

Suppl. Table 1

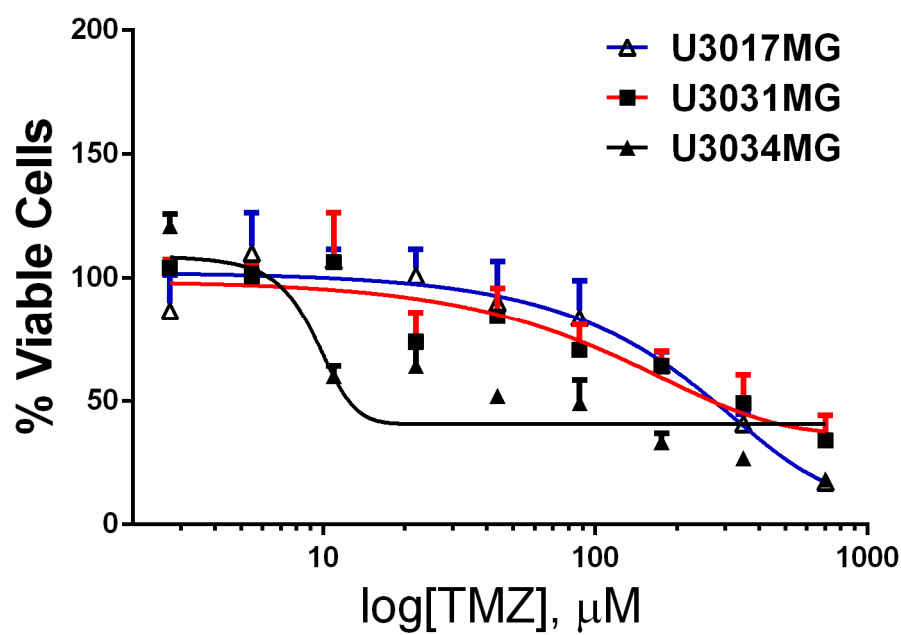
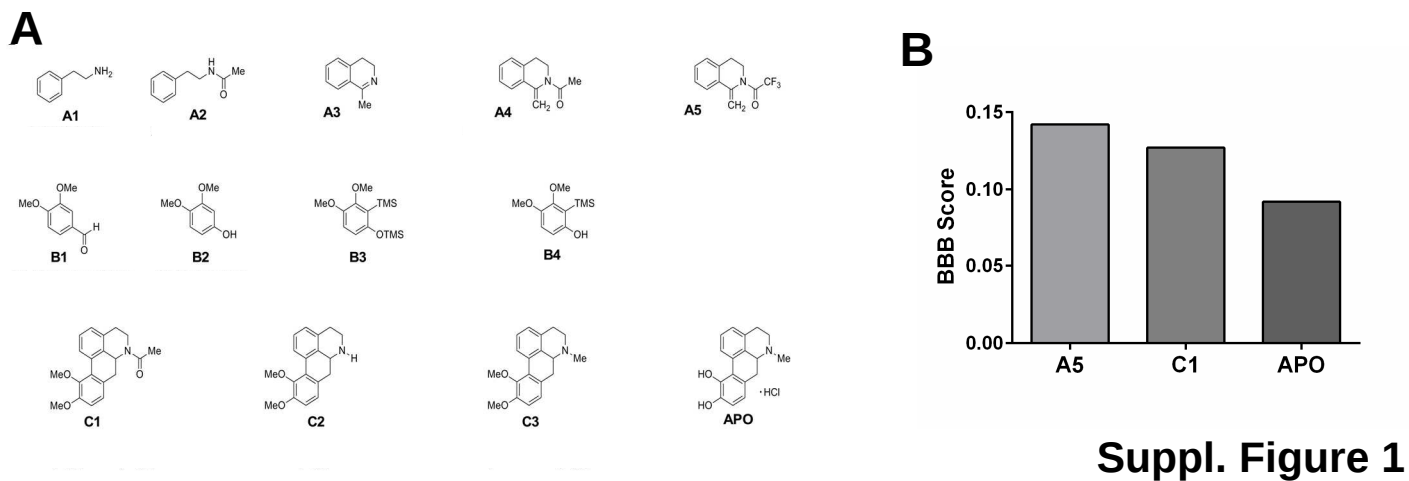
Term Description	FDR q-value	Matching Proteins
A5		
Adenylate cyclase-inhibiting g protein-coupled acetylcholine receptor signaling pathway	4.28E-08	CHRM3,CHRM1,CHRM5,CHRM2,CHRM4
Acetylcholine receptor signaling pathway	4.28E-08	CHRM3,CHRM1,CHRM5,CHRM2,CHRNA7,CHRM4
Cellular response to oxygen-containing compound	4.28E-08	PPP5C,APEX1,CHRM3,MAPK3,PRKCI,CHRM1,CDK19,HRH2,CHRM5,CHRM2,ESR1,CHRNA7,CHRM4,NR4A1
Cellular response to dopamine	4.28E-08	CHRM3,MAPK3,CHRM1,HRH2,CHRM5,CHRM2,CHRM4
Cellular response to stimulus	6.59E-08	PPP5C,APEX1,PARP2,CHRM3,CYP2C9,MAPK6,MAPK3,CAMK4,PRKCI,CHRM1,OXSRI,CYP2B6,CDK19,ZAK,HRH2,CHRM5,TSSK1B,CIT,MAP2K7,CHRM2,ESR1,CHRNA7,CHRM4,NR4A1
Cellular response to nitrogen compound	1.54E-07	APEX1,CHRM3,MAPK3,PRKCI,CHRM1,HRH2,CHRM5,CHRM2,CHRNA7,CHRM4,NR4A1
Response to stimulus	2.12E-07	PPP5C,APEX1,PARP2,CHRM3,CYP2C9,MAPK6,MAPK3,CAMK4,PRKCI,CHRM1,OXSRI,CYP2B6,CDK19,ZAK,HRH2,CHRM5,TSSK1B,CIT,MAP2K7,CHRM2,ESR1,CHRNA7,CHRM4,NR4A1,ABCB1
Cellular response to organic cyclic compound	5.21E-07	APEX1,CHRM3,MAPK3,CHRM1,HRH2,CHRM5,CHRM2,ESR1,CHRM4,NR4A1
Response to organonitrogen compound	6.78E-07	PPP5C,APEX1,CHRM3,MAPK3,PRKCI,CHRM1,HRH2,CHRM5,CHRM2,CHRNA7,CHRM4,NR4A1
Cellular response to organonitrogen compound	1.11E-06	APEX1,CHRM3,MAPK3,PRKCI,CHRM1,HRH2,CHRM5,CHRM2,CHRM4,NR4A1
Cellular response to chemical stimulus	2.10E-06	PPP5C,APEX1,CHRM3,CYP2C9,MAPK3,PRKCI,CHRM1,OXSRI,CYP2B6,CDK19,HRH2,CHRM5,CHRM2,ESR1,CHRNA7,CHRM4,NR4A1
Response to organic cyclic compound	3.87E-06	PPP5C,APEX1,CHRM3,MAPK3,CHRM1,HRH2,CHRM5,CHRM2,ESR1,CHRM4,NR4A1
Protein phosphorylation	5.65E-06	PPP5C,MAPK6,MAPK3,CAMK4,PRKCI,OXSRI,CDK19,ZAK,TSSK1B,CIT,MAP2K7
Signal transduction	7.28E-06	PPP5C,PARP2,CHRM3,MAPK6,MAPK3,CAMK4,PRKCI,CHRM1,OXSRI,ZAK,HRH2,CHRM5,TSSK1B,CIT,MAP2K7,CHRM2,ESR1,CHRNA7,CHRM4,NR4A1
Response to chemical	9.39E-06	PPP5C,APEX1,CHRM3,CYP2C9,MAPK3,PRKCI,CHRM1,OXSRI,CYP2B6,CDK19,HRH2,CHRM5,MAP2K7,CHRM2,ESR1,CHRNA7,CHRM4,NR4A1,ABCB1
C1		
G protein-coupled receptor signaling pathway, coupled to cyclic nucleotide second messenger	1.16E-10	HTR2B,ADRA2A,HTR5A,MTNR1A,DRD5,ADRA1B,HRH2,ADRA1D,ADRA2C,ADRA2B
Vascular process in circulatory system	3.00E-10	HTR2B,ADRA2A,DRD5,ADRA1B,HRH2,ADRA1D,ADRA2C,ABCB1,ADRA2B
Adenylate cyclase-activating adrenergic receptor signaling pathway	4.05E-10	ADRA2A,DRD5,ADRA1B,ADRA1D,ADRA2C,ADRA2B
Regulation of blood vessel diameter	1.20E-09	HTR2B,ADRA2A,DRD5,ADRA1B,HRH2,ADRA1D,ADRA2C,ADRA2B
Cyclic-nucleotide-mediated signaling	4.61E-09	HTR2B,ADRA2A,HTR5A,DRD5,ADRA1B,ADRA1D,ADRA2C,ADRA2B
Adenylate cyclase-modulating g protein-coupled receptor signaling pathway	2.64E-08	ADRA2A,HTR5A,MTNR1A,DRD5,ADRA1B,ADRA1D,ADRA2C,ADRA2B
Regulation of vasoconstriction	3.32E-08	ADRA2A,ADRA1B,HRH2,ADRA1D,ADRA2C,ADRA2B
Exogenous drug catabolic process	4.53E-08	CYP2C9,CYP2B6,CYP3A4,CYP2D6,CYP2C19
cAMP-mediated signaling	8.96E-08	ADRA2A,HTR5A,DRD5,ADRA1B,ADRA1D,ADRA2C,ADRA2B
Monoterpenoid metabolic process	1.22E-07	CYP2C9,CYP3A4,CYP2D6,CYP2C19
Response to drug	3.35E-06	HTR2B,CYP2C9,CYP2B6,CYP3A4,CYP2D6,CYP2C19,ABCB1
Cell-cell signaling	1.10E-05	HTR2B,ADRA2A,HTR5A,DRD5,ADRA1B,HRH2,ADRA1D,ADRA2C,CHRNA7,ADRA2B
Negative regulation of epinephrine secretion	1.73E-05	ADRA2A,ADRA2C,ADRA2B
Phospholipase c-activating g protein-coupled receptor signaling pathway	2.11E-05	HTR2B,ADRA2A,DRD5,ADRA1B,ADRA1D
Positive regulation of vasoconstriction	2.11E-05	ADRA1B,HRH2,ADRA1D,ADRA2C
APO		
G protein-coupled receptor signaling pathway, coupled to cyclic nucleotide second messenger	3.77E-14	DRD4,HTR2B,ADRA2A,HTR5A,HTR6,DRD5,ADRA1B,HTR1A,HTR7,HRH2,DRD1,ADRA2C,OPRM1,ADRA2B
Cellular response to dopamine	1.30E-12	DRD4,HTR2B,HTR5A,HTR6,DRD5,HTR1A,HTR7,HRH2,DRD1,OPRM1
Vascular process in circulatory system	1.77E-11	HTR2B,ADRA2A,DRD5,ADRA1B,HTR1A,HTR7,HRH2,DRD1,ADRA2C,ABCB1,ADRA2B
Regulation of blood vessel diameter	5.17E-11	HTR2B,ADRA2A,DRD5,ADRA1B,HTR1A,HTR7,HRH2,DRD1,ADRA2C,ADRA2B
Chemical synaptic transmission	2.03E-09	DRD4,HTR2B,HTR5A,HTR6,DRD5,HTR1A,HTR7,HRH2,DRD1,OPRM1,CHRNA7,PIP5K1C
Adenylate cyclase-modulating g protein-coupled receptor signaling pathway	2.72E-09	DRD4,ADRA2A,HTR5A,DRD5,ADRA1B,HTR1A,DRD1,ADRA2C,OPRM1,ADRA2B
Adenylate cyclase-activating adrenergic receptor signaling pathway	3.24E-09	ADRA2A,DRD5,ADRA1B,DRD1,ADRA2C,ADRA2B
Cell-cell signaling	4.44E-09	DRD4,HTR2B,ADRA2A,HTR5A,HTR6,DRD5,ADRA1B,HTR1A,HTR7,HRH2,DRD1,ADRA2C,OPRM1,CHRNA7,PIP5K1C,ADRA2B
Cellular response to chemical stimulus	7.80E-09	DRD4,APEX1,HTR2B,CYP2C9,SIGMAR1,ADRA2A,HTR5A,HTR6,DRD5,OXSRI,HTR1A,CYP2B6,CYP3A4,HTR7,PTPN22,CYP2D6,CYP2C19,HRH2,DRD1,OPRM1,CHRNA7,PIP5K1C
Cyclic-nucleotide-mediated signaling	8.67E-09	HTR2B,ADRA2A,HTR5A,DRD5,ADRA1B,DRD1,ADRA2C,OPRM1,ADRA2B
Cellular response to nitrogen compound	8.67E-09	DRD4,APEX1,HTR2B,HTR5A,HTR6,DRD5,HTR1A,HTR7,PTPN22,HRH2,DRD1,OPRM1,CHRNA7
G protein-coupled receptor signaling pathway	1.40E-08	DRD4,HTR2B,SIGMAR1,ADRA2A,HTR5A,HTR6,DRD5,ADRA1B,HTR1A,GRK1,HTR7,HRH2,DRD1,ADRA2C,OPRM1,ADRA2B
Cellular response to stimulus	1.40E-08	DRD4,APEX1,MAP3K10,HTR2B,CYP2C9,SIGMAR1,ADRA2A,HTR5A,HTR6,DRD5,ADRA1B,OXSRI,HTR1A,PLEC,CYP2B6,GRK1,CYP3A4,HTR7,PKN1,PTPN22,CYP2D6,CYP2C19,HRH2,DRD1,STK32A,ADRA2C,OPRM1,CHRNA7,PIP5K1C,ADRA2B
Response to stimulus	1.41E-08	DRD4,APEX1,MAP3K10,HTR2B,CYP2C9,SIGMAR1,ADRA2A,HTR5A,HTR6,DRD5,ADRA1B,OXSRI,HTR1A,PLEC,CYP2B6,GRK1,CYP3A4,HTR7,PKN1,PTPN22,CYP2D6,CYP2C19,HRH2,DRD1,STK32A,ADRA2C,OPRM1,CHRNA7,PIP5K1C,ABCB1,ADRA2B
Cellular response to organonitrogen compound	4.92E-08	DRD4,APEX1,HTR2B,HTR5A,HTR6,DRD5,HTR1A,HTR7,PTPN22,HRH2,DRD1,OPRM1

Suppl. Table 2

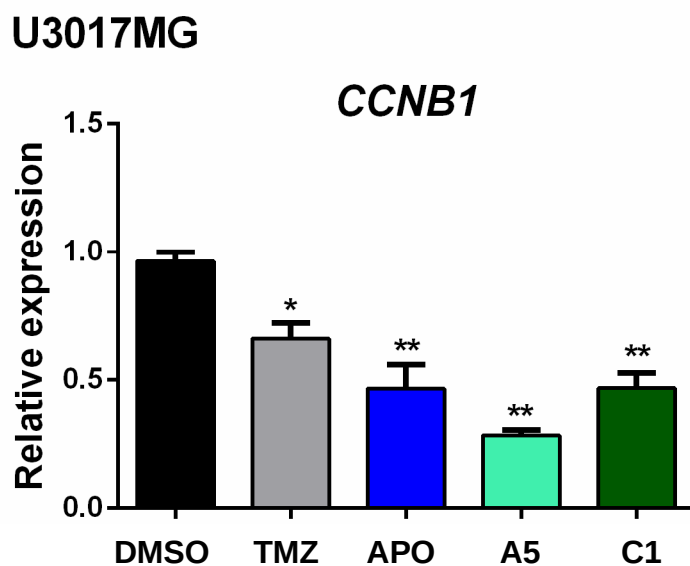
Term Description	FDR q-value	Matching Proteins
C1		
G protein-coupled receptor signaling pathway, coupled to cyclic nucleotide second messenger	5.93E-10	MTNR1B,MTNR1A,DRD5,HTR1A,PTGDR2,HTR7,DRD2,AGTR2,DRD3,DRD1,HTR2A
Chemical synaptic transmission	5.93E-10	MTNR1B,DRD5,HTR1A,HTR7,DRD2,SLC22A2,TH,DRD3,DRD1,HCRT1,CHRNA2,HTR2A,HCRT2
Cellular response to dopamine	1.87E-07	DRD5,HTR1A,HTR7,DRD2,DRD3,DRD1,HTR2A
Synaptic transmission, dopaminergic	3.99E-07	DRD5,DRD2,TH,DRD3,DRD1
Vascular process in circulatory system	6.70E-07	MTNR1B,DRD5,HTR1A,HTR7,SLC22A2,AGTR2,DRD1,HTR2A
Circulatory system process	7.61E-07	MTNR1B,DRD5,HTR1A,HTR7,DRD2,SLC22A2,AGTR2,DRD3,DRD1,HTR2A
Cell-cell signaling	7.61E-07	MTNR1B,DRD5,HTR1A,HTR7,DRD2,SLC22A2,AGTR2,TH,DRD3,DRD1,HCRT1,CHRNA2,HTR2A,HCRT2
Behaviour	7.94E-07	MTNR1A,DRD5,HTR1A,DRD2,AGTR2,TH,DRD3,DRD1,HCRT1,HTR2A,HCRT2
Dopamine metabolic process	1.67E-06	DRD2,AGTR2,TH,DRD3,DRD1
Regulation of biological quality	2.42E-06	MTNR1B,SLC22A3,PRELID1,DRD5,HTR1A,F3,HTR7,TUBB,DRD2,PARP1,SLC22A2,AGTR2,TH,DRD3,DRD1,PLAA,PARP3,FKBP1A,HCRT1,CHRNA2,HTR2A,HCRT2
Regulation of blood vessel diameter	2.42E-06	MTNR1B,DRD5,HTR1A,HTR7,AGTR2,DRD1,HTR2A
Phospholipase c-activating dopamine receptor signaling pathway	2.89E-06	DRD5,DRD2,DRD3,DRD1
Response to amphetamine	2.98E-06	DRD5,DRD2,TH,DRD3,DRD1
Phenol-containing compound metabolic process	4.43E-06	HTR1A,DRD2,AGTR2,TH,DRD3,DRD1
Blood circulation	5.69E-06	MTNR1B,DRD5,HTR1A,HTR7,DRD2,AGTR2,DRD3,DRD1,HTR2A
APO		
Cellular response to dopamine	4.38E-09	DRD4,DRD5,HTR1A,DRD2,DRD3,DRD1
Response to amphetamine	6.26E-09	DRD4,DRD5,DRD2,DRD3,DRD1
Regulation of dopamine uptake involved in synaptic transmission	1.78E-08	DRD4,DRD2,DRD3,DRD1
Response to cocaine	2.15E-08	DRD4,DRD5,DRD2,DRD3,DRD1
Phospholipase c-activating dopamine receptor signaling pathway	2.15E-08	DRD5,DRD2,DRD3,DRD1
Behavioural response to cocaine	4.37E-08	DRD4,DRD2,DRD3,DRD1
Adenylate cyclase-modulating g protein-coupled receptor signaling pathway	1.96E-07	DRD4,DRD5,HTR1A,DRD2,DRD3,DRD1
Phenol-containing compound metabolic process	2.22E-07	DRD4,HTR1A,DRD2,DRD3,DRD1
Adenylate cyclase-activating adrenergic receptor signaling pathway	2.27E-07	DRD5,DRD2,DRD3,DRD1
Dopamine metabolic process	5.37E-07	DRD4,DRD2,DRD3,DRD1
Cellular response to organonitrogen compound	5.45E-07	DRD4,DRD5,HTR1A,DRD2,PARP1,DRD3,DRD1
Adenylate cyclase-inhibiting dopamine receptor signaling pathway	2.28E-06	DRD4,DRD2,DRD3
Chemical synaptic transmission	4.48E-06	DRD4,DRD5,HTR1A,DRD2,DRD3,DRD1
Negative regulation of synaptic transmission	7.80E-06	DRD5,DRD2,DRD3,DRD1
Response to organic cyclic compound	7.86E-06	DRD4,DRD5,HTR1A,DRD2,PARP1,DRD3,DRD1

Suppl. Table 3

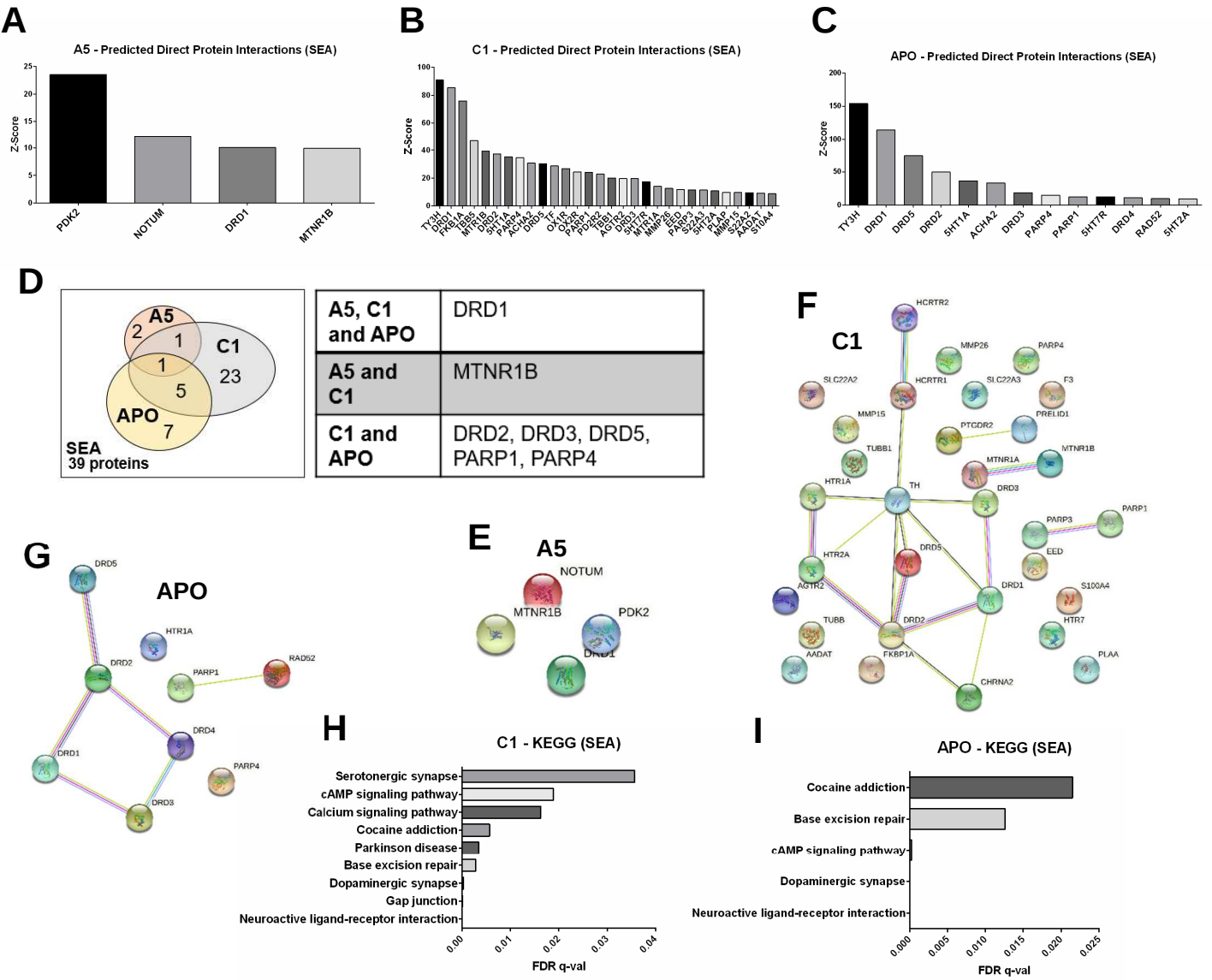
Gene Symbol	Forward (F) and Reverse (R) Primers Sequences (5'- 3')
<i>GAPDH</i>	F - GGAGTCAACGGATTTGGTCGTA R - GGCAACAATATCCACTTTACCA
<i>PROM1</i> (<i>CD133</i>)	F - ACCCAACATCATCCCTGTTCTT R - AGCTCTTCAAGGTGCTGTTTCATG
<i>NES</i>	F - AGCCCTGACCACTCCAGTTTAG R - CCCTCTATGGCTGTTTCTTTCTCT
<i>OCT4</i>	F - AGTGCCCGAAACCCACACT R - CTTCTGGCGCCGGTTACA
<i>CD44</i>	F - ATAATTGCCGCTTTGCAGGTGTATT R - ATAATGGCAAGGTGCTATTGAAAGCCT
<i>BAX</i>	F - CGACTGATGTCCCTGTCTCC R - CTCCCGCCACAAAGATGGT
<i>BECN1</i>	F - GCTCCCGAGGTGAAGAGCAT R - TGTGGTAAGTAATGGAGCTGTGA
<i>BCL2L11</i> (<i>BIM</i>)	F - CACTATCTCAGTGCAATGGCTTCC R - ATTCGTGGGTGGTCTTCGG
<i>CDKN1A</i> (<i>p21</i>)	F - CTGCCCAAGCTCTACCTTCC R - CAGGTCCACATGGTCTTCCT
<i>CCNB1</i>	F - ACCTGTGTCAGGCTTTCTCTG R - TGGTCTGACTGCTTGCTCTTC
<i>ABCB1</i>	F - GTCTGGACAAGCACTGAAA R - AACAAACGGTTCGGAAGTTT
<i>CYP2B6</i>	F - AGACGCCTTCAATCCTGACC R - CCTTCACCAAGACAAATCCGC
<i>CYP2C9</i>	F - TGGATGAAGGTGGCAATTTT R - GGGCTTCTCCCACACAAAT
<i>DRD1</i>	F - CTCCTCAACGTTTCGGAGCC R - AGCTCTCCAAACGCCTTGCCTT
<i>DRD5</i>	F - TCATCTATGCCTTCAACGCCGACT R - AGCTGCGATTTCTTGTGGAAGAC



Suppl. Figure 2

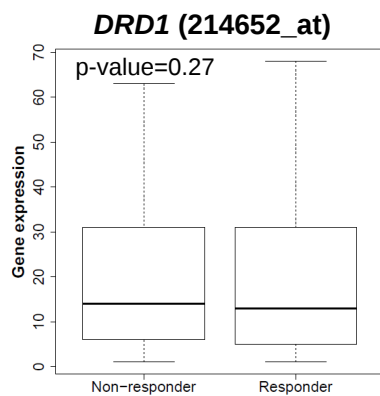


Suppl. Figure 3



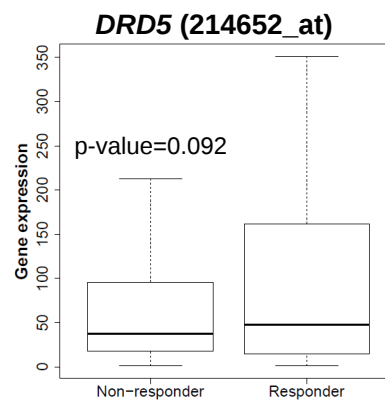
Suppl. Figure 7

A



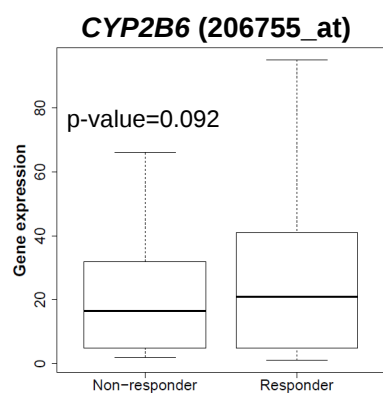
TMZ response	N of patients	Mean	SD	Median	Minimum	Maximum
Responder	165	21	28	13	1	264
Non-responder	154	27	41	14	1	314

B



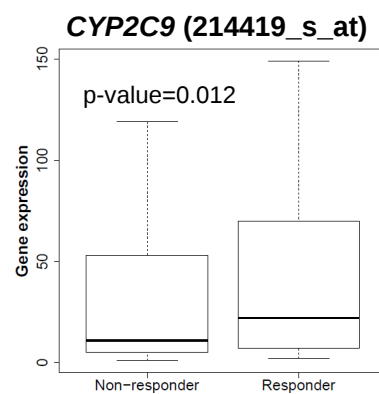
TMZ response	N of patients	Mean	SD	Median	Minimum	Maximum
Responder	165	91	92	48	1	351
Non-responder	154	79	97	38	1	646

C



TMZ response	N of patients	Mean	SD	Median	Minimum	Maximum
Responder	165	34	40	21	1	202
Non-responder	154	24	28	16	2	161

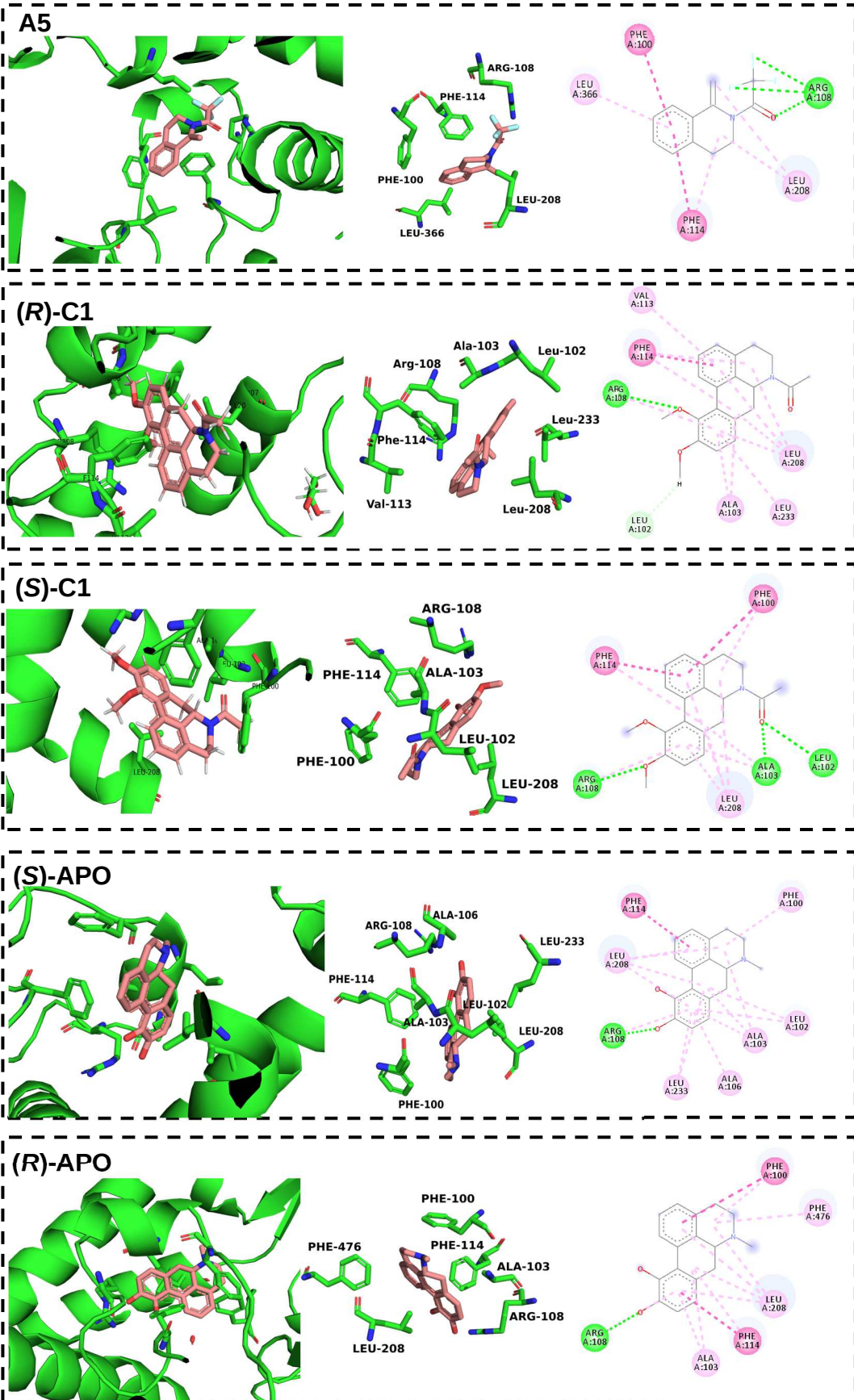
D



TMZ response	N of patients	Mean	SD	Median	Minimum	Maximum
Responder	165	41	42	22	2	165
Non-responder	154	36	54	11	1	482

Suppl. Figure 8

CYP2C9

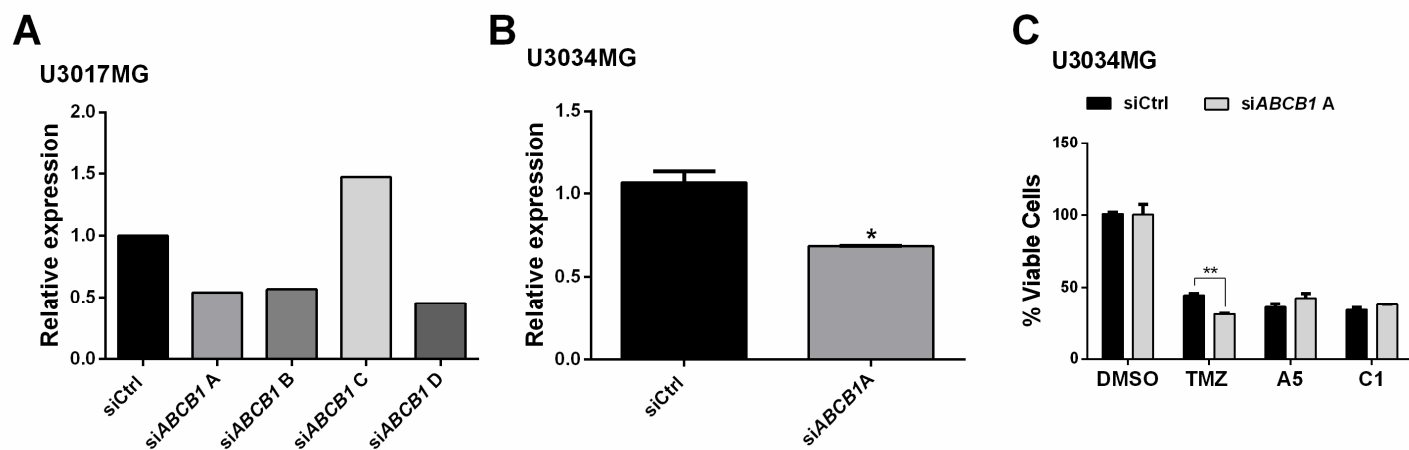


Interactions

	Conventional Hydrogen Bond		Pi-Stacked
	Carbon Hydrogen Bond		Alkyl

ΔG Binding Energy (kcal/mol)

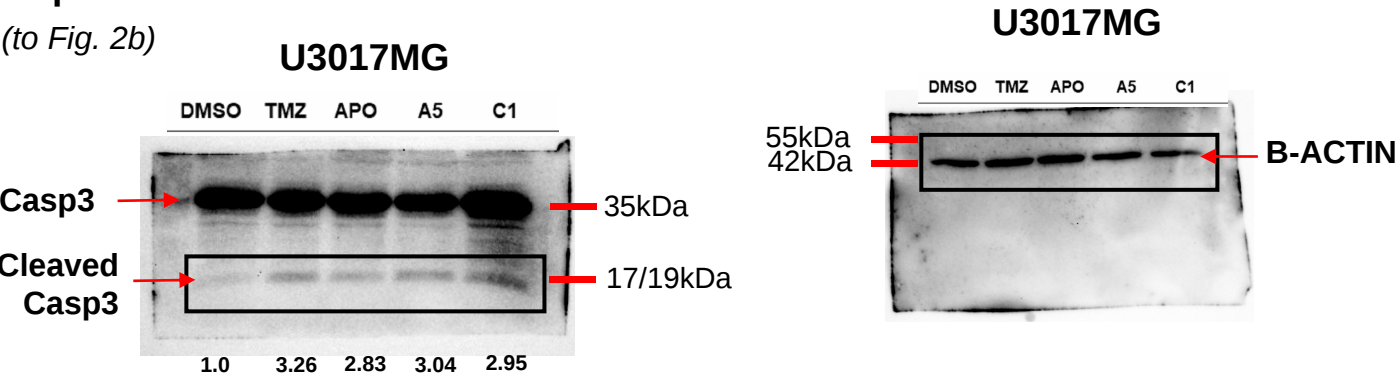
A5 = -25.69
 (R)-C1 = -36.62
 (S)-C1 = -38.40
 (R)-APO = -35.45
 (S)-APO = -28.51



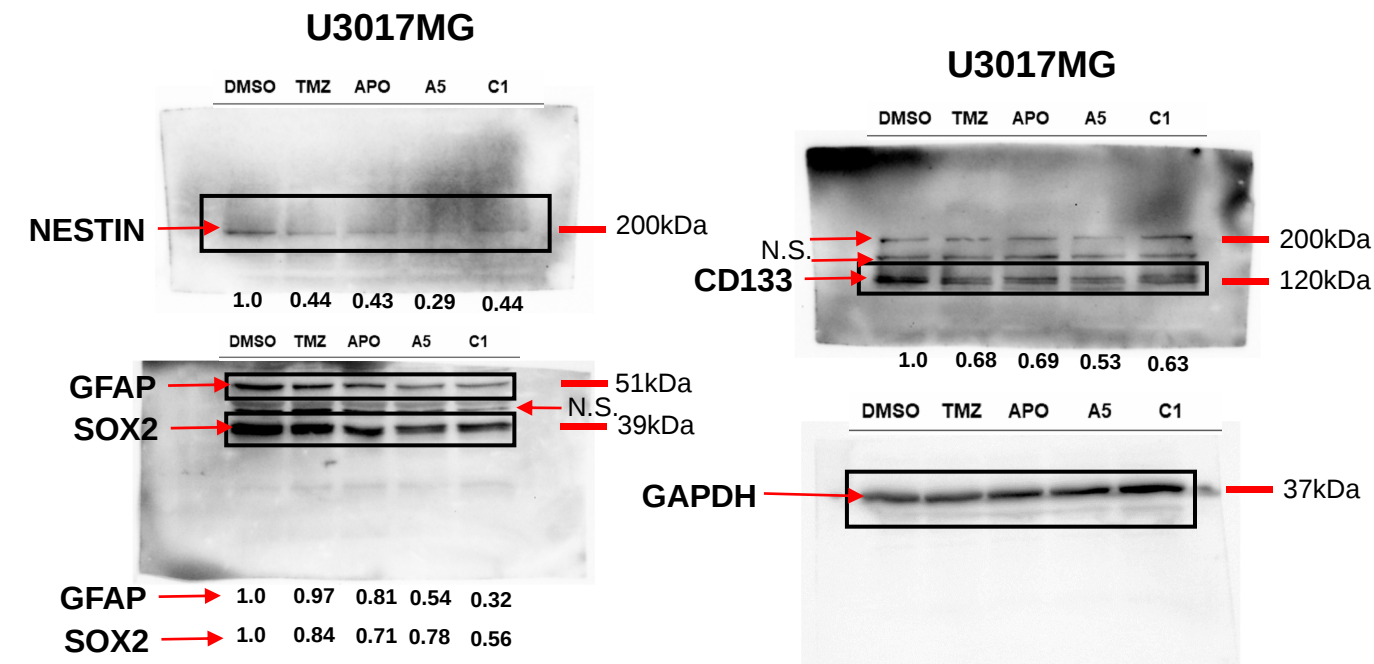
Suppl. Figure 10

Unprocessed immunoblots

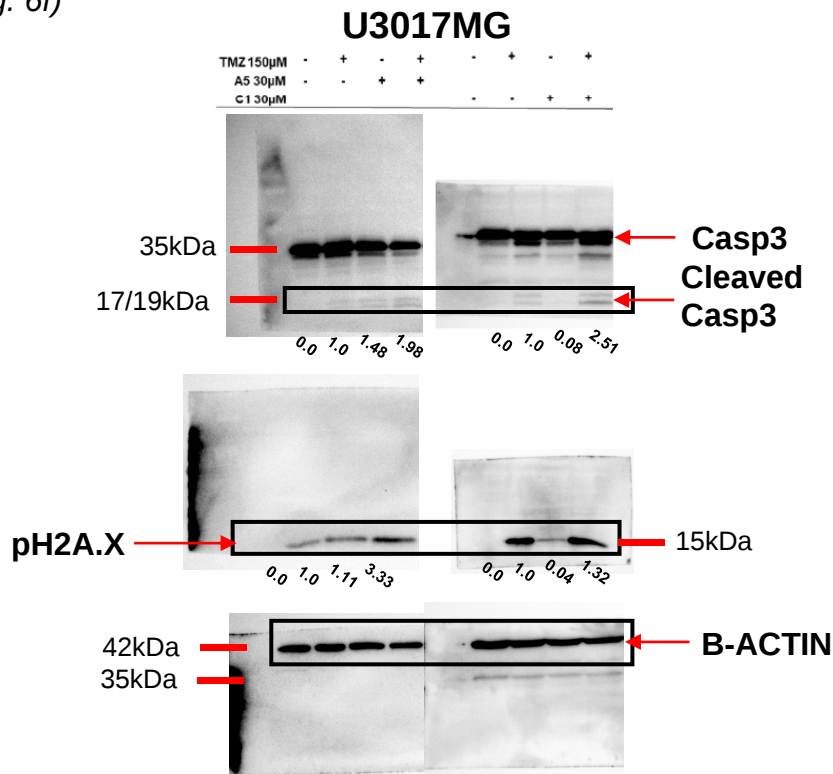
(to Fig. 2b)



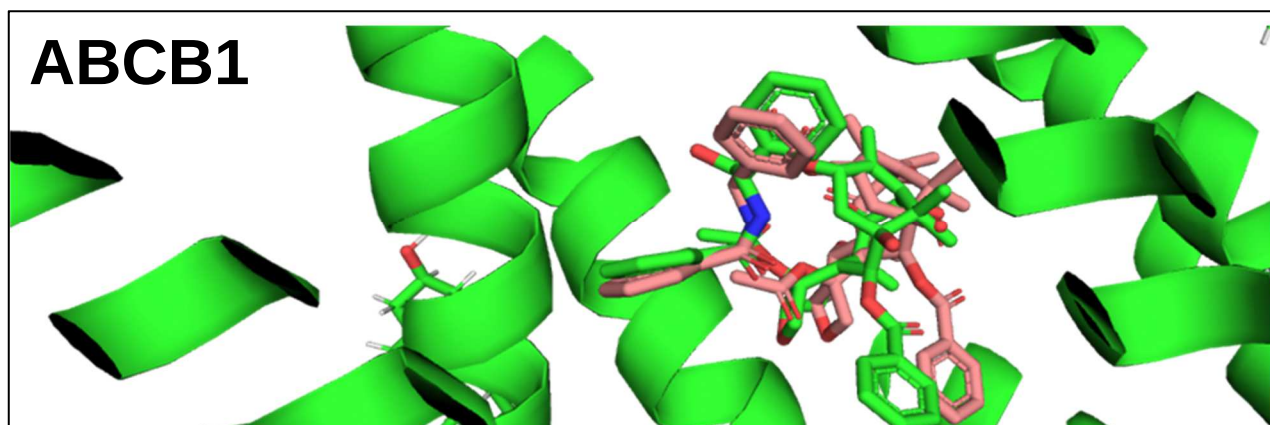
(to Fig. 3c)



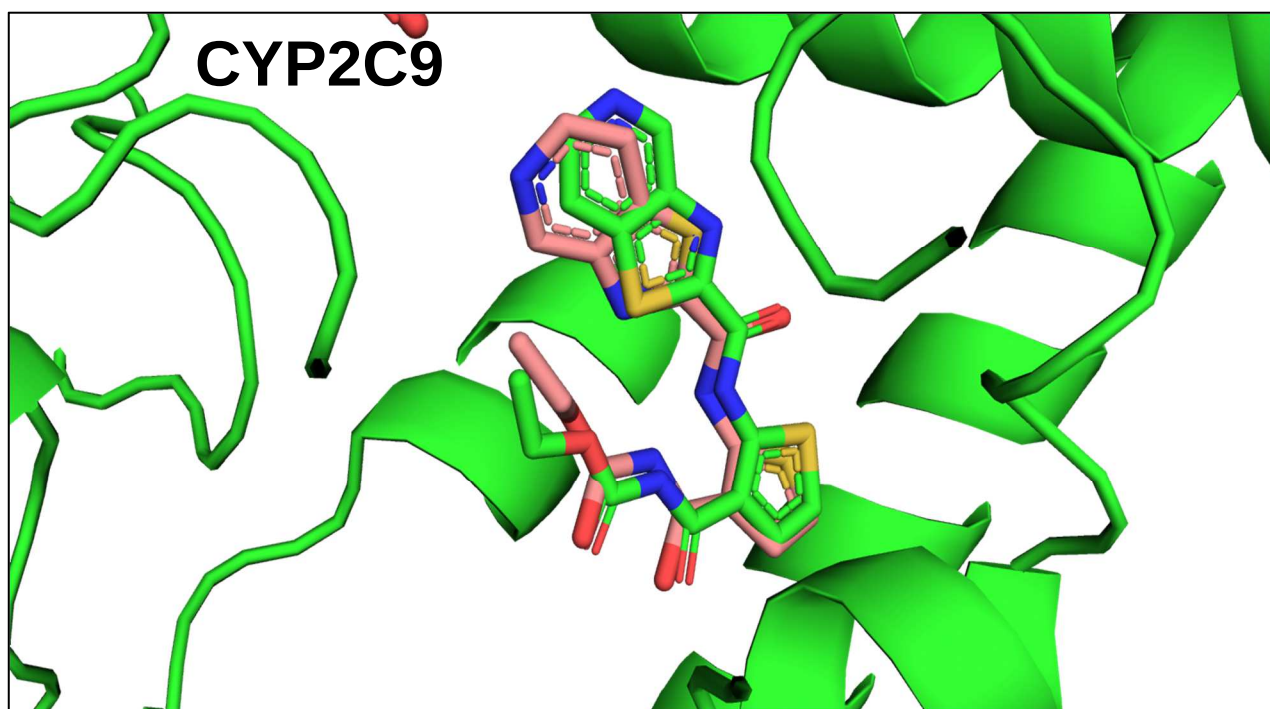
(to Fig. 6f)



A



B



Suppl. Figure 12