



Supplementary Information

DDT and Derivatives May Target Insulin Pathway Proteins

Diana Montes-Grajales, Jesus Olivero-Verbel and Maria Cabarcas-Montalvo*

*Environmental and Computational Chemistry Group, Faculty of Pharmaceutical Sciences,
 University of Cartagena, Campus of Zaragocilla, Cartagena, Colombia*

Table S1. Docking affinities (kcal mol⁻¹) for DDT and related compounds, optimized by MM, binding to insulin pathway proteins

Protein name	Short name	PDB_ID	<i>p,p'</i> -DDT	<i>m,p'</i> -DDD	<i>m,p'</i> -DDT	<i>o,o'</i> -DDT	<i>o,p'</i> -DDD	<i>o,p'</i> -DDE	<i>o,p'</i> -DDT	<i>p,p'</i> -DDD	<i>p,p'</i> -DDE
Celladhesion											
Flotillin 2	Flot2	1win	-6.4 ± 0.0	-6.0 ± 0.0	-6.5 ± 0.0	-6.2 ± 0.0	-6.1 ± 0.0	-6.0 ± 0.1	-6.2 ± 0.0	-5.9 ± 0.0	-6.0 ± 0.0
Cytokine/Cytokine regulator											
Eotaxin-3	TSC-1	1g2s	-5.5 ± 0.0	-5.4 ± 0.0	-5.5 ± 0.0	-5.4 ± 0.0	-5.2 ± 0.0	-5.6 ± 0.0	-5.4 ± 0.1	-5.3 ± 0.0	-5.6 ± 0.0
Suppressor of cytokinesignaling 3	SOCS3	2hnh	-7.3 ± 0.0	-7.1 ± 0.0	-8.0 ± 0.0	-7.1 ± 0.0	-7.1 ± 0.0	-7.1 ± 0.1	-7.6 ± 0.0	-7.1 ± 0.0	-6.7 ± 0.0
DNA binding protein											
Forkhead box protein O3	FOXO3 A	2k86	-5.0 ± 0.0	-5.4 ± 0.0	-5.4 ± 0.0	-5.7 ± 0.0	-5.7 ± 0.0	-6.1 ± 0.0	-5.0 ± 0.0	-5.6 ± 0.0	-5.1 ± 0.0
DNA binding protein											
Endocytosis/Exocytosis											
Cdc42-interacting protein 4	CIP4	2efk	-6.6 ± 0.0	-6.7 ± 0.0	-6.6 ± 0.0	-6.0 ± 0.0	-6.1 ± 0.1	-6.2 ± 0.0	-5.9 ± 0.0	-6.5 ± 0.0	-6.2 ± 0.0
Hormone/Growth factor											
Insulin	Insulin	1ms0	-5.9 ± 0.1	-5.9 ± 0.0	-5.7 ± 0.0	-5.5 ± 0.0	-5.5 ± 0.1	-5.4 ± 0.0	-5.4 ± 0.2	-5.6 ± 0.1	-5.9 ± 0.0
Transcription regulator											
Protein SinI	sinI	1b0n	-6.5 ± 0.0	-6.0 ± 0.0	-6.3 ± 0.1	-6.4 ± 0.0	-6.3 ± 0.0	-6.2 ± 0.0	-6.5 ± 0.0	-6.1 ± 0.0	-6.0 ± 0.0
Hydrolase											
Ras-likeprotein TC10	TC10	2atx	-5.8 ± 0.0	-5.9 ± 0.0	-6.2 ± 0.0	-5.9 ± 0.0	-5.6 ± 0.0	-6.2 ± 0.0	-5.6 ± 0.0	-5.9 ± 0.0	-5.9 ± 0.0
Tyr-protein phosphatase non-receptor type 11	Shp2	3o5x	-5.9 ± 0.0	-5.7 ± 0.1	-5.9 ± 0.0	-6.2 ± 0.0	-5.7 ± 0.1	-6.0 ± 0.0	-6.0 ± 0.1	-5.8 ± 0.0	-5.7 ± 0.0
Phosphatase and tensin homolog	PTEN	1d5r	-7.1 ± 0.0	-6.9 ± 0.0	-7.6 ± 0.0	-6.9 ± 0.0	-6.9 ± 0.0	-7.1 ± 0.0	-6.7 ± 0.0	-7.0 ± 0.0	-6.7 ± 0.0
Tyr-protein phosphatase non-receptor type 1	PTP-1B	3eax	-6.6 ± 0.2	-6.0 ± 0.0	-6.4 ± 0.0	-6.5 ± 0.0	-6.0 ± 0.0	-6.1 ± 0.0	-6.6 ± 0.0	-6.1 ± 0.2	-6.1 ± 0.0
Ser/Thr protein phosphatase PP1-β catalytic subunit	PP-1B	1s70	-4.9 ± 0.0	-4.9 ± 0.0	-5.0 ± 0.0	-4.9 ± 0.0	-4.5 ± 0.0	-4.9 ± 0.0	-4.9 ± 0.0	-5.0 ± 0.0	-4.9 ± 0.0
cAMP/cAMP-inhibited cGMP 3'. 5'-cyclic phosphodiesterase 10A	PDE10A	2wey	-7.4 ± 0.0	-7.9 ± 0.0	-7.4 ± 0.0	-6.8 ± 0.0	-7.6 ± 0.0	-7.5 ± 0.0	-7.0 ± 0.0	-8.2 ± 0.0	-8.5 ± 0.0
Immune system											
Tumor necrosis factor	TNF	319j	-5.8 ± 0.0	-5.8 ± 0.0	-6.0 ± 0.3	-5.7 ± 0.1	-5.9 ± 0.0	-6.1 ± 0.2	-5.8 ± 0.0	-6.0 ± 0.0	-5.8 ± 0.1
Insulin receptor substrate 2	IRS-2	3fqx	-3.3 ± 0.1	-3.2 ± 0.0	-3.3 ± 0.0	-3.1 ± 0.0	-3.2 ± 0.0	-3.4 ± 0.0	-3.1 ± 0.0	-3.2 ± 0.1	-3.1 ± 0.1
Ligase											
Amiloride-sensitive sodium channel subunit beta	ENaC	1i5h	-6.3 ± 0.0	-6.1 ± 0.0	-6.1 ± 0.0	-6.1 ± 0.0	-6.1 ± 0.0	-6.5 ± 0.0	-6.5 ± 0.0	-6.2 ± 0.0	-6.3 ± 0.0
Oxidoreductase/Metal binding protein											
Cytoplasmic protein NCK2	Nck-2	1u5s	-5.6 ± 0.2	-5.8 ± 0.0	-5.4 ± 0.0	-5.7 ± 0.1	-5.2 ± 0.0	-5.5 ± 0.0	-5.4 ± 0.0	-5.5 ± 0.2	-5.2 ± 0.0
EHdomain-containingprotein 1	EHD1	2jq6	-5.6 ± 0.0	-6.3 ± 0.1	-6.1 ± 0.0	-5.6 ± 0.1	-5.7 ± 0.0	-5.6 ± 0.0	-5.9 ± 0.3	-5.9 ± 0.1	-5.5 ± 0.0
Nitric oxide synthase, inducible	iNOS	3hr4	-7.3 ± 0.3	-7.4 ± 0.2	-7.3 ± 0.2	-7.0 ± 0.3	-7.4 ± 0.2	-7.5 ± 0.4	-7.2 ± 0.2	-7.3 ± 0.3	-7.6 ± 0.2
Phosphoinositide 3 Kinase Gamma											
Phosphatidylinositol 3-kinase catalytic subunit	PI3K p110	1e8y	-7.0 ± 0.0	-7.4 ± 0.0	-7.3 ± 0.1	-6.4 ± 0.0	-6.9 ± 0.0	-7.0 ± 0.0	-6.9 ± 0.1	-7.0 ± 0.0	-8.1 ± 0.0
Phosphotransferase											
Extracellularsignal-regulatedkinase 2	ERK-2	2erk	-6.7 ± 0.0	-6.8 ± 0.0	-6.9 ± 0.0	-6.6 ± 0.0	-6.5 ± 0.0	-6.6 ± 0.0	-6.6 ± 0.0	-6.4 ± 0.1	-6.4 ± 0.0

*e-mail: joliverov@unicartagena.edu.co

Table S1. continuation

Protein name	Short name	PDB_ID	<i>p,p'</i> -DDT	<i>m,p'</i> -DDD	<i>m,p'</i> -DDT	<i>o,o'</i> -DDT	<i>o,p'</i> -DDD	<i>o,p'</i> -DDE	<i>o,p'</i> -DDT	<i>p,p'</i> -DDD	<i>p,p'</i> -DDE
Protein binding/Transferase											
Adaptormoleculerck	Crk	lju5	-6.0 ± 0.0	-5.9 ± 0.1	-6.2 ± 0.0	-6.2 ± 0.0	-5.8 ± 0.0	-6.1 ± 0.1	-6.0 ± 0.0	-5.9 ± 0.0	-6.0 ± 0.0
Syntaxinbindingprotein 4	Synip	lwi4	-6.7 ± 0.0	-6.9 ± 0.0	-6.8 ± 0.0	-6.8 ± 0.0	-6.4 ± 0.0	-6.4 ± 0.1	-6.9 ± 0.1	-6.2 ± 0.0	-7.3 ± 0.0
Serine/ Threonine Protein Kinase											
Proto-oncogene c-RAF	cRAF	lrfa	-5.4 ± 0.0	-5.6 ± 0.0	-6.0 ± 0.0	-5.2 ± 0.0	-5.1 ± 0.0	-5.6 ± 0.0	-5.4 ± 0.1	-5.6 ± 0.0	-5.4 ± 0.0
Signal transduction											
Insulin receptor substrate 1	IRS-1	lqqg	-7.3 ± 0.1	-6.8 ± 0.1	-7.1 ± 0.1	-6.7 ± 0.1	-7.2 ± 0.0	-7.4 ± 0.1	-7.1 ± 0.1	-7.0 ± 0.0	-7.3 ± 0.0
Signaling protein / Gene regulation											
Growth factor receptor-bound protein 2	Grb2	ljjr	-5.7 ± 0.0	-5.5 ± 0.0	-6.0 ± 0.0	-5.6 ± 0.0	-5.4 ± 0.0	-5.6 ± 0.0	-5.3 ± 0.0	-5.5 ± 0.0	-5.4 ± 0.0
Signaling inositol polyphosphate phosphatase SHIP II	SHIP2	2ysx	-5.2 ± 0.0	-5.2 ± 0.0	-5.5 ± 0.0	-5.7 ± 0.0	-5.3 ± 0.0	-5.5 ± 0.0	-5.3 ± 0.1	-5.2 ± 0.2	-5.4 ± 0.0
SHC-transforming protein 1	SHC	loy2	-6.4 ± 0.0	-6.0 ± 0.1	-6.2 ± 0.0	-5.9 ± 0.0	-5.8 ± 0.0	-5.7 ± 0.0	-6.0 ± 0.1	-6.2 ± 0.1	-6.4 ± 0.1
Son of sevenless protein homolog 1	SOS-1	lxd4	-7.8 ± 0.4	-7.6 ± 0.5	-7.3 ± 0.1	-6.9 ± 0.1	-7.6 ± 0.4	-7.6 ± 0.0	-7.3 ± 0.3	-8.0 ± 0.1	-7.1 ± 0.3
Son of sevenless protein homolog 1	SOS-1	ldbh	-6.8 ± 0.0	-7.2 ± 0.0	-6.8 ± 0.0	-6.6 ± 0.0	-6.1 ± 0.0	-6.6 ± 0.0	-6.8 ± 0.0	-7.1 ± 0.0	-6.8 ± 0.1
Agouti signaling protein	ASP	ly7j	-5.4 ± 0.1	-5.4 ± 0.0	-5.4 ± 0.0	-5.5 ± 0.0	-4.9 ± 0.0	-5.4 ± 0.0	-5.1 ± 0.1	-5.1 ± 0.0	-5.2 ± 0.0
Tumor necrosis factor receptor 1	TNFR-1	lxtt	-6.1 ± 0.1	-5.9 ± 0.0	-6.2 ± 0.2	-6.2 ± 0.0	-5.8 ± 0.0	-6.1 ± 0.1	-6.1 ± 0.0	-5.9 ± 0.1	-6.1 ± 0.1
GTP-binding protein Rheb	RHEB	lxts	-7.4 ± 0.0	-7.3 ± 0.2	-7.2 ± 0.2	-6.2 ± 0.0	-6.5 ± 0.0	-6.9 ± 0.3	-6.6 ± 0.0	-7.2 ± 0.0	-7.7 ± 0.0
Structural protein/Protein binding											
EH domain-bindingprotein 1	EHBP1	2d89	-5.8 ± 0.0	-5.6 ± 0.0	-5.8 ± 0.0	-5.4 ± 0.0	-5.5 ± 0.0	-5.9 ± 0.0	-5.8 ± 0.0	-5.7 ± 0.0	-5.9 ± 0.0
Transcription											
Forkhead box protein O1	FOXO1	3co6	-5.3 ± 0.0	-5.3 ± 0.0	-5.2 ± 0.0	-5.3 ± 0.0	-5.0 ± 0.0	-5.2 ± 0.1	-5.1 ± 0.0	-5.3 ± 0.0	-5.1 ± 0.1
Forkhead box protein O4	FOXO4	3l2c	-5.2 ± 0.0	-5.3 ± 0.1	-5.5 ± 0.0	-5.5 ± 0.0	-5.1 ± 0.1	-5.3 ± 0.0	-5.4 ± 0.0	-5.2 ± 0.0	-5.0 ± 0.0
Transferase											
Protein kinase C theta type	PKCθ	lxjd	-7.3 ± 0.0	-7.6 ± 0.0	-7.8 ± 0.0	-6.9 ± 0.0	-7.7 ± 0.0	-8.0 ± 0.0	-7.4 ± 0.0	-7.5 ± 0.1	-8.1 ± 0.0
Proto-oncogene tyrosine-protein kinase FYN	Fyn	lzbj	-7.8 ± 0.1	-7.3 ± 0.1	-7.4 ± 0.0	-6.8 ± 0.0	-7.0 ± 0.0	-7.7 ± 0.0	-7.7 ± 0.0	-7.1 ± 0.0	-7.3 ± 0.1
GlgA glycogen synthase	GS	2bfw	-5.9 ± 0.0	-5.8 ± 0.1	-5.9 ± 0.0	-5.7 ± 0.0	-5.4 ± 0.1	-5.9 ± 0.0	-5.3 ± 0.0	-5.6 ± 0.0	-5.8 ± 0.0
Insulin receptor	IR	lir3	-6.7 ± 0.0	-7.0 ± 0.0	-6.9 ± 0.1	-6.6 ± 0.0	-6.4 ± 0.0	-7.0 ± 0.2	-6.4 ± 0.0	-6.7 ± 0.0	-7.2 ± 0.0
Phosphatidylinositol 3-kinase	PI3K p85	lh9o	-5.6 ± 0.0	-5.5 ± 0.0	-5.9 ± 0.0	-5.4 ± 0.0	-5.4 ± 0.0	-6.1 ± 0.0	-5.3 ± 0.0	-5.5 ± 0.0	-5.9 ± 0.1
C-Jun N-terminal kinase 3	JNK	2p33	-7.5 ± 0.0	-7.5 ± 0.0	-7.7 ± 0.1	-6.8 ± 0.1	-7.1 ± 0.0	-7.1 ± 0.0	-7.4 ± 0.0	-7.4 ± 0.0	-7.5 ± 0.0
Ribosomal protein S6 kinase beta-1	P70S6K	3a62	-7.6 ± 0.0	-7.7 ± 0.0	-7.8 ± 0.0	-6.9 ± 0.0	-6.7 ± 0.0	-7.4 ± 0.0	-7.0 ± 0.0	-6.9 ± 0.0	-7.1 ± 0.0
Glycogen synthase kinase-3 beta	GSK3B	luy5	-7.5 ± 0.0	-7.9 ± 0.0	-7.3 ± 0.0	-6.8 ± 0.0	-7.0 ± 0.0	-6.6 ± 0.0	-6.7 ± 0.0	-8.0 ± 0.0	-8.3 ± 0.0
Ser/Thr-protein kinase Sgk1	SGK	3hdn	-7.9 ± 0.0	-7.6 ± 0.1	-7.8 ± 0.1	-7.3 ± 0.3	-7.5 ± 0.0	-7.9 ± 0.6	-7.9 ± 0.4	-7.6 ± 0.0	-8.0 ± 0.0
Mammalian target of rapamycin	MTOR	2npu	-7.6 ± 0.0	-7.2 ± 0.0	-7.5 ± 0.1	-7.0 ± 0.0	-6.7 ± 0.1	-7.4 ± 0.1	-7.0 ± 0.0	-7.5 ± 0.0	-7.1 ± 0.0
Rac-gamma Ser/Thr-protein kinase	AKT-3	2x18	-7.3 ± 0.0	-7.2 ± 0.0	-7.1 ± 0.0	-7.3 ± 0.0	-6.8 ± 0.2	-7.3 ± 0.2	-7.0 ± 0.0	-7.0 ± 0.3	-7.1 ± 0.5
Rac-beta Ser/Thr-protein kinase	AKT-2	2x39	-7.1 ± 0.0	-6.9 ± 0.0	-7.6 ± 0.0	-7.4 ± 0.0	-7.1 ± 0.0	-6.9 ± 0.1	-7.5 ± 0.0	-6.8 ± 0.0	-7.0 ± 0.0
Rac-alpha Ser/Thr-protein kinase	AKT-1	3cqu	-7.9 ± 0.1	-8.7 ± 0.0	-8.9 ± 0.0	-5.9 ± 0.0	-8.1 ± 0.7	-8.6 ± 0.8	-7.5 ± 0.6	-8.7 ± 0.0	-9.5 ± 0.0
5'-AMP-activated protein kinase	AMPK	2v8q	-7.7 ± 0.1	-8.0 ± 0.1	-8.2 ± 0.4	-7.6 ± 0.2	-7.8 ± 0.1	-8.2 ± 0.0	-7.7 ± 0.6	-7.7 ± 0.1	-7.9 ± 0.1
ATP-citrate synthase	ACL	3mwd	-7.9 ± 0.0	-7.9 ± 0.1	-7.9 ± 0.0	-7.1 ± 0.0	-7.8 ± 0.0	-7.5 ± 0.0	-7.1 ± 0.0	-8.0 ± 0.0	-7.8 ± 0.1
Dual specificity mitogen-activated protein kinase kinase 2	MEK2	ls9i	-7.3 ± 0.7	-7.6 ± 0.5	-7.3 ± 0.2	-6.3 ± 0.3	-6.8 ± 0.7	-7.4 ± 0.7	-6.6 ± 0.0	-7.9 ± 0.0	-7.6 ± 0.7
Dual specificity mitogen-activated protein kinase kinase 1	MEK1	2p55	-6.7 ± 0.0	-7.2 ± 0.0	-7.0 ± 0.0	-6.1 ± 0.1	-6.3 ± 0.3	-6.4 ± 0.0	-6.1 ± 0.0	-6.8 ± 0.1	-7.1 ± 0.0
Transferase/Transferase inhibitor											
cAMP-dependent protein kinase, alpha-catalytic subunit	PKA	2qcs	-8.1 ± 0.2	-8.4 ± 0.5	-8.0 ± 0.5	-7.1 ± 0.0	-7.4 ± 0.6	-7.7 ± 0.1	-7.6 ± 0.0	-8.4 ± 0.1	-7.7 ± 0.0
Translation											
Eukaryotic translation initiation factor 4E	eIF4E	1kwk	-8.6 ± 0.0	-8.1 ± 0.2	-8.5 ± 0.0	-7.8 ± 0.0	-8.2 ± 0.0	-8.3 ± 0.0	-8.6 ± 0.0	-8.4 ± 0.0	-8.3 ± 0.0
Translation initiation factor eIF2B subunit alpha	eIF2B	3ecs	-6.6 ± 0.1	-6.3 ± 0.0	-6.3 ± 0.0	-6.4 ± 0.0	-6.0 ± 0.0	-6.5 ± 0.1	-6.6 ± 0.0	-6.1 ± 0.1	-6.6 ± 0.0
Translation initiation factor eIF2B, subunit delta	eIF2B	lt5o	-6.7 ± 0.0	-6.6 ± 0.0	-6.9 ± 0.0	-7.1 ± 0.0	-6.3 ± 0.1	-6.9 ± 0.1	-6.8 ± 0.0	-6.8 ± 0.0	-6.7 ± 0.0
Translation initiation factor eIF2B subunit epsilon	eIF2B	3jui	-5.9 ± 0.1	-5.6 ± 0.0	-6.0 ± 0.0	-5.5 ± 0.0	-5.5 ± 0.0	-5.7 ± 0.0	-5.7 ± 0.0	-5.6 ± 0.0	-5.7 ± 0.0
Eukaryotic translation initiation factor 4E binding protein 1	4E-BP1	3hxx	-5.1 ± 0.0	-4.7 ± 0.0	-5.0 ± 0.0	-4.9 ± 0.0	-4.5 ± 0.0	-4.8 ± 0.0	-4.6 ± 0.0	-5.1 ± 0.0	-4.8 ± 0.0