G

¹ The pathway analysis was performed in Ingenuity pathway analysis software. The target genes of the 12 smoking cessation persistent miRNAs were used. See methods for detail. The pathways were ranked by p value.

² Fisher's exact test.

³ Number of target genes in a given pathway divided by total number of genes that make up that pathway.

⁴ Only target genes of the smoking cessation persistent miRNAs in a given pathway were shown.