

Wu et al.:

Computational Systems Biology as an Animal-Free Approach to Characterize Toxicological Effects of Persistent Organic Pollutants

Supplementary Data

Tab. S1: Chemical-protein associations, with adverse outcome pathways (AOPs), biological assays and cytotoxicity information

Chemical name		CompTox (July 2019)			AOPwiki		ToxCast (July 2019)
		Cytotoxicity	AC50	Assay	AOP	event	Gene symbol
The initial 12 POPs							
Aldrin	Aldrin	7.23 µM	3.09	ATG_DR5_CIS_up	-	-	RARB
Aldrin	Aldrin	7.23 µM	1.9	ATG_PXRE_CIS_up	60	245	NR1I2
Aldrin	Aldrin	7.23 µM	4.04	ATG_PXR_TRANS_up	60	245	NR1I2
Aldrin	Aldrin	7.23 µM	0.912	ATG_RARg_TRANS_up	-	-	RARG
Aldrin	Aldrin	7.23 µM	7.17	ATG_RXRb_TRANS_up	-	-	RXRB
Aldrin	Aldrin	7.23 µM	2.2	BSK_BE3C_uPA_up	-	-	PLAU
Aldrin	Aldrin	7.23 µM	4.45	BSK_hDFCGF_Proliferation_down	-	-	\
Aldrin	Aldrin	7.23 µM	0.571	TOX21_p53_BLA_p4_ratio	-	-	TP53
Aldrin	Aldrin	7.23 µM	0.8	NHEERL_ZF_144hpf_TERATOSCORE_up	-	-	\
Aldrin	Aldrin	7.23 µM	2.41	TOX21_ERa_LUC_BG1_Agonist_Counterscreen	200	1181	ESR1
Chlordane	Chlordane	9.56 µM	1.33	NVS_ENZ_hPTPRF_Activator	-	-	PTPRF
Chlordane	Chlordane	9.56 µM	1.78	ATG_DR5_CIS_up	-	-	RARB
Chlordane	Chlordane	9.56 µM	2.04	ATG_PXRE_CIS_up	60	245	NR1I2
Chlordane	Chlordane	9.56 µM	3.21	ATG_VDRE_CIS_up	-	-	VDR
Chlordane	Chlordane	9.56 µM	4.32	BSK_hDFCGF_VCAM1_down	-	-	VCAM1
Chlordane	Chlordane	9.56 µM	4.5	BSK_hDFCGF_CollagenIII_down	-	-	COL3A1
Chlordane	Chlordane	9.56 µM	4.63	NVS_ADME_hCYP2C19	-	-	CYP2C19
Chlordane	Chlordane	9.56 µM	4.91	NVS_ENZ_hPTPN1_Activator	-	-	PTPN1
Chlordane	Chlordane	9.56 µM	5.02	BSK_hDFCGF_IP10_down	-	-	CXCL10
Chlordane	Chlordane	9.56 µM	5.07	BSK_hDFCGF_MCSF_down	-	-	CSF1
Chlordane	Chlordane	9.56 µM	5.52	BSK_hDFCGF_Proliferation_down	-	-	\
Chlordane	Chlordane	9.56 µM	6.17	ACEA_ER_80hr	200	1181	ESR1
Chlordane	Chlordane	9.56 µM	6.23	BSK_hDFCGF_TIMP1_down	-	-	TIMP1
Chlordane	Chlordane	9.56 µM	6.27	BSK_SAg_Proliferation_down	-	-	\
Chlordane	Chlordane	9.56 µM	6.41	NVS_ADME_hCYP2B6	-	-	CYP2B6
Chlordane	Chlordane	9.56 µM	6.45	BSK_hDFCGF_MMP1_down	-	-	MMP1
Chlordane	Chlordane	9.56 µM	6.49	BSK_hDFCGF_MIG_down	-	-	CXCL9

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Chlordane	Chlordane	9.56 µM	6.88	ATG_RARg_TRANS_up	-	-	RARG
Chlordane	Chlordane	9.56 µM	7.13	NVS_NR_hGR	66	654	NR3C1
Chlordane	Chlordane	9.56 µM	7.25	BSK_hDFCGF_PA11_down	-	-	SERPINE1
Chlordane	Chlordane	9.56 µM	7.38	BSK_hDFCGF_IL8_down	-	-	CXCL8
Chlordane	Chlordane	9.56 µM	7.44	ATG_PXR_TRANS_up	60	245	NR112
Chlordane	Chlordane	9.56 µM	7.72	ACEA_AR_antagonist_80hr	187	1134	AR
Chlordane	Chlordane	9.56 µM	7.96	TOX21_ARE_BLA_Agonist_ch2	-	-	\
Chlordane	Chlordane	9.56 µM	7.99	TOX21_TSHR_Agonist_ratio	-	-	TSHR
Chlordane	Chlordane	9.56 µM	8.09	OT_ER_ERbERb_0480	-	-	ESR2
Chlordane	Chlordane	9.56 µM	8.21	TOX21_ARE_BLA_agonist_ratio	-	-	NFE2L2
Chlordane	Chlordane	9.56 µM	8.24	BSK_hDFCGF_SRB_down	-	-	\
Chlordane	Chlordane	9.56 µM	8.86	TOX21_TSHR_HTRF_Agonist_ch1	-	-	\
Chlordane	Chlordane	9.56 µM	8.94	NHEERL_ZF_144hpf_TERATOSCORE_up	-	-	\
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	4.74	ATG_ERE_CIS_up	200	1181	ESR1
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	4.31	ATG_PXRE_CIS_up	60	245	NR112
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	4.41	ATG_ERa_TRANS_up	200	1181	ESR1
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	5.58	BSK_CASM3C_Thrombomodulin_up	-	-	THBD
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	4.36	BSK_hDFCGF_Proliferation_down	-	-	\
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	0.164	NVS_ENZ_hPTPN2_Activator	-	-	PTPN2
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	4.72	OT_ERa_EREGFP_0120	200	1181	ESR1
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	3.26	OT_ERa_EREGFP_0480	200	1181	ESR1
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	5.21	TOX21_ERa_LUC_BG1_Agonist	200	1181	ESR1
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	3.8	NHEERL_ZF_144hpf_TERATOSCORE_up	-	-	\
Dichlorodiphenyltrichloroethane (DDT)	DDT	5.74 µM	5.57	TOX21_DT40_657	-	-	\
Dieldrin	Dieldrin	8.84 µM	4.13	ACEA_ER_80hr	200	1181	ESR1
Dieldrin	Dieldrin	8.84 µM	0.579	ATG_DR5_CIS_up	-	-	RARB
Dieldrin	Dieldrin	8.84 µM	1	ATG_ERE_CIS_up	200	1181	ESR1
Dieldrin	Dieldrin	8.84 µM	1.92	ATG_PXRE_CIS_up	60	245	NR112
Dieldrin	Dieldrin	8.84 µM	4.71	ATG_ERa_TRANS_up	200	1181	ESR1
Dieldrin	Dieldrin	8.84 µM	2.55	ATG_PXR_TRANS_up	60	245	NR112
Dieldrin	Dieldrin	8.84 µM	0.77	ATG_RARa_TRANS_up	-	-	RARA
Dieldrin	Dieldrin	8.84 µM	1.68	ATG_RARg_TRANS_up	-	-	RARG
Dieldrin	Dieldrin	8.84 µM	0.0406	BSK_CASM3C_SAA_up	-	-	SAA1
Dieldrin	Dieldrin	8.84 µM	6.3	BSK_hDFCGF_Proliferation_down	-	-	\
Dieldrin	Dieldrin	8.84 µM	2.74	BSK_LPS_TNFa_up	-	-	TNF
Dieldrin	Dieldrin	8.84 µM	4.79	NVS_ADME_hCYP2B6	-	-	CYP2B6
Dieldrin	Dieldrin	8.84 µM	3.64	NVS_ADME_hCYP2C19	-	-	CYP2C19
Dieldrin	Dieldrin	8.84 µM	1.01	ATG_M_19_TRANS_dn	-	-	\
Dieldrin	Dieldrin	8.84 µM	6.74	NHEERL_ZF_144hpf_TERATOSCORE_up	-	-	\
Dieldrin	Dieldrin	8.84 µM	7.42	TOX21_AP1_BLA_Agonist_ch2	-	-	\
Dieldrin	Dieldrin	8.84 µM	4.55	TOX21_TSHR_HTRF_Agonist_ch1	-	-	\
Dieldrin	Dieldrin	8.84 µM	3.72	TOX21_TSHR_Agonist_ratio	-	-	TSHR
Endrin	Endrin	4.69 µM	0.806	ATG_DR5_CIS_up	-	-	RARB
Endrin	Endrin	4.69 µM	0.272	ATG_ERE_CIS_up	200	1181	ESR1
Endrin	Endrin	4.69 µM	1.38	ATG_PXRE_CIS_up	60	245	NR112
Endrin	Endrin	4.69 µM	2.42	ATG_VDRE_CIS_up	-	-	VDR
Endrin	Endrin	4.69 µM	2.25	ATG_PXR_TRANS_up	60	245	NR112
Endrin	Endrin	4.69 µM	1.61	ATG_RARb_TRANS_up	-	-	RARB
Endrin	Endrin	4.69 µM	1.7	ATG_RARg_TRANS_up	-	-	RARG

Endrin	Endrin	4.69 µM	4.33	BSK_4H_MCP1_down	-	-	CCL2
Endrin	Endrin	4.69 µM	4.63	BSK_hDFCGF_Proliferation_down	-	-	\
Endrin	Endrin	4.69 µM	3.37	BSK_LPS_TNFa_up	-	-	TNF
Endrin	Endrin	4.69 µM	4.2	BSK_SAg_PBMCCytotoxicity_up	-	-	\
Endrin	Endrin	4.69 µM	0.222	NVS_GPCR_gANPA	-	-	Nppa
Endrin	Endrin	4.69 µM	1.7	CEETOX_H295R_OHPREG_dn	-	-	PGR
Endrin	Endrin	4.69 µM	3.54	CEETOX_H295R_PROG_dn	-	-	PGR
Endrin	Endrin	4.69 µM	4.31	ATG_DR4_LXR_CIS_dn	58	167	NR1H3
Endrin	Endrin	4.69 µM	4.5	ATG_TCF_b_cat_CIS_dn	-	-	TCF7
Endrin	Endrin	4.69 µM	0.0109	NHEERL_ZF_144hpf_TERATOSCORE_up	-	-	\
Heptachlor	Heptachlor	8.24 µM	5.73	BSK_3C_Proliferation_down	-	-	\
Heptachlor	Heptachlor	8.24 µM	5.05	BSK_hDFCGF_CollagenIII_down	-	-	COL3A1
Heptachlor	Heptachlor	8.24 µM	6.38	BSK_hDFCGF_IP10_down	-	-	CXCL10
Heptachlor	Heptachlor	8.24 µM	6.88	BSK_hDFCGF_MCSF_down	-	-	CSF1
Heptachlor	Heptachlor	8.24 µM	7.21	BSK_hDFCGF_PAI1_down	-	-	SERPINE1
Heptachlor	Heptachlor	8.24 µM	6.81	BSK_hDFCGF_Proliferation_down	-	-	\
Heptachlor	Heptachlor	8.24 µM	7.3	BSK_hDFCGF_TIMP1_down	-	-	TIMP1
Heptachlor	Heptachlor	8.24 µM	6.05	BSK_hDFCGF_VCAM1_down	-	-	VCAM1
Heptachlor	Heptachlor	8.24 µM	3.36	NHEERL_ZF_144hpf_TERATOSCORE_up	-	-	\
Heptachlor	Heptachlor	8.24 µM	7.74	TOX21_AP1_BLA_Agonist_ch2	-	-	\
Heptachlor	Heptachlor	8.24 µM	5.97	TOX21_TSHR_HTRF_Agonist_ch1	-	-	\
Heptachlor	Heptachlor	8.24 µM	3.93	TOX21_TSHR_Agonist_ratio	-	-	TSHR
Hexachlorobenzene (HCB)	HCB	\ (no bioactive record)	\	\	\	\	\
Mirex	Mirex	0.04 µM	0.0114	BSK_LPS_PGE2_up	-	-	PTGER2
Toxaphene	Toxaphene	8.11 µM	4.23	TOX21_ERa_BLA_Antagonist_ratio	200	1181	ESR1
Toxaphene	Toxaphene	8.11 µM	4.27	TOX21_MMP_ratio_down	-	-	\
Toxaphene	Toxaphene	8.11 µM	4.33	TOX21_MMP_rhodamine	-	-	\
Toxaphene	Toxaphene	8.11 µM	7.28	TOX21_PPARg_BLA_Agonist_ch2	-	-	\
Toxaphene	Toxaphene	8.11 µM	5.43	TOX21_TR_LUC_GH3_Antagonist_viability	-	-	\
Toxaphene	Toxaphene	8.11 µM	4.74	TOX21_DT40	-	-	\
Toxaphene	Toxaphene	8.11 µM	4.99	TOX21_DT40_100	-	-	\
Toxaphene	Toxaphene	8.11 µM	3.4	TOX21_DT40_657	-	-	\
Polychlorinated biohenyls (PCB)*							
→ 2,2'-Dichlorobiphenyl	PCB_4	12.39 µM	11.9	TOX21_MMP_fitc			\
→ 2,2'-Dichlorobiphenyl	PCB_4	12.39 µM	6.93	TOX21_AP1_BLA_Agonist_ch2			\
→ 2,2',3,4',5,5',6-Heptachloro-1,1'-biphenyl	PCB_187	2.72 µM	0.000804	BSK_BE3C_MMP1_down	-	-	MMP1
→ 2,2',3,4',5,5',6-Heptachloro-1,1'-biphenyl	PCB_187	2.72 µM	1.34	BSK_BE3C_uPAR_up	-	-	PLAUR
→ 2,2',3,4',5,5',6-Heptachloro-1,1'-biphenyl	PCB_187	2.72 µM	0.06	BSK_CASM3C_Proliferation_up	-	-	\
→ 2,2',3,4',5,5',6-Heptachloro-1,1'-biphenyl	PCB_187	2.72 µM	0.12	BSK_CASM3C_SRB_down	-	-	\
→ 2,2',3,4',5,5',6-Heptachloro-1,1'-biphenyl	PCB_187	2.72 µM	0.61	BSK_CASM3C_uPAR_down	-	-	PLAUR
→ 2,2',3,4',5,5',6-Heptachloro-1,1'-biphenyl	PCB_187	2.72 µM	0.09	BSK_CASM3C_VCAM1_down	-	-	VCAM1
→ 2,2',3,4',5,5',6-Heptachloro-1,1'-biphenyl	PCB_187	2.72 µM	0.07	BSK_LPS_MCP1_down	-	-	CCL2
→ 2,2',3,4',5,5',6-Heptachloro-1,1'-biphenyl	PCB_187	2.72 µM	0.81	ATG_DR5_CIS_dn	-	-	RARB
→ 2,2',4,4',5,5'-Hexachlorobiphenyl	PCB_153	1000 µM	35.4	TOX21_TR_LUC_GH3_Antagonist	-	-	Thrb
→ 2,2',4,4',5,5'-Hexachlorobiphenyl	PCB_153	1000 µM	22.8	TOX21_AP1_BLA_Agonist_ch2	-	-	\
Polychlorinated dibenzo-p-dioxins (PCDD)*							

→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.279	TOX21_AR_BLA_Antagonist_viability	-	-	\
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.0004 43	TOX21_ERa_LUC_BG1_Antagonist_Specificity	200	1181	ESR1
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.0002 64	TOX21_AhR_LUC_Agonist	150	18	AHR
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.0004 14	TOX21_ARE_BLA_Agonist_ch2	-	-	\
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.0004 7	TOX21_ARE_BLA_agonist_ratio	-	-	NFE2L2
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.0017 3	TOX21_CAR_Agonist	107	715	NR1I3
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.0035 8	TOX21_ERa_LUC_BG1_Antagonist	200	1181	ESR1
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.0024 5	TOX21_PGC_ERR_Antagonist	-	-	ESRRA
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.165	TOX21_RT_HEK293_GLO_08hr_viability	-	-	\
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.245	TOX21_RT_HEK293_GLO_16hr_viability	-	-	\
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.245	TOX21_RT_HEK293_GLO_24hr_viability	-	-	\
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.245	TOX21_RT_HEK293_GLO_32hr_viability	-	-	\
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.245	TOX21_RT_HEK293_GLO_40hr_viability	-	-	\
→ 2,3,7,8-Tetrachlorodibenzodioxin (=TCDD)	TCDD	0.05 µM	0.0327	TOX21_RT_HEPG2_FLO_40hr_ctrl_viability	-	-	\
Polychlorinated dibenzofurans (PCDF)*							
→2,3,7,8-PCDF (no record in database)	2,3,7,8-PCDF	\	\	\	\	\	\
→1,2,3,7,8-Pentachlorodibenzofuran (no record in database)	1,2,3,7,8-PCDF	\	\	\	\	\	\
The 16 new POPs							
Alpha Hexachlorocyclohexane	aHCH	9.52 µM	(no AC50< =9.52)	\	\	\	\
Beta Hexachlorocyclohexane	bHCH	10.09 µM	5.78	ACEA_ER_80hr	200	1181	ESR1
Beta Hexachlorocyclohexane	bHCH	10.09 µM	2.53	ATG_DR5_CIS_up	-	-	RARB
Beta Hexachlorocyclohexane	bHCH	10.09 µM	0.863	ATG_ERE_CIS_up	200	1181	ESR1
Beta Hexachlorocyclohexane	bHCH	10.09 µM	1.6	ATG_PXRE_CIS_up	60	245	NR1I2
Beta Hexachlorocyclohexane	bHCH	10.09 µM	0.543	ATG_ERa_TRANS_up	200	1181	ESR1
Beta Hexachlorocyclohexane	bHCH	10.09 µM	0.909	ATG_PXR_TRANS_up	60	245	NR1I2
Beta Hexachlorocyclohexane	bHCH	10.09 µM	1.37E- 02	NVS_ENZ_hHDAC6	-	-	HDAC6
Beta Hexachlorocyclohexane	bHCH	10.09 µM	2.83	TOX21_ERa_LUC_BG1_Agonist	200	1181	ESR1
Beta Hexachlorocyclohexane	bHCH	10.09 µM	5.59	ATG_HIF1a_CIS_dn	-	-	HIF1A
Beta Hexachlorocyclohexane	bHCH	10.09 µM	3.76E- 02	TOX21_RT_HEK293_FLO_08hr_viability	-	-	\
Beta Hexachlorocyclohexane	bHCH	10.09 µM	2.75	TOX21_ERb_BLA_Agonist_ch2	-	-	\
Beta Hexachlorocyclohexane	bHCH	10.09 µM	2.85	TOX21_ERb_BLA_Agonist_ratio	-	-	ESR2
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7	APR_HepG2_MitoMemPot_24h_dn	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.4	ATG_AP_1_CIS_up	-	-	FOS
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.619	ATG_ERE_CIS_up	200	1181	ESR1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	4.17	ATG_GLI_CIS_up	-	-	GLI1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.73	ATG_NRF2_ARE_CIS_up	-	-	NFE2L2
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.727	ATG_PXRE_CIS_up	60	245	NR1I2
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.16	ATG_Sox_CIS_up	-	-	SOX1

Chlordecone (=Kepone)	Chlordecone	7.89 µM	2.18	ATG_VDRE_CIS_up	-	-	VDR
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.607	ATG_ERa_TRANS_up	200	1181	ESR1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	1.74	ATG_PXR_TRANS_up	60	245	NR1I2
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.2	ATG_RXRb_TRANS_up	-	-	RXRb
Chlordecone (=Kepone)	Chlordecone	7.89 µM	4.21	ATG_THRa1_TRANS_up	-	-	THRA
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.97	BSK_3C_HLADR_down	-	-	HLA-DRA
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.01	BSK_3C_Proliferation_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.15	BSK_3C_SRB_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.3	BSK_3C_TissueFactor_down	-	-	F3
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.26	BSK_3C_uPAR_down	-	-	PLAUR
Chlordecone (=Kepone)	Chlordecone	7.89 µM	4.92	BSK_3C_Vis_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.09	BSK_4H_Eotaxin3_down	-	-	CCL26
Chlordecone (=Kepone)	Chlordecone	7.89 µM	4.98	BSK_4H_MCP1_down	-	-	CCL2
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.55	BSK_4H_Pselectin_down	-	-	SELP
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.55	BSK_4H_SRB_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.73	BSK_4H_uPAR_down	-	-	PLAUR
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.97	BSK_4H_VCAM1_down	-	-	VCAM1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.49	BSK_4H_VEGFR1I_down	43	305	KDR
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.83	BSK_BE3C_HLADR_down	-	-	HLA-DRA
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.29	BSK_BE3C_IP10_down	-	-	CXCL10
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.76	BSK_BE3C_MIG_down	-	-	CXCL9
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.04	BSK_BE3C_MMP1_down	-	-	MMP1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.23	BSK_BE3C_PA11_down	-	-	SERPINE1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.24	BSK_BE3C_SRB_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	4.63	BSK_BE3C_TGFB1_down	-	-	TGFB1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	2.3	BSK_BE3C_tPA_down	-	-	PLAT
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.62	BSK_BE3C_uPA_down	-	-	PLAU
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.79	BSK_BE3C_uPAR_down	-	-	PLAUR
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.44	BSK_CASM3C_LDLR_down	-	-	LDLR
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.49	BSK_CASM3C_Proliferation_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.21	BSK_hDFCGF_CollagenIII_down	-	-	COL3A1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	1.31	BSK_hDFCGF_EGFR_down	-	-	EGFR
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.76	BSK_hDFCGF_IP10_down	-	-	CXCL10
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.66	BSK_hDFCGF_PA11_down	-	-	SERPINE1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	1.01	BSK_hDFCGF_Proliferation_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	4.18	BSK_hDFCGF_VCAM1_down	-	-	VCAM1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.4	BSK_KF3CT_MMP9_down	-	-	MMP9
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.82	BSK_KF3CT_SRB_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.7	BSK_KF3CT_TGFB1_down	-	-	TGFB1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.74	BSK_LPS_CD40_down	-	-	CD40
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.75	BSK_LPS_IL1a_down	-	-	IL1A
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.85	BSK_LPS_PGE2_down	-	-	PTGER2
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.17	BSK_LPS_SRB_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.83	BSK_LPS_VCAM1_down	-	-	VCAM1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.36	BSK_SAg_CD38_down	-	-	CD38
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.7	BSK_SAg_CD40_down	-	-	CD40
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.27	BSK_SAg_CD69_down	-	-	CD69
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.1	BSK_SAg_PBMCCytotoxicity_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.13	BSK_SAg_Proliferation_down	-	-	\

Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.97	BSK_SAg_SRB_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.796	NVS_ADME_hCYP2B6	-	-	CYP2B6
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.533	NVS_ADME_hCYP2C18	-	-	CYP2C18
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.341	NVS_ADME_hCYP2C19	-	-	CYP2C19
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.08	NVS_ADME_hCYP2C9	-	-	CYP2C9
Chlordecone (=Kepone)	Chlordecone	7.89 µM	1.54	NVS_ADME_rCYP2B1	-	-	Cyp2b1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.168	NVS_ADME_rCYP2C11	-	-	Cyp2c11
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5	NVS_ADME_rCYP2C6	-	-	Cyp2c6v1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.48	NVS_ADME_rCYP3A1	-	-	Cyp3a23/3a1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	1.14	NVS_ADME_rCYP3A2	-	-	Cyp3a2
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.41	NVS_ENZ_hMMP7	-	-	MMP7
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.137	NVS_GPCR_h5HT5A	-	-	HTR5A
Chlordecone (=Kepone)	Chlordecone	7.89 µM	1.63	NVS_GPCR_h5HT7	-	-	HTR7
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.115	NVS_GPCR_hAdoRA2a	-	-	ADORA2A
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.925	NVS_GPCR_hAdrb1	-	-	ADRB1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	1.16	NVS_GPCR_hDRD1	-	-	DRD1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	1.83	NVS_GPCR_hOpiate_mu	-	-	OPRM1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.57	NVS_NR_hER	200	1181	ESR1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.217	NVS_NR_hGR	66	654	NR3C1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.309	NVS_NR_mERa	200	1181	Esr1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.748	NVS_NR_rAR	187	1134	Ar
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.951	NVS_TR_hNET	-	-	SLC6A2
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.91	OT_ERa_EREGFP_0120	200	1181	ESR1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.39	OT_ERa_EREGFP_0480	200	1181	ESR1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.54	TOX21_ERa_BLA_Agonist_ch2	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.06	TOX21_ERa_LUC_BG1_Agonist	200	1181	ESR1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	0.913	TOX21_MMP_ratio_down	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	1.06	TOX21_MMP_rhodamine	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.34	Tanguay_ZF_120hpf_AXIS_up	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.25	Tanguay_ZF_120hpf_PIG_up	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.74	Tanguay_ZF_120hpf_TR_up	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.26	ATG_DR4_LXR_CIS_dn	58	167	NR1H3
Chlordecone (=Kepone)	Chlordecone	7.89 µM	2.72	ATG_E_Box_CIS_dn	-	-	USF1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	2.68	ATG_GRE_CIS_dn	66	654	NR3C1
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.72	ATG_STAT3_CIS_dn	-	-	STAT3
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.52	NHEERL_ZF_144hpf_TERATOSCORE_up	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	6.47	TOX21_AP1_BLA_Agonist_ch2	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.73	ACEA_ER_AUC_viability	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	7.78	ACEA_AR_antagonist_80hr	187	1134	AR
Chlordecone (=Kepone)	Chlordecone	7.89 µM	5.7	TOX21_ERb_BLA_Antagonist_ch2	-	-	\
Chlordecone (=Kepone)	Chlordecone	7.89 µM	3.64	TOX21_ERb_BLA_Antagonist_ratio	-	-	ESR2
Decabromodiphenyl ether (DecaBDE = BDE 209 = 1,1'-Oxybis(2,3,4,5,6-pentabromobenzene)	BDE209	1000 µM	0.311	NVS_ENZ_hPTEN_Activator	-	-	PTEN
Decabromodiphenyl ether (DecaBDE = BDE 209 = 1,1'-Oxybis(2,3,4,5,6-pentabromobenzene)	BDE209	1000 µM	6.45	ACEA_ER_AUC_viability	-	-	\
Hexabromobiphenyl	PBB-153	\ (no bioactive record)	\	\	\	\	\

Hexabromocyclododecane	HBCD	\ (no bioactive record)	\	\	\	\	\
Hexabromodiphenyl ether	PBDE-153	\ (no bioactive record)	\	\	\	\	\
Heptabromodiphenyl ether	PBDE-173	\ (no bioactive record)	\	\	\	\	\
Hexachlorobutadiene	HCBd	5.05 µM	4.96	BSK_CASM3C_Proliferation_down	-	-	\
Hexachlorobutadiene	HCBd	5.05 µM	2.51	BSK_CASM3C_SRB_down	-	-	\
Hexachlorobutadiene	HCBd	5.05 µM	0.152	BSK_CASM3C_Thrombomodulin_down	-	-	THBD
Hexachlorobutadiene	HCBd	5.05 µM	0.0033	BSK_CASM3C_TissueFactor_down	-	-	F3
Hexachlorobutadiene	HCBd	5.05 µM	1.45	BSK_hDFCGF_PA11_down	-	-	SERPINE1
Hexachlorobutadiene	HCBd	5.05 µM	0.0097	BSK_LPS_PGE2_up	-	-	PTGER2
Hexachlorobutadiene	HCBd	5.05 µM	0.0003	TOX21_p53_BLA_p5_ch2	-	-	\
Hexachlorobutadiene	HCBd	5.05 µM	0.0000	TOX21_p53_BLA_p5_ratio	-	-	TP53
Lindane	Lindane	8.51 µM	5.74	ATG_NRF2_ARE_CIS_up	-	-	NFE2L2
Lindane	Lindane	8.51 µM	5.86	ATG_PBREM_CIS_up	107	715	NR1I3
Lindane	Lindane	8.51 µM	5.68	ATG_PXRE_CIS_up	60	245	NR1I2
Lindane	Lindane	8.51 µM	6.52	ATG_VDRE_CIS_up	-	-	VDR
Lindane	Lindane	8.51 µM	6.68	NVS_TR_hDAT	-	-	SLC6A3
Lindane	Lindane	8.51 µM	1.43	CLD_CYP2B6_6hr	-	-	CYP2B6
Lindane	Lindane	8.51 µM	1.67	CLD_CYP2B6_24hr	-	-	CYP2B6
Lindane	Lindane	8.51 µM	2.29	CLD_CYP3A4_24hr	-	-	CYP3A4
Lindane	Lindane	8.51 µM	0.10	CLD_CYP2B6_48hr	-	-	CYP2B6
Lindane	Lindane	8.51 µM	0.588	CLD_CYP3A4_48hr	-	-	CYP3A4
Lindane	Lindane	8.51 µM	1.89	CLD_SULT2A_48hr	-	-	SULT2A1
Lindane	Lindane	8.51 µM	7.3	TOX21_TSHR_Agonist_ratio	-	-	TSHR
Pentachlorobenzene	PeCB	4.91 µM	0.104	ACEA_ER_80hr	200	1181	ESR1
Pentachlorobenzene	PeCB	4.91 µM	0.352	BSK_CASM3C_uPAR_up	-	-	PLAUR
Pentachlorophenol	PeCB	3.32 µM	2.45	ATG_PPRe_CIS_up	58	468	PPARA
Pentachlorophenol	PeCB	3.32 µM	2.5	ATG_PPARG_TRANS_up	163	1028	PPARG
Pentachlorophenol	PeCB	3.32 µM	1.12	BSK_BE3C_PA11_down	-	-	SERPINE1
Pentachlorophenol	PeCB	3.32 µM	2.97	BSK_BE3C_tPA_down	-	-	PLAT
Pentachlorophenol	PeCB	3.32 µM	2.08	BSK_hDFCGF_CollagenIII_down	-	-	COL3A1
Pentachlorophenol	PeCB	3.32 µM	2.95	BSK_hDFCGF_Proliferation_down	-	-	\
Pentachlorophenol	PeCB	3.32 µM	1.96	TOX21_MMP_ratio_down	-	-	\
Pentachlorophenol	PeCB	3.32 µM	2.02	TOX21_MMP_rhodamine	-	-	\
Pentachlorophenol	PeCB	3.32 µM	2.85	TOX21_AhR_LUC_Agonist	150	18	AHR
Pentachlorophenol	PeCB	3.32 µM	3.05	TOX21_FXR_BLA_antagonist_viability	-	-	\
Pentachlorophenol	PeCB	3.32 µM	0.657	TOX21_PPARG_BLA_antagonist_ratio	163	1028	PPARG
Pentachlorophenol	PeCB	3.32 µM	2.18	TOX21_FXR_BLA_agonist_viability	-	-	\
Pentachlorophenol	PeCB	3.32 µM	1.73	TOX21_PPARG_BLA_Agonist_viability	-	-	\
Pentachlorophenol	PeCB	3.32 µM	1.16	TOX21_PPARG_BLA_Antagonist_ch2	-	-	\
Pentachlorophenol	PeCB	3.32 µM	2.54	TOX21_p53_BLA_p2_ratio	-	-	TP53

Pentachlorophenol	PeCB	3.32 µM	1.36	TOX21_p53_BLA_p3_ch1	-	-	\
Pentachlorophenol	PeCB	3.32 µM	2.43	TOX21_p53_BLA_p3_ratio	-	-	TP53
Pentachlorophenol	PeCB	3.32 µM	0.588	Tanguay_ZF_120hpf_MORT_up	-	-	\
Pentachlorophenol	PeCB	3.32 µM	0.142	ATG_STAT3_CIS_dn	-	-	STAT3
Pentachlorophenol	PeCB	3.32 µM	0.623	NHEERL_ZF_144hpf_TERATOSCORE_up	-	-	\
Pentachlorophenol	PeCB	3.32 µM	0.556	Tanguay_ZF_120hpf_ActivityScore	-	-	\
Pentachlorophenol	PeCB	3.32 µM	0.958	NIS_RAIU_inhibition	-	-	SLC5A5
Pentachlorophenol	PeCB	3.32 µM	1.2	TOX21_HRE_BLA_Agonist_viability	-	-	\
Pentachlorophenol	PeCB	3.32 µM	0.118	NIS_HEK293T_CTG_Cytotoxicity	-	-	\
Pentachlorophenol	PeCB	3.32 µM	2.38	TOX21_ERb_BLA_Agonist_viability	-	-	\
Pentachlorophenol	PeCB	3.32 µM	2.91	TOX21_ERb_BLA_Antagonist_viability	-	-	\
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	5.43	APR_HepG2_p53Act_72h_up	-	-	TP53
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	5.82	ATG_NRF2_ARE_CIS_up	-	-	NFE2L2
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	5.85	BSK_LPS_IL8_up	-	-	CXCL8
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	4.14	NVS_ADME_hCYP19A1	153	964	CYP19A1
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	0.822	NVS_ADME_hCYP2C18	-	-	CYP2C18
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	4.91	NVS_ADME_hCYP2C19	-	-	CYP2C19
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	4.7	NVS_ADME_hCYP2C8	-	-	CYP2C8
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	0.0217	NVS_ADME_hCYP2C9	-	-	CYP2C9
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	1.53	NVS_ADME_hCYP4F12	-	-	CYP4F12
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	0.09	NVS_ADME_rCYP2C11	-	-	Cyp2c11
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	5.47	NVS_ENZ_hAMPKa1	-	-	PRKAA1
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	0.471	NVS_ENZ_hBACE	-	-	BACE1
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	0.406	NVS_ENZ_hCSF1R_Activator	-	-	CSF1R
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	1.73	NVS_ENZ_hMMP7	-	-	MMP7
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	5.39	NVS_ENZ_hPPP2CA	-	-	PPP2CA
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	0.0533	NVS_ENZ_hPTPN1	-	-	PTPN1
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	5.17	NVS_GPCR_hAdoRA2a	-	-	ADORA2A
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	2.27	NVS_NR_hGR	66	654	NR3C1
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	5.94	NVS_NR_hPPARg	163	1028	PPARG
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	4.27	NVS_NR_rAR	187	1134	Ar
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	0.547	Tanguay_ZF_120hpf_MORT_up	-	-	\
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	2.39	Tanguay_ZF_120hpf_AXIS_up	-	-	\
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	1.92	Tanguay_ZF_120hpf_TR_up	-	-	\
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	3.45	Tanguay_ZF_120hpf_ActivityScore	-	-	\
Perfluorooctane sulfonic acid (PFOS)	PFOS	7.21 µM	0.1	NIS_HEK293T_CTG_Cytotoxicity	-	-	\
Perfluorooctane sulfonyl fluoride (PFOSF) (no record in database)	PFOSF	\	\	\	\	\	\
Pentabromodiphenyl ether	PBDE-99	7.31 µM	4.69	TOX21_p53_BLA_p3_ch2	\	\	\
Tetrabromodiphenyl ether	PBDE-47	\ (no bioactive record)	\	\	\	\	\
Polychlorinated naphthalenes*							
→1-Chloronaphthalene	CINap	7.79 µM	(no AC50< 7.79 µM)	\	\	\	\
Technical endosulfan	t-Endosulfan	\ (no record in	\	\	\	\	\

		database)					
Endosulfan	Endosulfan	8.36 µM	0.894	ATG_DR5_CIS_up	-	-	RARB
Endosulfan	Endosulfan	8.36 µM	1.35	ATG_ERE_CIS_up	200	1181	ESR1
Endosulfan	Endosulfan	8.36 µM	1.24	ATG_PBREM_CIS_up	107	715	NR1I3
Endosulfan	Endosulfan	8.36 µM	1.12	ATG_PXRE_CIS_up	60	245	NR1I2
Endosulfan	Endosulfan	8.36 µM	1.73	ATG_ERa_TRANS_up	200	1181	ESR1
Endosulfan	Endosulfan	8.36 µM	4.89	NVS_ADME_hCYP2B6	-	-	CYP2B6
Endosulfan	Endosulfan	8.36 µM	1.92	NVS_ADME_hCYP2C19	-	-	CYP2C19
Endosulfan	Endosulfan	8.36 µM	0.164	NVS_NR_hCAR_Antagonist	107	715	NR1I3
Endosulfan	Endosulfan	8.36 µM	3.98	NVS_NR_hGR	66	654	NR3C1
Endosulfan	Endosulfan	8.36 µM	4.91	TOX21_ERa_LUC_BG1_Agonist	200	1181	ESR1
Endosulfan	Endosulfan	8.36 µM	3.5	NHEERL_ZF_144hpf_TERATOSCORE_up	-	-	\
Endosulfan	Endosulfan	8.36 µM	2.42	CLD_CYP2B6_6hr	-	-	CYP2B6
Endosulfan	Endosulfan	8.36 µM	2.56	CLD_CYP2B6_24hr	-	-	CYP2B6
Endosulfan	Endosulfan	8.36 µM	5.02	CLD_CYP3A4_24hr	-	-	CYP3A4
Endosulfan	Endosulfan	8.36 µM	4.46	CLD_UGT1A1_24hr	-	-	UGT1A1
Endosulfan	Endosulfan	8.36 µM	1.04	CLD_CYP2B6_48hr	-	-	CYP2B6
Endosulfan	Endosulfan	8.36 µM	4.59	CLD_CYP3A4_48hr	-	-	CYP3A4
Endosulfan	Endosulfan	8.36 µM	0.257	NHEERL_MHC_CellCount_up	-	-	\
Endosulfan	Endosulfan	8.36 µM	3.52	NHEERL_MHC_MHCvCellCount_dn	-	-	\
Endosulfan	Endosulfan	8.36 µM	6.47	TOX21_AP1_BLA_Agonist_ch2	-	-	\
Endosulfan	Endosulfan	8.36 µM	6.36	TOX21_TSHR_HTRF_Agonist_ch1	-	-	\
Endosulfan	Endosulfan	8.36 µM	4.91	TOX21_TSHR_Agonist_ratio	-	-	TSHR
Short chain chlorinated paraffins (SCCPs)*							
→ chlorinated paraffins: C12, 60% chlorine	clParaf	8.35 µM	3.09	ATG_DR5_CIS_up	-	-	RARB
→ chlorinated paraffins: C12, 60% chlorine	clParaf	8.35 µM	3.16	ATG_PBREM_CIS_up	107	715	NR1I3
→ chlorinated paraffins: C12, 60% chlorine	clParaf	8.35 µM	0.855	ATG_PXRE_CIS_up	60	245	NR1I2
→ chlorinated paraffins: C12, 60% chlorine	clParaf	8.35 µM	4.22	ATG_VDRE_CIS_up	-	-	VDR
→ chlorinated paraffins: C12, 60% chlorine	clParaf	8.35 µM	1.5	ATG_PXR_TRANS_up	60	245	NR1I2
→ chlorinated paraffins: C12, 60% chlorine	clParaf	8.35 µM	0.0016 5	TOX21_RT_HEK293_FLO_24hr_viability	-	-	\
→ chlorinated paraffins: C12, 60% chlorine	clParaf	8.35 µM	0.0016 5	TOX21_RT_HEK293_FLO_32hr_viability	-	-	\
→ chlorinated paraffins: C12, 60% chlorine	clParaf	8.35 µM	0.0016 5	TOX21_RT_HEK293_FLO_40hr_viability	-	-	\

Tab. S2: List of protein-protein associations from the POP-PPAN model

Protein	Protein	oS (overlapping score)
ESR1	NR1I2	8
RARB	NR1I2	7
RARB	ESR1	6
VDR	NR1I2	5
CYP2B6	NR1I2	5
RARB	RARG	4
NR3C1	CYP2C19	4
SERPINE1	COL3A1	4
RARG	ESR1	4
RARG	NR1I2	4
TSHR	CYP2B6	4
TSHR	NR1I2	4
CYP2C19	ESR1	4
CYP2C19	CYP2B6	4
CYP2C19	NR1I2	4
ESR1	CYP2B6	4
MMP1	VCAM1	3
NFE2L2	NR3C1	3
NFE2L2	VDR	3
NFE2L2	AR	3
NFE2L2	CYP2C19	3
NFE2L2	ESR1	3
NFE2L2	CYP2B6	3
NFE2L2	NR1I2	3
RARB	TSHR	3
RARB	VDR	3
RARB	CYP2C19	3
RARB	CYP2B6	3
NR3C1	AR	3
NR3C1	ESR1	3
NR3C1	CYP2B6	3
NR3C1	NR1I2	3
SERPINE1	VCAM1	3
SERPINE1	CXCL10	3
SERPINE1	ESR1	3
TSHR	CYP2C19	3
TSHR	ESR1	3
VCAM1	COL3A1	3
VCAM1	CXCL10	3
VDR	ESR1	3
VDR	CYP2B6	3
ESR2	ESR1	3
ESR2	NR1I2	3
COL3A1	CXCL10	3
COL3A1	ESR1	3
AR	CYP2C19	3
NR1I3	NR1I2	3

Tab. S3: Adverse outcome pathways (name, AOP-wiki ID) and the events (name, AOP-wiki ID) for the identified proteins

Protein	AOP ID	AOP name	Event ID	Event type	Event name
AR	19	Androgen_receptor_antagonism_leading_to_adverse_effects_in_the_male_foetus_(mammals)	286	KE	Decreased, Transcription of genes by AR
AR	288	Inhibition_of_17a-hydrolase/C_10,20-lyase_(Cyp17A1)_activity_leads_to_birth_reproductive_defects_(cryptorchidism)_in_male_(mammals)	1614	KE	Decrease, androgen receptors (AR) activation
AR	187	Anticoagulant_rodenticide_inhibition_of_vitamin_K_epoxide_reductase_resulting_coagulopathy_and_hemorrhage	1134	MIE	Irreversible inhibition of hepatic VKOR by binding of AR at tyrosine 139, Failure to cycle vitamin K epoxide to vitamin K to form vitamin K hydroquinone
ESR1	29	Estrogen_receptor_agonism_leading_to_reproductive_dysfunction	111	MIE	Agonism, Estrogen receptor
ESR1	30	Estrogen_receptor_antagonism_leading_to_reproductive_dysfunction	112	MIE	Antagonism, Estrogen receptor
ESR1	52	ER_agonism_leading_to_skewed_sex_ratios_due_to_altered_sexual_differentiation_in_males	111	MIE	Agonism, Estrogen receptor
ESR1	112	Increased_dopaminergic_activity_leading_to_endometrial_adenocarcinomas_(in_Wistar_rat)	748	KE	Increased, Estrogen receptor (ER) activity
ESR1	167	Early-life_estrogen_receptor_activity_leading_to_endometrial_carcinoma_in_the_mouse	1064	MIE	prepubertal increase, Estrogen receptor (ER) activity
ESR1	200	Estrogen_receptor_activation_leading_to_breast_cancer	1181	MIE	Activation, Estrogen receptor
ESR1	167	Early-life_estrogen_receptor_activity_leading_to_endometrial_carcinoma_in_the_mouse.	1065	KE	Activation, estrogen receptor alpha
ESR2	29	Estrogen_receptor_agonism_leading_to_reproductive_dysfunction	111	MIE	Agonism, Estrogen receptor
ESR2	30	Estrogen_receptor_antagonism_leading_to_reproductive_dysfunction	112	MIE	Antagonism, Estrogen receptor
ESR2	52	ER_agonism_leading_to_skewed_sex_ratios_due_to_altered_sexual_differentiation_in_males	111	MIE	Agonism, Estrogen receptor
ESR2	112	Increased_dopaminergic_activity_leading_to_endometrial_adenocarcinomas_(in_Wistar_rat)	748	KE	Increased, Estrogen receptor (ER) activity
ESR2	167	Early-life_estrogen_receptor_activity_leading_to_endometrial_carcinoma_in_the_mouse	1064	MIE	prepubertal increase, Estrogen receptor (ER) activity
ESR2	200	Estrogen_receptor_activation_leading_to_breast_cancer	1181	MIE	Activation, Estrogen receptor
NR112	11	Percellome_Toxicogenomics_Approach_for_AOP_Building:_Case_study_on_Pentachlorophenol	245	MIE	Activation, PXR/SXR
NR112	60	NR112_(Pregnane_X_Receptor,_PXR)_activation_leading_to_hepatic_steatosis	245	MIE	Activation, PXR/SXR
NR113	107	Constitutive_androstane_receptor_activation_leading_to_hepatocellular_adenomas_and_carcinomas_in_the_mouse_and_the_rat	715	MIE	Activation, Constitutive androstane receptor
NR113	58	NR113_(CAR)_suppression_leading_to_hepatic_steatosis	456	MIE	Suppression, Constitutive androstane receptor, NR113
NR3C1	66	Modulation_of_Adult_Leydig_Cell_Function_Subsequent_Glucocorticoid_Activation_in_the_Fetal_Testis	654	MIE	Decreased testosterone by the fetal Leydig cells, Activation by other glucocorticoid receptor agonists
NR3C1	14	Glucocorticoid_Receptor_Activation_Leading_to_Increased_Disease_Susceptibility	122	MIE	Activation, Glucocorticoid Receptor

NR3C1	64	Glucocorticoid_Receptor_(GR)_Mediated_Adult_Leydig_Cell_Dysfunction_Leading_to_Deceased_Male_Fertility	494	MIE	Glucocorticoid Receptor Agonist, Activation
NR3C1	71	Modulation_of_Adult_Leydig_Cell_Function_Subsequent_to_Glucocorticoid_Activation	651	KE	Glucocorticoid Receptor mediated alterations in steroidogenic enzymes, Decreased testosterone by adult Leydig cells
NR3C1	214	Network_of_SSRI_s_(selective_serotonin_reuptake_inhibitors)	122	KE	Activation, Glucocorticoid Receptor
NR3C1	221	Mental_stress_to_depression	1396	MIE	Increased, glucocorticoid receptor activity
NR3C1	222	Mental_stress_to_agitation	1396	MIE	Increased, glucocorticoid receptor activity
CXCL10	39	Sensitisation_of_the_Respiratory_Tract_induced_by_Covalent_Binding_of_Low_Molecular_Weight_Organic_Chemicals_to_Proteins	151	KE	Activation, Inflammatory cytokines, chemokines, cytoprotective gene pathways

Tab. S4: Dicofol

Tab. S4a: Compiled known proteins linked to dicofol

Gene symbol*	Gene name	Entrez gene
AR	androgen receptor	367
CCL2	C-C motif chemokine ligand 2	6347
COL3A1	collagen type III alpha 1 chain	1281
CSF1	colony stimulating factor 1	1435
CXCL10	C-X-C motif chemokine ligand 10	3627
CYP1A1	cytochrome P450 family 1 subfamily A member 1	1543
CYP2B6	cytochrome P450 family 2 subfamily B member 6	1555
CYP2C19	cytochrome P450 family 2 subfamily C member 19	1557
CYP2C9	cytochrome P450 family 2 subfamily C member 9	1559
CYP3A4	cytochrome P450 family 3 subfamily A member 4	1576
ESR1	estrogen receptor 1	2099
ESR2	estrogen receptor 2	2100
IL1A	interleukin 1 alpha	3552
MMP1	matrix metalloproteinase 1	4312
MMP9	matrix metalloproteinase 9	4318
NFE2L2	nuclear factor, erythroid 2 like 2	4780
NR112	nuclear receptor subfamily 1 group I member 2	8856
NR113	nuclear receptor subfamily 1 group I member 3	9970
NR3C1	nuclear receptor subfamily 3 group C member 1	2908
RARB	retinoic acid receptor beta	5915
RARG	retinoic acid receptor gamma	5916
SERPINE1	serpin family E member 1	5054
SULT2A1	sulfotransferase family 2A member 1	6822
THBD	thrombomodulin	7056
TIMP1	TIMP metalloproteinase inhibitor 1	7076
TSHR	thyroid stimulating hormone receptor	7253
VCAM1	vascular cell adhesion molecule 1	7412
VDR	vitamin D receptor	7421

*in bold are the ones extracted from ToxCast

Tab. S4b: Predicted proteins using the POP-PPAN model

Protein	Protein	binS
RARB	NR1I2	-1.146128036
RARB	CYP2B6	-1.079181246
RARB	CYP2C19	-1.204119983
ESR1	NR1I2	-0.77815125
ESR1	CYP2B6	-1
ESR1	CYP2C19	-1.079181246
ESR1	NR3C1	-1.204119983
AR	NR1I2	-1.380211242
NFE2L2	NR1I2	-1.204119983
NFE2L2	CYP2B6	-0.903089987
NFE2L2	CYP2C19	-1.079181246
NFE2L2	NR3C1	-0.77815125
NR1I2	VDR	-1.255272505
NR1I2	ESR2	-1.380211242
NR1I2	RARG	-1.342422681
NR1I2	CYP2B6	-1.079181246
NR1I2	CYP2C19	-1.146128036
NR1I2	NR3C1	-1.255272505
NR1I2	NR1I3	-1.414973348
NR1I2	TSHR	-1.255272505
VDR	CYP2B6	-1
VCAM1	COL3A1	-0.77815125
VCAM1	CXCL10	-0.77815125
VCAM1	MMP1	-1
VCAM1	SERPINE1	-0.77815125
COL3A1	CXCL10	-0.602059991
COL3A1	SERPINE1	-0.602059991
CXCL10	SERPINE1	-0.602059991
CYP2B6	CYP2C19	-0.77815125
CYP2B6	NR3C1	-1
CYP2B6	TSHR	-1
CYP2C19	NR3C1	-0.903089987
CYP2C19	TSHR	-0.903089987
CCL2	Ni*	
COL3A1	Ni	
CYP3A4	Ni	
IL1A	Ni	
THBD	Ni	

* Ni = No interacting protein in the model

Tab. S4c: Linkage of known and predicted proteins to adverse outcome pathways (AOPs) and their corresponding events (MIE, molecular initiative event; KE, key event)

Protein	AOP ID*	AOP name	Event ID*	Event type	Event name
AR	19	Androgen_receptor_antagonism_leading_to_adverse_effects_in_the_male_foetus_(mammals)	286	KE	Decreased, Transcription of genes by AR
AR	288	Inhibition_of_17a-hydrolase/C_10,20-lyase_(Cyp17A1)_activity_leads_to_birth_reproductive_defects_(cryptorchidism)_in_male_(mammals)	1614	KE	Decrease, androgen receptors (AR) activation
AR	187	Anticoagulant_rodenticide_inhibition_of_vitamin_K_epoxide_reductase_resulting_coagulopathy_and_hemorrhage	1134	MIE	Irreversible inhibition of hepatic VKOR by binding of AR at tyrosine 139, Failure to cycle vitamin K epoxide to vitamin K to form vitamin K hydroquinone
ESR1	29	Estrogen_receptor_agonism_leading_to_reproductive_dysfunction	111	MIE	Agonism, Estrogen receptor
ESR1	30	Estrogen_receptor_antagonism_leading_to_reproductive_dysfunction	112	MIE	Antagonism, Estrogen receptor
ESR1	52	ER_agonism_leading_to_skewed_sex_ratios_due_to_altered_sexual_differentiation_in_males	111	MIE	Agonism, Estrogen receptor
ESR1	112	Increased_dopaminergic_activity_leading_to_endometrial_adenocarcinomas_(in_Wistar_rat)	748	KE	Increased, Estrogen receptor (ER) activity
ESR1	167	Early-life_estrogen_receptor_activity_leading_to_endometrial_carcinoma_in_the_mouse	1064	MIE	prepubertal increase, Estrogen receptor (ER) activity
ESR1	200	Estrogen_receptor_activation_leading_to_breast_cancer	1181	MIE	Activation, Estrogen receptor
ESR1	167	Early-life_estrogen_receptor_activity_leading_to_endometrial_carcinoma_in_the_mouse.	1065	KE	Activation, estrogen receptor alpha
ESR2	29	Estrogen_receptor_agonism_leading_to_reproductive_dysfunction	111	MIE	Agonism, Estrogen receptor
ESR2	30	Estrogen_receptor_antagonism_leading_to_reproductive_dysfunction	112	MIE	Antagonism, Estrogen receptor
ESR2	52	ER_agonism_leading_to_skewed_sex_ratios_due_to_altered_sexual_differentiation_in_males	111	MIE	Agonism, Estrogen receptor
ESR2	112	Increased_dopaminergic_activity_leading_to_endometrial_adenocarcinomas_(in_Wistar_rat)	748	KE	Increased, Estrogen receptor (ER) activity
ESR2	167	Early-life_estrogen_receptor_activity_leading_to_endometrial_carcinoma_in_the_mouse	1064	MIE	prepubertal increase, Estrogen receptor (ER) activity
ESR2	200	Estrogen_receptor_activation_leading_to_breast_cancer	1181	MIE	Activation, Estrogen receptor
NR112	11	Percellome_Toxicogenomics_Approach_for_AOP_Building:_Case_study_on_Pentachlorophenol	245	MIE	Activation, PXR/SXR
NR112	60	NR112_(Pregnane_X_Receptor,_PXR)_activation_leading_to_hepatic_steatosis	245	MIE	Activation, PXR/SXR
NR113	107	Constitutive_androstane_receptor_activation_leading_to_hepatocellular_adenomas_and_carcinomas_in_the_mouse_and_the_rat	715	MIE	Activation, Constitutive androstane receptor
NR113	58	NR113_(CAR)_suppression_leading_to_hepatic_steatosis	456	MIE	Suppression, Constitutive androstane receptor, NR113
NR3C1	66	Modulation_of_Adult_Leydig_Cell_Function_Subsequent_Glucocorticoid_Activation_in_the_Fetal_Testis	654	MIE	Decreased testosterone by the fetal Leydig cells, Activation by other glucocorticoid receptor agonists
NR3C1	14	Glucocorticoid_Receptor_Activation_Leading_to_Increased_Disease_Susceptibility	122	MIE	Activation, Glucocorticoid Receptor

NR3C1	64	Glucocorticoid_Receptor_(GR)_Mediated_Adult_Leydig_Cell_Dysfunction_Leading_to_Decreased_Male_Fertility	494	MIE	Glucocorticoid Receptor Agonist, Activation
NR3C1	71	Modulation_of_Adult_Leydig_Cell_Function_Subsequent_to_Glucocorticoid_Activation	651	KE	Glucocorticoid Receptor mediated alterations in steroidogenic enzymes, Decreased testosterone by adult Leydig cells
NR3C1	214	Network_of_SSRI_s_(selective_serotonin_reuptake_inhibitors)	122	KE	Activation, Glucocorticoid Receptor
NR3C1	221	Mental_stress_to_depression	1396	MIE	Increased, glucocorticoid receptor activity
NR3C1	222	Mental_stress_to_agitation	1396	MIE	Increased, glucocorticoid receptor activity
CXCL10	39	Sensitisation_of_the_Respiratory_Tract_induced_by_Covalent_Binding_of_Low_Molecular_Weight_Organic_Chemicals_to_Proteins	151	KE	Activation, Inflammatory cytokines, chemokines, cytoprotective gene pathways

*ID are the one extracted from the AOP-wiki database

Tab. 5: Results from the biological and disease enrichments for dicofol

KEGG					
description of the pathways	size	overlap	pValue	FDR	Proteins from the input set
AGE-RAGE signaling pathway in diabetic complications	99	6	6.73E-07	2.19E-04	CCL2;COL3A1;IL1A;SERPINE1;THBD;VCAM1
Metabolism of xenobiotics by cytochrome P450	76	5	4.33E-06	5.14E-04	CYP1A1;CYP2B6;CYP2C9;CYP3A4;SULT2A1
Fluid shear stress and atherosclerosis	139	6	4.94E-06	5.14E-04	CCL2;IL1A;MMP9;NFE2L2;THBD;VCAM1
Chemical carcinogenesis	82	5	6.31E-06	5.14E-04	CYP1A1;CYP2C19;CYP2C9;CYP3A4;SULT2A1
TNF signaling pathway	110	5	2.66E-05	0.001732164	CCL2;CSF1;CXCL10;MMP9;VCAM1
Retinol metabolism	67	4	6.49E-05	0.00352771	CYP1A1;CYP2B6;CYP2C9;CYP3A4
Drug metabolism	72	4	8.62E-05	0.004013052	CYP2B6;CYP2C19;CYP2C9;CYP3A4
Linoleic acid metabolism	29	3	1.14E-04	0.00465793	CYP2C19;CYP2C9;CYP3A4
Rheumatoid arthritis	90	4	2.06E-04	0.007443792	CCL2;CSF1;IL1A;MMP1
IL-17 signaling pathway	93	4	2.33E-04	0.007603576	CCL2;CXCL10;MMP1;MMP9
Arachidonic acid metabolism	63	3	0.001152388	0.034152585	CYP2B6;CYP2C19;CYP2C9
Pathways in cancer	526	7	0.001297519	0.03524928	AR;ESR1;ESR2;MMP1;MMP9;NFE2L2;RARB
Endocrine resistance	98	3	0.004085957	0.102463221	ESR1;ESR2;MMP9
Bladder cancer	41	2	0.008143055	0.189616852	MMP1;MMP9
Relaxin signaling pathway	130	3	0.008957419	0.194674564	COL3A1;MMP1;MMP9
Estrogen signaling pathway	137	3	0.010335941	0.203351483	ESR1;ESR2;MMP9
Endocrine and other factor-regulated calcium reabsorption	47	2	0.010604218	0.203351483	ESR1;VDR
Malaria	49	2	0.011489152	0.208081302	CCL2;VCAM1
Cytokine-cytokine receptor interaction	294	4	0.015477909	0.265568333	CCL2;CSF1;CXCL10;IL1A
Steroid hormone biosynthesis	60	2	0.016908955	0.275615968	CYP1A1;CYP3A4
Reactome					
description of the pathways	size	overlap	pValue	FDR	Proteins from the input set
Nuclear Receptor transcription pathway	50	9	2.44E-15	4.22E-12	AR;ESR1;ESR2;NR1I2;NR1I3;NR3C1;RARB;RARG;VDR
Xenobiotics	24	5	3.05E-09	2.63E-06	CYP1A1;CYP2B6;CYP2C19;CYP2C9;CYP3A4

SUMOylation of intracellular receptors	30	5	1.01E-08	5.82E-06	AR;ESR1;NR1I2;NR3C1;VDR
Interleukin-10 signaling	47	5	1.06E-07	4.56E-05	CCL2;CSF1;CXCL10;IL1A;TIMP1
Interleukin-4 and Interleukin-13 signaling	108	6	2.48E-07	8.58E-05	CCL2;IL1A;MMP1;MMP9;TIMP1;VCAM1
Cytochrome P450 - arranged by substrate type	66	5	5.95E-07	1.71E-04	CYP1A1;CYP2B6;CYP2C19;CYP2C9;CYP3A4
Synthesis of epoxy (EET) and dihydroyeicosatrienoic acids (DHET)	8	3	8.29E-07	2.05E-04	CYP1A1;CYP2C19;CYP2C9
Synthesis of (16-20)-hydroxyeicosatetraenoic acids (HETE)	9	3	1.24E-06	2.68E-04	CYP1A1;CYP2C19;CYP2C9
CYP2E1 reactions	11	3	2.43E-06	4.67E-04	CYP2B6;CYP2C19;CYP2C9
Phase I - Functionalization of compounds	107	5	6.59E-06	0.001138889	CYP1A1;CYP2B6;CYP2C19;CYP2C9;CYP3A4
Biosynthesis of DHA-derived SPMs	17	3	9.91E-06	0.001557508	CYP1A1;CYP2C9;CYP3A4
Signaling by Interleukins	462	8	1.35E-05	0.001871597	CCL2;CSF1;CXCL10;IL1A;MMP1;MMP9;TIMP1;VCAM1
Biosynthesis of specialized proresolving mediators (SPMs)	19	3	1.41E-05	0.001871597	CYP1A1;CYP2C9;CYP3A4
Biological oxidations	223	6	1.70E-05	0.002096257	CYP1A1;CYP2B6;CYP2C19;CYP2C9;CYP3A4;SULT2A1
Activation of Matrix Metalloproteinases	33	3	7.74E-05	0.008852913	MMP1;MMP9;TIMP1
SUMO E3 ligases SUMOylate target proteins	181	5	8.34E-05	0.008852913	AR;ESR1;NR1I2;NR3C1;VDR
Extracellular matrix organization	301	6	9.14E-05	0.008852913	COL3A1;MMP1;MMP9;SERPINE1;TIMP1;VCAM1
Biosynthesis of maresin-like SPMs	6	2	9.39E-05	0.008852913	CYP2C9;CYP3A4
SUMOylation	187	5	9.73E-05	0.008852913	AR;ESR1;NR1I2;NR3C1;VDR
Biosynthesis of maresins	8	2	1.75E-04	0.015104215	CYP2C9;CYP3A4
GO biological process					
GO ID	GO name	nb of proteins from the input set involved			
GO:0008152	metabolic process	27			
GO:0050896	response to stimulus	27			
GO:0065007	biological regulation	25			
GO:0007154	cell communication	21			
GO:0032501	multicellular organismal process	20			
GO:0032502	developmental process	18			
GO:0016043	cellular component organization	16			
GO:0051179	localization	15			
GO:0008283	cell proliferation	14			
GO:0051704	multi-organism process	13			
GO:0000003	reproduction	10			
GO:0040007	growth	6			
GO molecular function					
GO ID	GO name	nb of proteins from the input set involved			
GO:0005515	protein binding	25			
GO:0043167	ion binding	21			

GO:0060089	molecular transducer activity	11			
GO:0003676	nucleic acid binding	10			
GO:0008289	lipid binding	6			
GO:0030234	enzyme regulator activity	4			
GO:0016740	transferase activity	3			
GO:0019825	oxygen binding	3			
GO:0003682	chromatin binding	2			
GO:0016787	hydrolase activity	2			
GO:0005198	structural molecule activity	1			
GO cellular component					
GO ID	GO name	nb of proteins from the input set involved			
GO:0005515	protein binding	25			
GO:0043167	ion binding	21			
GO:0060089	molecular transducer activity	11			
GO:0003676	nucleic acid binding	10			
GO:0008289	lipid binding	6			
GO:0030234	enzyme regulator activity	4			
GO:0016740	transferase activity	3			
GO:0019825	oxygen binding	3			
GO:0003682	chromatin binding	2			
GO:0016787	hydrolase activity	2			
GO:0005198	structural molecule activity	1			
DisGeNET					
disease names	size	overlap	pValue	FDR	Proteins from the input set
Depressive Symptoms	30	6	3.02E-10	1.11E-06	CYP1A1;CYP3A4;MMP9;SERPINE1;TIMP1;VDR
Prostatic Neoplasms	492	12	9.24E-09	1.15E-05	AR;CYP1A1;CYP2C19;CYP3A4;ESR1;ESR2;MMP9;NFE2L2;NR3C1;SERPINE1;SULT2A1;VDR
Chemical and Drug Induced Liver Injury	212	9	9.41E-09	1.15E-05	CCL2;COL3A1;CXCL10;CYP2C19;CYP2C9;IL1A;NFE2L2;NR1I2;NR1I3
Hypertensive disease	302	10	1.29E-08	1.18E-05	AR;CCL2;COL3A1;CYP1A1;MMP9;NR3C1;SERPINE1;TIMP1;VCAM1;VDR
Mammary Neoplasms	448	10	5.29E-07	3.88E-04	AR;CSF1;CYP1A1;CYP3A4;ESR1;ESR2;MMP1;MMP9;RARB;VDR
Atherosclerosis	59	5	9.25E-07	5.67E-04	CCL2;ESR1;MMP1;SERPINE1;VCAM1
Astrocytoma	29	4	1.74E-06	7.98E-04	AR;ESR1;ESR2;MMP9
Female infertility	29	4	1.74E-06	7.98E-04	AR;ESR1;ESR2;NR1I2
Prostatic Intraepithelial Neoplasias	11	3	4.48E-06	0.001659081	AR;ESR1;ESR2
Pulmonary Fibrosis	81	5	4.52E-06	0.001659081	CCL2;COL3A1;MMP9;NFE2L2;TIMP1

Unipolar Depression	256	7	1.03E-05	0.003225043	CCL2;CXCL10;CYP2C19;CYP2C9;ESR2;NR3C1;SERPINE1
Kidney Failure, Chronic	45	4	1.05E-05	0.003225043	CCL2;CYP2B6;CYP2C19;SERPINE1
Major Depressive Disorder	262	7	1.20E-05	0.003400027	CCL2;CXCL10;CYP2C19;CYP2C9;ESR2;NR3C1;SERPINE1
Oral Submucous Fibrosis	16	3	1.50E-05	0.003944437	MMP1;MMP9;TIMP1
Endometrial Neoplasms	53	4	2.03E-05	0.00498405	CCL2;ESR1;ESR2;NFE2L2
Metabolic Syndrome X	20	3	3.03E-05	0.006967248	CCL2;NR1I2;NR1I3
Liver carcinoma	244	6	8.88E-05	0.019186412	AR;CYP1A1;ESR1;MMP9;NFE2L2;VCAM1
Lead Poisoning	6	2	1.41E-04	0.028784564	MMP9;VDR
Diabetic Nephropathy	35	3	1.69E-04	0.032640524	CCL2;NFE2L2;SERPINE1
Brain Ischemia	92	4	1.79E-04	0.032796184	CCL2;CXCL10;IL1A;MMP9

Tab. S6: Perfluorooctanoic acid (PFOA)

Tab. S6a: Compiled known proteins linked to PFOA

Gene symbol*	Gene name	Entrez gene
ACP1	acid phosphatase 1	52
BACE1	beta-secretase 1	23621
CYP2A2	cytochrome P450 family 2 subfamily A member 2	24895
CYP2B6	cytochrome P450 family 2 subfamily B member 6	1555
CYP2C11	cytochrome P450 family 2 subfamily C member 11	29277
CYP2C19	cytochrome P450 family 2 subfamily C member 19	1557
ESR1	estrogen receptor 1	2099
GSTA2	glutathione S-transferase alpha 2	2939
NFE2L2	nuclear factor, erythroid 2 like 2	4780
NR1I2	nuclear receptor subfamily 1 group I member 2	8856
NR3C1	nuclear receptor subfamily 3 group C member 1	2908
PLAUR	plasminogen activator, urokinase receptor	5329
PPP1CA	protein phosphatase 1 catalytic subunit alpha	5499
RARB	retinoic acid receptor beta	5915
RORA	RAR related orphan receptor A	6095
TSHR	thyroid stimulating hormone receptor	7253
VDR	vitamin D receptor	7421

*in bold are the ones extracted from ToxCast

Tab. S6b: Predicted proteins using the POP-PPAN model

Protein	Protein	binS
RARB	CYP2B6	-1.079181246
ESR1	CYP2B6	-1
NFE2L2	CYP2B6	-0.903089987
NR1I2	CYP2B6	-1.079181246
VDR	CYP2B6	-1
CYP2B6	CYP2C19	-0.77815125
CYP2B6	NR3C1	-1
CYP2B6	TSHR	-1
ACP1	Ni	
BACE1	Ni	
CYP2A2	Ni	
CYP2C11	Ni	
GSTA2	Ni	
PLAUR	Ni	
PPP1CA	Ni	
RORA	Ni	

* Ni = No interacting protein in the model

Tab. S6c: Linkage of known and predicted proteins to AOPs

Protein	AOP ID*	AOP name	Event ID*	Event type	Event name
NR1I2	60	NR1I2 (Pregnane X Receptor, PXR) activation leading to hepatic steatosis	245	MIE	Activation, PXR/SXR
ESR1	200	Estrogen_receptor_activation_leading_to_breast_cancer	1181	MIE	Activation, Estrogen receptor
NR3C1	66	Modulation_of_Adult_Leydig_Cell_Function_Subsequent_Glucocorticoid_Activation_in_the_Fetal_Testis	654	MIE	Decreased testosterone by the fetal Leydig cells, Activation by other glucocorticoid receptor agonists

*ID are the ones extracted from the AOP-wiki database

Tab. S7: Results from the biological and disease enrichments for PFOA

KEGG					
description of the pathways	size	overlap	pValue	FDR	Proteins from the input set
Drug metabolism	72	3	2.90E-04	0.094455406	CYP2B6;CYP2C19;GSTA2
Endocrine and other factor-regulated calcium reabsorption	47	2	0.003361219	0.486514945	ESR1;VDR
Proteoglycans in cancer	201	3	0.005613113	0.486514945	ESR1;PLAUR;PPP1CA
Arachidonic acid metabolism	63	2	0.005969509	0.486514945	CYP2B6;CYP2C19
Metabolism of xenobiotics by cytochrome P450	76	2	0.008591001	0.540441433	CYP2B6;GSTA2
Chemical carcinogenesis	82	2	0.009946775	0.540441433	CYP2C19;GSTA2
Pathways in cancer	526	4	0.01378901	0.607348012	ESR1;GSTA2;NFE2L2;RARB
Riboflavin metabolism	8	1	0.014904246	0.607348012	ACP1
Fluid shear stress and atherosclerosis	139	2	0.027030202	0.965025253	GSTA2;NFE2L2
Thiamine metabolism	16	1	0.029602002	0.965025253	ACP1
Hepatocellular carcinoma	168	2	0.038331897	1	GSTA2;NFE2L2
cAMP signaling pathway	199	2	0.052086639	1	PPP1CA;TSHR
Linoleic acid metabolism	29	1	0.053052251	1	CYP2C19
Circadian rhythm	31	1	0.056612919	1	RORA
Mineral absorption	51	1	0.091542215	1	VDR
Neuroactive ligand-receptor interaction	277	2	0.093035307	1	NR3C1;TSHR
Autoimmune thyroid disease	53	1	0.094968277	1	TSHR

Regulation of lipolysis in adipocytes	54	1	0.096676805	1	TSHR
Glutathione metabolism	56	1	0.100084879	1	GSTA2
Inflammatory bowel disease (IBD)	65	1	0.11527398	1	RORA
Reactome					
description of the pathways	size	overlapp	pValue	FDR	Proteins from the input set
Nuclear Receptor transcription pathway	50	6	1.39E-11	2.40E-08	ESR1;NR1I2;NR3C1;RARB;RORA;VDR
SUMOylation of intracellular receptors	30	5	1.66E-10	1.43E-07	ESR1;NR1I2;NR3C1;RORA;VDR
SUMO E3 ligases SUMOylate target proteins	181	5	1.62E-06	8.20E-04	ESR1;NR1I2;NR3C1;RORA;VDR
SUMOylation	187	5	1.90E-06	8.20E-04	ESR1;NR1I2;NR3C1;RORA;VDR
Circadian Clock	70	3	7.62E-05	0.022048019	NR3C1;PPP1CA;RORA
CYP2E1 reactions	11	2	7.66E-05	0.022048019	CYP2B6;CYP2C19
Xenobiotics	24	2	3.81E-04	0.093982086	CYP2B6;CYP2C19
Generic Transcription Pathway	1169	6	0.001571062	0.339349384	ESR1;NR1I2;NR3C1;RARB;RORA;VDR
Biological oxidations	223	3	0.002275852	0.43696365	CYP2B6;CYP2C19;GSTA2
RNA Polymerase II Transcription	1292	6	0.002655856	0.45143648	ESR1;NR1I2;NR3C1;RARB;RORA;VDR
Cytochrome P450 - arranged by substrate type	66	2	0.002873728	0.45143648	CYP2B6;CYP2C19
Regulation of RUNX2 expression and activity	73	2	0.003503746	0.504539369	ESR1;NR3C1
Post-translational protein modification	1425	6	0.004402944	0.553263895	ESR1;NR1I2;NR3C1;PLAUR;RORA;VDR
Gene expression (Transcription)	1430	6	0.004482462	0.553263895	ESR1;NR1I2;NR3C1;RARB;RORA;VDR
PTK6 Expression	5	1	0.00614481	0.707882156	NR3C1
RUNX1 regulates estrogen receptor mediated transcription	6	1	0.007369582	0.70890504	ESR1
RUNX1 regulates transcription of genes involved in WNT signaling	6	1	0.007369582	0.70890504	ESR1
Phase I - Functionalization of compounds	107	2	0.007384428	0.70890504	CYP2B6;CYP2C19
Attachment of GPI anchor to uPAR	7	1	0.008592961	0.78150715	PLAUR
Transcriptional regulation by RUNX2	121	2	0.00936214	0.796270215	ESR1;NR3C1
GO biological process					
GO ID	GO name	nb of proteins from the input set involved			
GO:0008152	metabolic process	15			
GO:0050896	response to stimulus	14			
GO:0007154	cell communication	12			
GO:0065007	biological regulation	12			
GO:0032501	multicellular organismal process	10			
GO:0032502	developmental process	8			
GO:0051179	localization	6			
GO:0016043	cellular component organization	6			
GO:0008283	cell proliferation	5			
GO:0051704	multi-organism process	3			
GO:0000003	reproduction	2			
GO:0040007	growth	2			
GO molecular function					
GO ID	GO name	nb of proteins from the input set involved			
GO:0005515	protein binding	14			
GO:0043167	ion binding	9			
GO:0060089	molecular transducer activity	8			
GO:0003676	nucleic acid binding	7			

GO:0008289	lipid binding	4			
GO:0016787	hydrolase activity	3			
GO:0016740	transferase activity	2			
GO:0019825	oxygen binding	1			
GO:0003682	chromatin binding	1			
GO:0030234	enzyme regulator activity	1			
GO cellular component					
GO ID	GO name	nb of proteins from the input set involved			
GO:0031974	membrane-enclosed lumen	10			
GO:0016020	membrane	9			
GO:0005634	nucleus	8			
GO:0032991	protein-containing complex	8			
GO:0012505	endomembrane system	6			
GO:0031982	vesicle	5			
GO:0005829	cytosol	5			
GO:0005783	endoplasmic reticulum	4			
GO:0005615	extracellular space	3			
GO:0005794	Golgi apparatus	3			
GO:0042995	cell projection	3			
GO:0005694	chromosome	3			
GO:0005856	cytoskeleton	3			
GO:0005768	endosome	1			
GO:0005773	vacuole	1			
GO:0005739	mitochondrion	1			
DisGeNET					
disease names	size	overla p	pValue	FDR	Proteins from the input set
Prostatic Neoplasms	492	6	5.56E-05	0.093606014	CYP2C19;ESR1;NFE2L2;NR3C1;PLAUR;VDR
Ovarian Failure, Premature	9	2	8.16E-05	0.093606014	CYP2C19;NFE2L2
Delayed epiphyseal ossification	10	2	1.02E-04	0.093606014	ESR1;VDR
Delayed maturation of end part of long bone	10	2	1.02E-04	0.093606014	ESR1;VDR
Hypophosphatemia	18	2	3.44E-04	0.252790123	NR1I2;VDR
Mental Depression	260	4	5.57E-04	0.341342944	CYP2C19;ESR1;NR3C1;RORA
Adenocarcinoma	114	3	6.65E-04	0.349039779	ESR1;NR1I2;RARB
Female infertility	29	2	9.04E-04	0.415141487	ESR1;NR1I2
Acne	34	2	0.001243482	0.507616917	ESR1;NR3C1
Kidney Failure, Chronic	45	2	0.002172877	0.798315151	CYP2B6;CYP2C19
Endometrial Neoplasms	53	2	0.003002893	0.953166523	ESR1;NFE2L2
Depressive disorder	413	4	0.003113228	0.953166523	CYP2C19;ESR1;NR3C1;RORA
Chemical and Drug Induced Liver Injury	212	3	0.003953387	1	CYP2C19;NFE2L2;NR1I2
Lung Neoplasms	213	3	0.00400614	1	ESR1;RARB;TSHR
Acute kidney injury	72	2	0.005476082	1	CYP2C19;NFE2L2
Unipolar Depression	256	3	0.006698561	1	ACP1;CYP2C19;NR3C1
Bipolar Disorder	516	4	0.006921251	1	ESR1;NR3C1;RORA;VDR
Major Depressive Disorder	262	3	0.007142646	1	ACP1;CYP2C19;NR3C1
Substance abuse problem	5	1	0.007813334	1	CYP2C19
Enlargement of the wrists	5	1	0.007813334	1	VDR