Supplemental Table Legends

Supplemental Table 1. TGFβ treatment decreased SMAD3 mRNA level across gene expression studies. Data from the GEO database was used to determine the generality of the effect of TGFβ on SMAD gene expression. The vast majority of the studies found substantial repression of SMAD3 but not SMAD2 mRNA by TGFβ.

Supplemental Table 2. Antipsychotics alter SMAD3 responsive genes in Mudge et al. dataset. p-values were calculated by the Nextbio algorithm for the significance of the association between the Experimental/Random Gene list (columns) and the Biogroup gene lists (rows).

Supplemental Table 3. Antipsychotics alter SMAD3 responsive genes in Narayan et al. dataset. p-values were calculated by the Nextbio algorithm for the significance of the association between the Experimental/Random Gene list (columns) and the Biogroup gene lists (rows).

Supplemental Table 4. Analysis of genes with SMAD binding sites in their promoters showing altered expression in the brains of patients with schizophrenia.

Supplemental Figure Legends

Supplemental Figure 1. Dose-response analysis of antipsychotic-induced activation of the insulin promoter in T6PNE cells. (A) SAR of antipsychotic effects on the endogenous insulin promoter; values listed are from Figure 1A. (**B)** Dose-response analysis of antipsychotic-induced activation of the insulin promoter in T6PNE cells. Ziprasidone was autoflourescent and therefore not included. All antipsychotics were cytotoxic at 40uM. Fluphenazine, perphenazine, and trifluoperazine were cytotoxic at 20uM (n=12), error bars are SEM.

Supplemental Figure 2. Neurotransmitter receptors and Activin-like kinase receptor family members are expressed in T6PNE and human islets. (A-B) Microarray analysis using Illumina BeadArrays was performed on T6PNE cells and primary human islets (GSE18821)[4]. The y-axis represents the level of hybridization to the oligonucleotide on the array. **(A)** Neurotransmitter receptors acted on by antipsychotics were expressed at comparable levels in the T6PNE and primary human islets. **(B)** TGFβ receptor family members were expressed at comparable levels in the T6PNE and primary human islets, with ALK4/5/7, targets of SB-505124, expressed at detectable levels in both.

Supplemental Figure 3 SB-505124 is a dose-responsive inhibitor of the T6PNE Insulin Promoter Asssay. SB-505124 shows dose responsive inhibition in the 48

hour T6PNE Ins-GFP Assay. (n=12). Error bars are SEM, * indicates $p<0.05$ relative to DMSO control.

Supplemental Figure 4. SB-505124 and TGFb Family Members show dose-responsive inhibition in the T6PNE Insulin Promoter Asssay. (A-C) TGFβ1 (A), TGFβ2 (B), and Activin A (C) all showed dose responsive inhibition in the 48 hour T6PNE Ins-GFP Assay. (n=12). Error bars are SEM, * indicates $p<0.05$ relative to DMSO control.

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PMID/GEO Reference Series	Title	Description	Species	SMAD3 Fold Change	SMAD2 Fold Change
unpublished/GSE6676	TGFβ overexpression effect on the cornea	TGFb expressed under Strong lens-specific promoter (Transgenic vs. Control)	Mouse	**-1.40**	**1.38**
19615063/GSE6653	TGFβ effect on immortalized ovarian surface epithelial cell line	IOSE cells (TGFb1 12hr vs untreated)	Human	**-2.43**	**-1.00**
15477587/GSE1805	TGFβ effect on acute myelogenous leukemia cells	M091 Cells (200 pM TGFb 4hr vs untreated)	Human	**-1.30**	**-1.14**
15477587/GSE1802	TGFβ effect on CD34+ hematopoietic stem cells	CB-CD34 CD34+ hematopoietic stem cells (200 pM TGFb 4hr vs untreated)	Human	**-1.52**	**1.04**
16078232/GSE2705	GFAP-negative lamina cribrosa cell response to TGFβ	GFAP-negative lamina cribrosa glial cell (10 ng/ml TGF-beta1 24 hours vs untreated)	Human	**-2.07**	**1.08**
20197308/GSE20247	Proinsulin C-peptide and TGFβ effect on proximal tubular cell line: time course	HK2 cells (TGFb 48hr vs untreated)	Human	**-1.49**	**-1.12**
20007254/GSE17708	TGFβ-induced epithelial-mesenchymal transition model	A549 Cells (TGFb 72hr vs. untreated)	Human	**-1.51**	**1.08**
17178593/GSE2558	TGFβ effect on renal mesangial cells	MES-13 Cells (100ng/ml TGFb 24hr vs untreated)	Mouse	**-1.23**	**-1.09**
15571627/GSE1724	Idiopathic and scleroderma-associated pulmonary fibrosis derived fibroblasts response-TGFβ	Adult Lung Fibroblasts, Normal Tissue (4ng/ml 4hr vs untreated)	Human	**-1.93**	**-1.23**
19701206 /GSE17518	mRNA expression profile in IMR-90 cells in response to TGFβ	IMR90 fetal lung mesenchymal cells (2ng/ml TGF-beta1 48hr vs untreated)	Human	**-6.82**	**-1.05**
Unpublished/GSE23952	Expression data from TGFβ treated Panc-1 pancreatic adenocarcinoma cell line	Panc-1 cells (serum-starved, 24 h, 5 ng/mL TGFbeta1 48hr vs untreated)	Human	**-1.98**	**-1.42**

Supplemental Table 1. TGFb treatment decreased SMAD3 mRNA level across gene expression studies.

	Genes Altered in AP Treated Patients (1291 genes)	Random Gene Lists (1291 genes)	Genes Altered in Patients Taking APs Most Potent in T6PNE (819 genes)	Random Gene Lists (819 genes)
Golgi Apparatus	0.00037	0.19	0.11	0.25
Post-Golgi Vesicle-Mediated Transport	0.0089	0.38	0.03	0.79
Gene Promoters with SMAD1 Binding Sites	0.11	0.16	0.18	0.28
Gene Promoters with SMAD3 Binding Sites	0.054	0.28	0.0096	0.14

Supplemental Table 2. Antipsychotics alter SMAD3 responsive genes in Mudge et al. dataset.

	Genes Altered in AP Treated Patients (Narayan et al., 415 genes)	Random Gene Lists (415 genes)	Genes Altered in Patients Taking APs Most Potent in T6PNE (Narayan et al., 732 genes)	Random Gene Lists (732 genes)
Gene Promoters with SMAD1 Binding Sites	0.18	0.12	0.16	0.23
Gene Promoters with SMAD3 Binding Sites	0.071	0.26	0.043	0.30

Supplemental Table 3. Antipsychotics alter SMAD3 responsive genes in Narayan et al. dataset.

Supplemental Table 4. Analysis of genes with SMAD sites in the brains of patients with schizophrenia.

Genes with SMAD binding sites (from Xie et al.[46])

SMAD1	SMAD3
ACTR1A	ABHD15
ADCY8	ACTN2
AGPAT4	ACVR1
ANKRD35	ADAMTSL2
ANP32E	AGER
ARAP3	AGPAT4
ARHGDIB	ALDH4A1
ARHGEF19	ANKMY2
ARID1A	ANKS1B
ARID5A	ANKS6
ATP2B4	ANXA9
ATP6V1E2	APBB2
AUP1	ARHGEF19
BCL2	ARID1A
BCOR	ASAP1
BMF	ASB2
BMP4	ATP6V1E2
BZRAP1	ATXN7L1
C10orf140	B3GALT2
C11orf45	BAMBI
C12orf11	BAZ2A
C16orf47	BCL9L
C17orf91	BHLHE41
C1QTNF5	BMPR2
C5orf38	BTBD3
C7orf51	BZW2
CACNB2	C11orf53
CACNG2	C11orf87
CACNG6	C16orf53
CADPS	C17orf61
CALD1	C1orf61
CBX5	C1QB
CCNI	C1QTNF5
CD68	C20orf117
CDC45L	C2orf66
CEP57	CABP2
CHD6	CACNB2
CHRM1	CACNB3
CHRNB2	CBFA2T3
CKS1B	CCDC140
CNIH2	CCDC33
CNOT4	CDK5
CPNE1	CDK5R2
CREM	CDKN1A
CRIM1	CEACAM19
CRK	CGRRF1
CSNK1E	CHD2
CTDSPL2	CHDH
DACH2	CHRM1
DCHS1	CHST9
DDOST	CLDN16
DDX17	CLTC
DIO3	CNTFR
DMXL1	COL11A2
DNAJC11	CPNE6
DQX1	CRABP2
DUSP2	CRAT
DUSP5	CSDA
DYNC1I1	CSF3
EIF4E	CXCR7
EIF4G2	CYTSB
ELAVL2	DARC

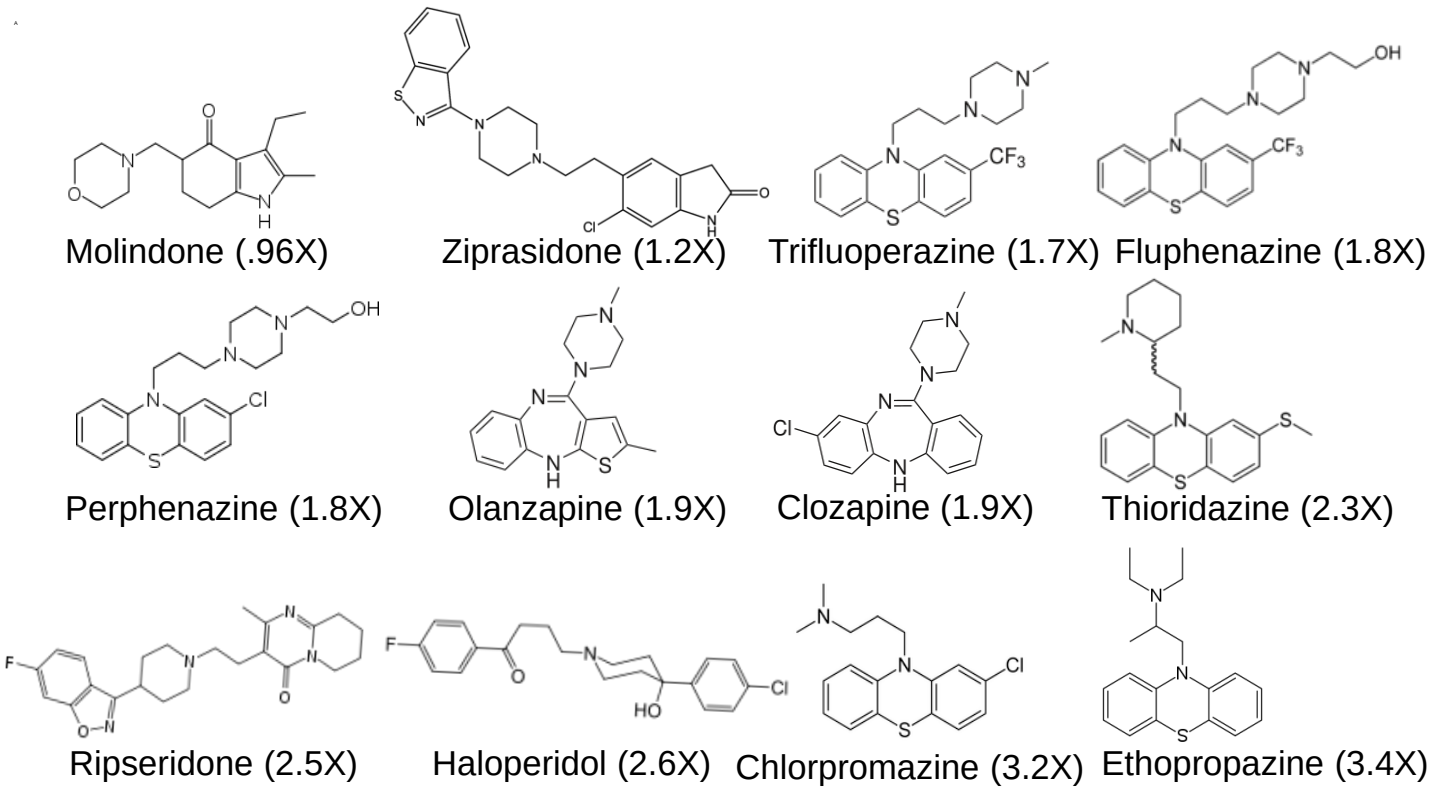
Genes with SMAD3 Binding Sites that were revealed by the NextBio analysis to be differentially expressed in the brains of schizophrenic patients compared with controls

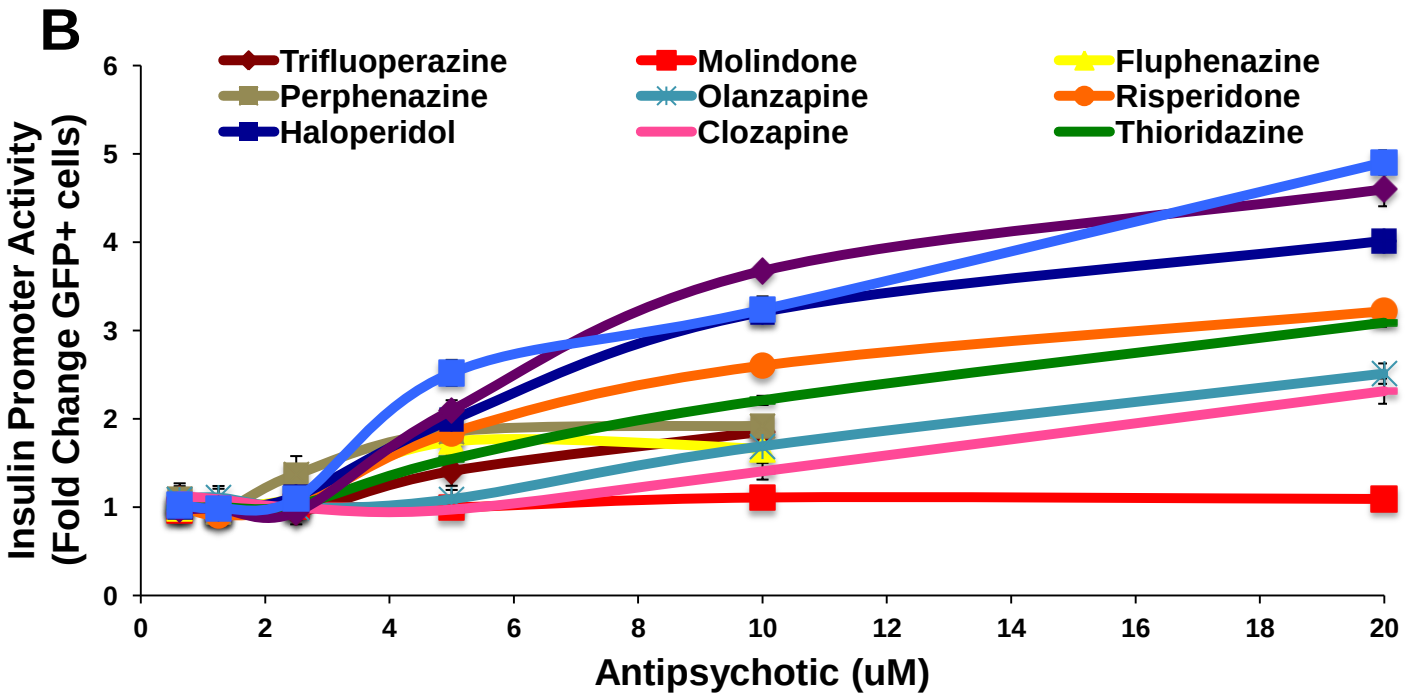
Subject 1 Chlopromazine	Subject 2 Clozapine	Subject 3 Clozapine	Subject 4 Fluphenazine	Subject 5 Haloperidol	Subject 6 Haloperidol	Subject 7 Olanzapine	Subject 8 Olanzapine	Subject 9 Olanzapine	Subject 10 Olanzapine	Subject 11 Perphanzine	Subject 12 Perphanazine	Subject 13 Risperidone	Subject 14 Thioridazine
ACVR1	ABHD15	C2orf66	CCDC140	ACVR1	BTBD3	C2orf66	C2orf66	B3GALT2	CCDC33	C1QB	C11orf53	ASB2	ADAMTSL2
ANKS1B	C11orf53	CHRM1	CHRM1	ASB2	CCDC140	CXCR7	CABP2	C11orf53	DLX3	CCDC33	CDKN1A	C11orf53	ASAP1
ANXA9	CCDC140	CSF3	HCRT	ATXN7L1	CLDN16	FAP	EYA4	CCDC140	FAP	DLX3	CHST9	C2orf66	ATXN7L1
APBB2	CHRM1	EYA4	HES7	C1orf61	EPHX4	HES7	FGF23	CCDC33	HES7	EYA4	CSF3	CCDC140	C11orf53
ASAP1	DLX3	FOXB1	HMCN1	C1QTNF5	FAP	HOXB1	LHX6	CHRM1	HOXC6	FAP	EDN1	CLDN16	CRABP2
BCL9L	EYA4	HOXC4	HOXC6	C2orf66	FGF23	KIRREL	LTBP1	DLX3	LCOR	HES7	FAP	EMID1	CXCR7
BTBD3	FAP	PITX3	IRX5	CCDC140	FGF7	MN1	OTX2	EPHX4	LHX6	HOXB1	HOXB1	FAP	EIF3J
C11orf87	HOXC4	PRLHR	NKX2-1	CCDC33	FGF7	NKX2-1	PRLHR	EYA1	MN1	NKX2-1	HOXC4	HCRT	EPHX4
C1QB	LCOR	WNT8B	OTX2	CHST9	HOXC6	OTX2	S100A14	GPC3	NKX2-1	OTX2	KIRREL	IRX5	EYA1
C2orf66	NKX2-1		PFKFB1	CLDN16	ITIH3	POU4F1		HES7	OLIG3	PRLHR	LCOR	LRP2	HS3ST2
CDKN1A	NYX		PITX3	CXCR7	NKX2-1	SMTN		LCOR	PAX3		LOX	MN1	ITIH3
CHDH	POU3F4		POU4F1	EPHX4	OTX2	ST6GALNAC5		LHX6	PFKFB1		NKX2-1	PAX3	JMJD1C
CHRM1	PURA		PTPN7	EYA1	PDE4D	TGFB2		NKX2-1	PURA		OTX2	PITX3	KIRREL
CSF3	R3HDML		R3HDML	EYA4	PITX3			OTX2	R3HDML		PAK3	POU3F4	LCOR
DOCK9	TFAP2D		SLC6A9	FAP	PRLHR			PAK3	S100A14		PLCXD2	RFX4	LHX6
ERG	TIMP4			FGF23	PTPN7			PRLHR	SMTN		POU4F1	SLC6A9	NKX2-1
EYA1	TLX1			FGF7	RFX5			PURA	TIMP4		PRLHR	SMTN	OLIG3
FAP	WNT10B			GRRP1	ST6GALNAC5			R3HDML			PURA	TEAD3	PAK3
FGF23	WNT8B			HOXC4	TNRC4			WNT10B			R3HDML	TGFB2	PFKFB1
FRY				HOXC6	WNT10B							TIMP4	PURA
FZD1				HS3ST2	WNT8B							WNT10B	R3HDML
GABRE				IRX5	ZNF654							ZNF654	ST6GALNAC5
GRIN2D				JMJD1C									SYNPO
GRRP1				LCOR									WNT8B
H1F0				MN1									ZNF654
HMCN1				OLIG3									
HOXB1				OTX2									
HOXC6				PAK3									
KCNJ8				PURA									
KIRREL				R3HDML									
KLF7				SMTN									
LRP2				TEAD3									
MN1				TFDP2									
MYCL1				TIMP4									
NKX2-1				WNT10B									
NR2F2				ZNF654									
NRXN3													
OTX2													
PITX3													
POU4F1													
PRLHR													
PURA													
RASL11B													
RFX5													
RIMS1													
RLIM													
SERINC2													
SHANK1													
SYNPO													
SYT7													
TIMP4													
TMEM164													
WNT8B													
WNT10B													
ZNF654													

ELK3	DCTN2
ELN	DLX3
EN1	DMPK
ENTPD1	DOCK9
EVX1	DUSP3
FAM5B	EDA
FAM70A	EDN1
FAM76B	EIF3J
FBXW7	ELOVL1
FGFR1OP2	EMID1
FHL3	EPB41
FLJ39739	EPHX4
GABRB1	ERG
GARNL3	ESRRG
GATA1	EYA1
GDNF	EYA4
GLRA1	FAP
GPR3	FGF11
GPRC5D	FGF14
GRHL3	FGF23
GRIN2D	FGF7
GTF2A1	FOXB1
H3F3B	FOXP1
HCLS1	FRY
HNRNPA1	FXR1
HNRNPUL1	FZD1
HOXB1	GABRE
HOXC13	GADD45G
HPCA	GIT1
HPX	GPC3
HTRA2	GRIN2D
IGF2BP3	GRRP1
IGFBP5	H1F0
IL1RAPL1	HAPLN2
IRX2	HCRT
JAKMIP2	HES7
JMJD1C	HEXIM1
JUB	HMCN1
KCNA1	HMGB1
KCNC1	HOXB1
KCNH2	HOXC4
KCNN4	HOXC6
KCNQ5	HS3ST2
KIAA0182	IL17RB
KIAA0913	IRX5
KIAA1967	ITGAE
KLK14	ITIH3
LAG3	JARID2
LAMA3	JMJD1C
LAMB3	JUB
LCOR	KCNJ8
LEFTY1	KCTD15
LEFTY2	KDM3A
LHX6	KIAA1191
LIN28	KIAA1468
LRRTM3	KIRREL
LTBP1	KLF7
MAGED2	LAMC2
MBNL1	LCOR
MEX3B	LHX6
MEX3C	LIMD2
MLL5	LIN28
MRPS18B	LOX
MYBPC2	LRP2
MYH6	LRRC48
MYL6B	LTBP1

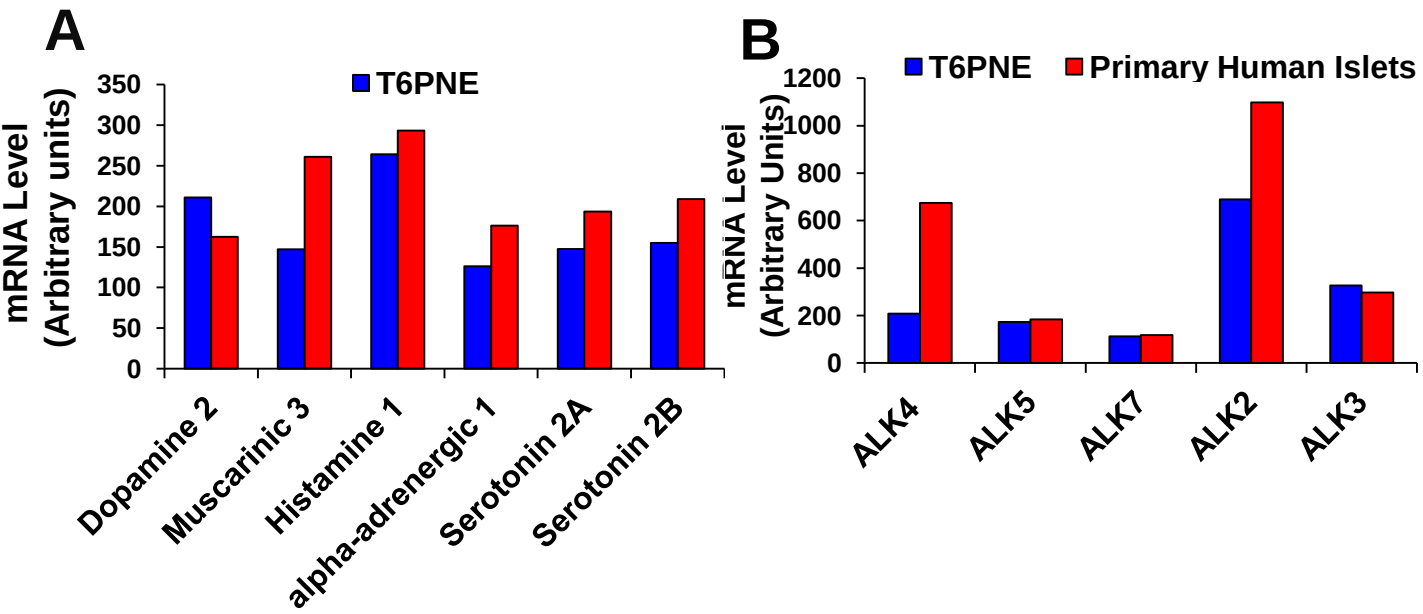
NCDN	LUC7L3
NCKAP5	MAP2
NDUFS4	MAP7D1
NEUROD1	MARCKSL1
NFE2	MEIS1
NOTCH3	MFAP4
NRGN	MN1
NRP1	MORF4L2
NSD1	MRC2
NXPH4	MTMR4
ONECUT2	MYCL1
OTX2	MYT1
PAFAH2	NAT8L
PDGFB	NDUFS2
PHC1	NIN
PHF12	NKX2-1
PHF17	NLGN2
PI4KB	NNAT
PIAS3	NOS3
PIK3CG	NR2F2
PIK3R1	NRXN3
PIM1	NTRK3
PLA2G2F	NXPH4
PMEPA1	NYX
POLD4	OLIG3
POLG	OTX2
PPP1R10	PABPC5
PPP1R15B	PAK3
PRMT1	PAX2
PRMT3	PAX3
PRX	PDE4D
PSD	PDLIM2
PSD4	PELI3
PSMB1	PFKFB1
PSMB2	PHF15
PTCH1	PIK3R3
PTGFRN	PITX3
RAB5C	PLCXD2
RARA	PLEKHA6
RASAL1	PLEKHH2
RBM12	POU3F4
RBMS1	POU4F1
RDH10	PPP3CB
RGL2	PRLHR
RHCE	PTPN6
RHD	PTPN7
RHOG	PURA
RIMS1	PVRL1
RNF144B	R3HDML
RNF152	RAI1
ROCK1	RARB
RORA	RASL11B
RPL7	RFX4
RPP21	RFX5
RPRD2	RIMS1
RPS14	RLIM
RRM1	RNF19B
RTCD1	RUFY3
RUNX2	RUSC1
S1PR1	S100A14
SEMA4A	S100A16
SERPINB5	SAV1
SERTAD3	SCRG1
SGCD	SERINC2
SH3KBP1	SHANK1
SHC1	SIAH3

SIPA1
SKAP1
SLAIN1
SLC25A4
SLC26A9
SLC4A2
SLC8A3
SMARCA1
SMG1
SMYD2
SNPH
SNX12
SOX21
SP3
SPOP
SPTAN1
SRRM1
ST18
STMN1
STX5
SUFU
SYT11
SYVN1
TAGLN
TARBP2
TBP
TEAD1
TENC1
THADA
TIAF1
TINAGL1
TPR
TSHZ1
TSSK3
TWIST1
UBE2Q1
UBE4B
UBXN10
UFD1L
VEGFA
WBP2NL
WDR81
WT1
XPO4
YBX2
ZEB2
ZFP91
ZNF324B
ZNF362
ZNF366
ZNF462
ZNF532
ZNF827
ZSCAN20
SIPA1
SKIL
SKP1
SLC4A2
SLC6A9
SMAD6
SMG5
SMPX
SMTN
SNIP
SOX14
SSBP3
ST5
ST6GALNAC5
STX16
SYNPO
SYT7
TAF6L
TEAD3
TFAP2D
TFDP2
TGFB2
TGIF2
THBS2
TIMP4
TLX1
TMEM164
TMEM79
TNRC4
TOP1
TRAIP
TSHZ3
TXNDC12
WNT10B
WNT8B
ZADH2
ZDHHC22
ZEB2
ZHX2
ZMYND17
ZMYND8
ZNF654
ZRANB1

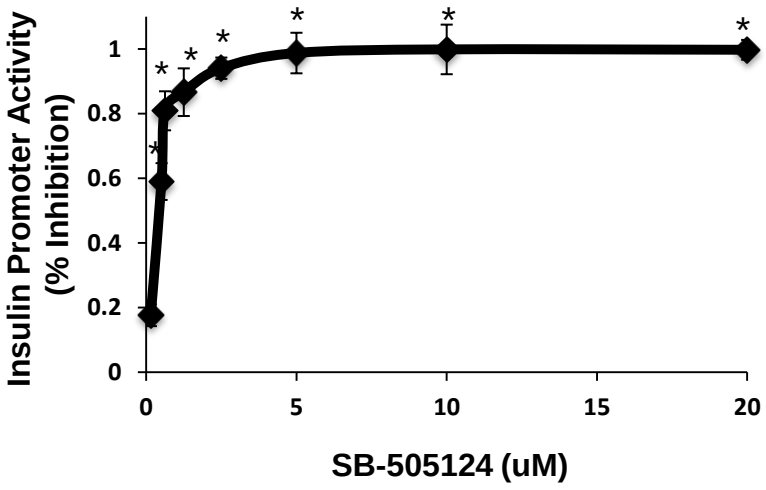




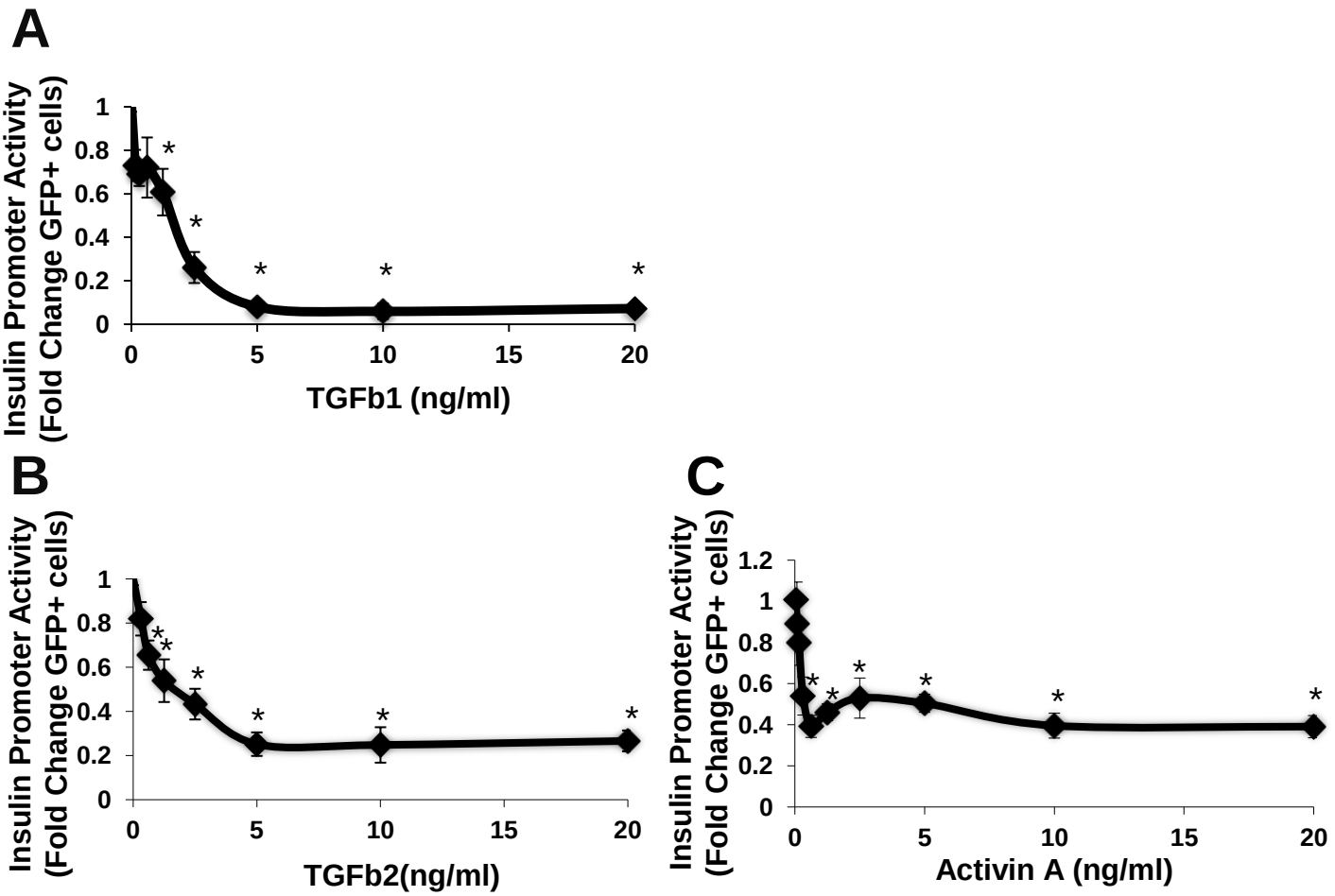
Supplemental Figure 1. Dose-response analysis of antipsychotic-induced activation of the insulin promoter in T6PNE cells.



Supplemental Figure 2. Neurotransmitter receptors and Activin-like kinase receptor family members are expressed in T6PNE and human islets.



Supplemental Figure 3. SB-505124 is a dose-responsive inhibitor of the T6PNE Insulin Promoter Asssay



Supplemental Figure 4. TGFb Family Members show dose-responsive inhibition in the T6PNE Insulin Promoter Asssay.