Supporting Information for

TPPU, a Selective and Potent Dual Inhibitor of Soluble Epoxide Hydrolase and p38 Kinase Intervenes in Alzheimer's Signaling in Human Nerve Cells

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S1. In Vitro Kinase Selectivity Screening for TPPU

The Kinase Selectivity Profiling System includes kinase and substrate pairs. Percentage kinase activities upon treatment of compound TPPU at 1 μM in a panel of 40 human protein kinases were measured by the ADP-Glo Kinase Assay Kit according to the manufacturer's protocol. The kinase inhibitor staurosporine was used at 1 μM as a reference control. Data were the mean of duplicate of each of six independent experiments with ± SEM (n = 6). The percentage of kinase activity was calculated and normalized according to below formula:

Kinase activity (%) = 100*[(drug treated kinase signal)–(background blank signal)]/[(no drug treated kinase signal) – (background blank signal)]

Assay Kinase	Substrate/Co-Factor	Kinase Activity (%)
ERK2	MBP	105.6 ± 1.5
GSK3β	GSK3 Substrate	72.2 ± 1.7
JNK1	p38 Substrate	105.3 ± 5.4
JNK3	p38 Substrate	105.9 ± 6.4
p38α	p38 Substrate	75.3 ± 3.2
p38β	p38 Substrate	35.6 ± 2.1
p38δ	p38 Substrate	101.5 ± 7.4
p38γ	p38 Substrate	48.8 ± 2.2
CDK1/CyclinA2	Histone H1 Protein	105.9 ± 4.8
CDK2/CyclinE1	Histone H1 Protein	104.3 ± 2.0
CDK3/CyclinE1	Histone H1 Protein	100.1 ± 5.5
CDK5/p25	Histone H1 Protein	91.7 ± 4.0
CDK5/p35	Histone H1 Protein	105.1 ± 3.6
CDK6/CyclinD3	Histone H1 Protein	84.3 ± 6.5
CDK9/CyclinK	PDKtide	80.9 ± 3.8

CLK3	MBP	93.7 ± 5.0
AKT1	AKT (PKB) Substrate	95.8 ± 8.9
p70S6Kβ	RSK Substrate	103.2 ± 7.6
PDK1	PDKtide	107.0 ± 3.7
PKA	Kemptide	92.1 ± 2.7
PKC	Neurogranin Peptide Substrate	102.0 ± 2.9
PRKG1	RSK Substrate	96.1 ± 7.6
ROCK1	S6K Substrate	98.3 ± 8.0
RSK2	RSK Substrate	94.8 ± 3.5
AMPK A1/B1/G1	SAMStide	105.9 ± 4.4
AMPK A1/B1/G2	SAMStide	106.8 ± 5.1
AMPK A2/B1/G1	SAMStide	70.6 ± 6.5
CAMK2α	Autocamtide-2	84.5 ± 2.3
CAMK2γ	Autocamtide-2	90.1 ± 3.0
CAMK4	Autocamtide-2	104.9 ± 2.6
DAPK1	MBP	103.8 ± 2.3
STK33	MBP	102.8 ± 7.1
Aurora A	MBP	106.1 ± 2.6
Aurora B	MBP	94.8 ± 2.6
CK2α1	Casein	103.2 ± 4.5
DNA-PK	DNA-PK Peptide Substrate	95.7 ± 5.8
CK1α1	De-Phospho Casein	65.8 ± 4.6
CK1ε	De-Phospho Casein	106.8 ± 2.8
CK1γ1	Casein	109.5 ± 4.7
VRK2	Casein	106.8 ± 5.4