

Development of an *in silico* platform to assess developmental and reproductive toxicity (DART)

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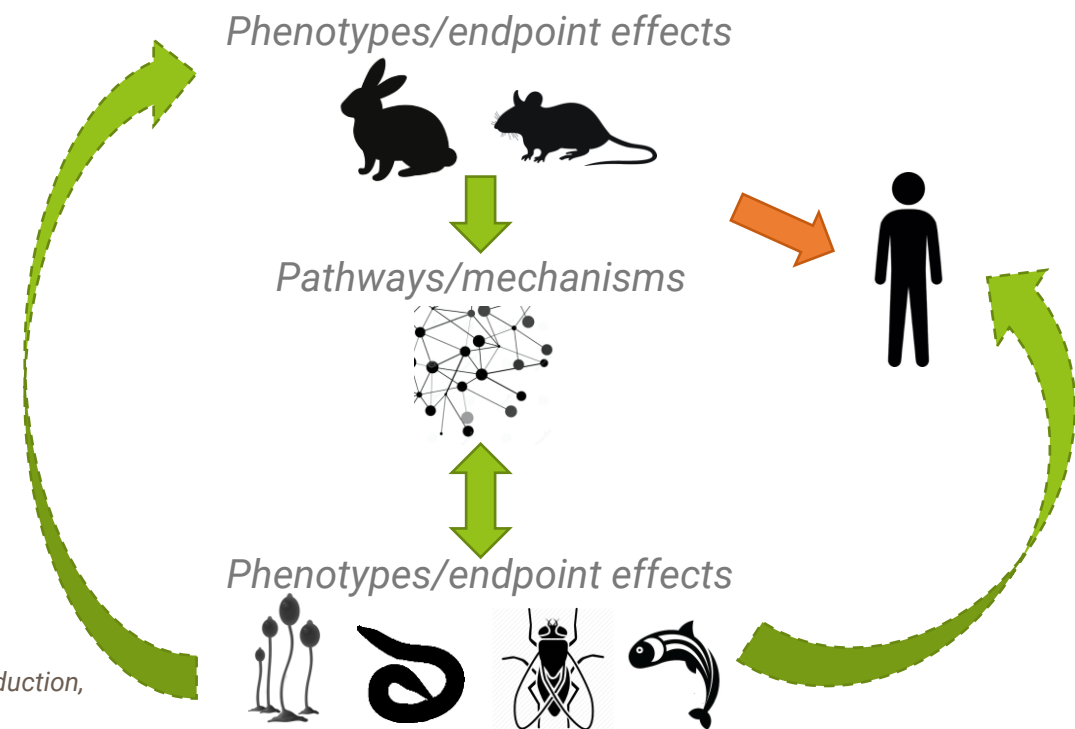
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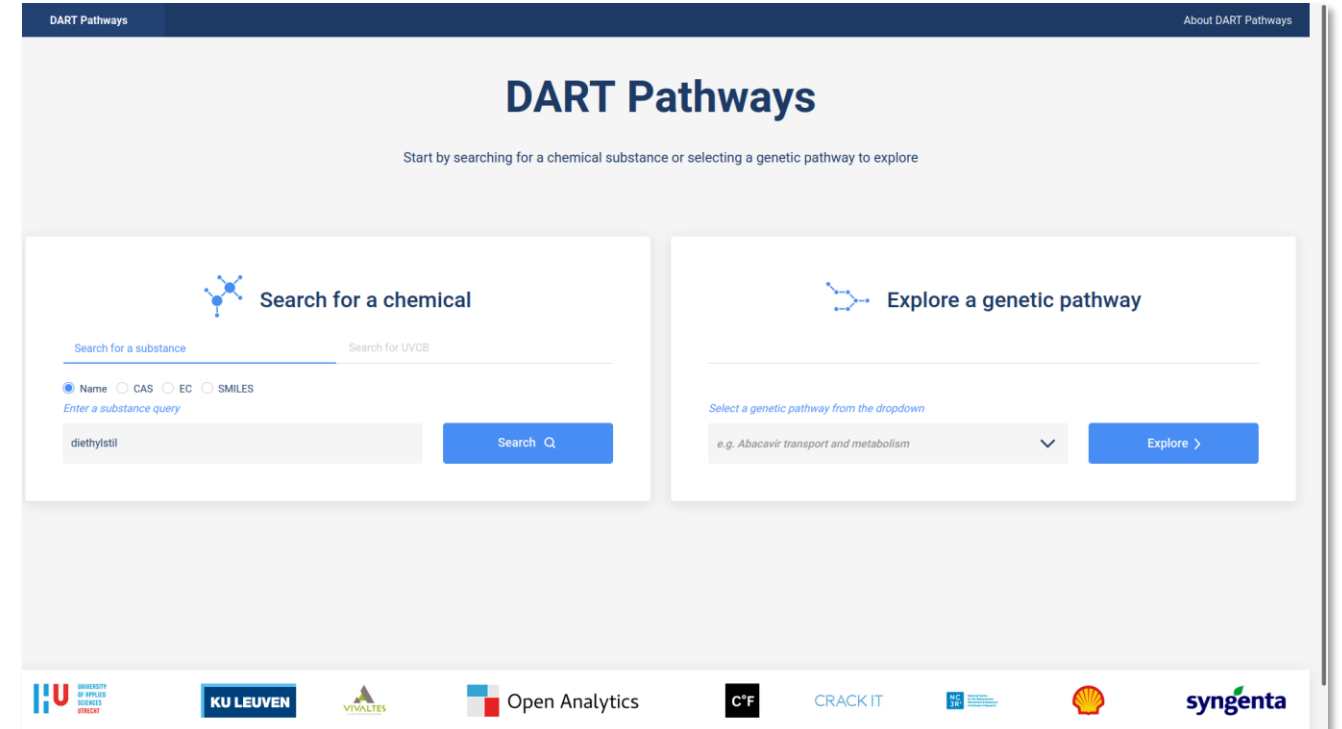
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To reduce the amount of animal testing in the assessment of DART, we have designed a user-friendly web-based platform - "DARTpaths" - that discloses scientific knowledge. This enables us to predict evolutionary-conserved adverse outcome pathways. Moreover, it advises relevant biological tests as alternatives to mammalian testing.

Map mammalian test data to 3R* methods And improve human toxicity prediction



Select a chemical or pathway of interest To start data analytics



Explore similar chemicals and test results

Name	Standardized structure	Regulatory Conclusions	CLP	In vitro hits	Phenotypes	Similarity
4-isopropylphenol					7	0.333
p-isopropylphenol					7	0.349
meso-hexestrol					46	0.429
tert-butyl 4-hydroxybenzoate					5	0.312
4-hydroxyacetophenone		total 8/3 rat 8/3				0.326
1-(4-hydroxyphenyl)-2-(methylamino)ethanol					2	0.327
4-(butan-2-yl)phenol		total 1/1 rat 1/1			17	0.386
sec-butylparaben					7	0.321
2,2-bis[4-(4-hydroxyphenyl)-1,1,1-trichloroethane]					83	0.304

Inspect phenotypes and test results

Source DB	Phenotype	Gene	Details	Species
ZFIN	cardiac ventricle shape, abnormal			zebrafish
ZFIN	cardiac ventricle morphology, abnormal			zebrafish
ZFIN	heart development process quality, abnormal			zebrafish
ZFIN	thyroid gland development process quality, abnormal			zebrafish
pipeline + manual curation	increased body weight		Compared to the vehicle group, the ratio of uterus/body weight in all NP groups, DES doses of 0.50, 1.00, 2.00, and 4.00 -de-g/kg body weight, and BPA dose of 240 mg/kg body weight were significantly increased (all P < 0.05).	mammalian
pipeline + manual curation	increased body weight		Compared with the blank and solvent controls, LH was significantly increased in rats treated with NP at dosages of 120 and 240 mg/kg body weight (both P < 0.05).	mammalian
pipeline + manual curation	increased body weight		The above results revealed significantly increased the uterus/body weight ratio in treated groups, indicating the ratio is the most sensitive parameter to assess the estrogenic effect.	mammalian
pipeline + manual curation	edema		Interestingly, compared with the other groups, DES induced interstitial edema and vill-like changes at the highest dosage.	mammalian
pipeline + manual curation	increased uterus weight		Compared to the vehicle group, the ratio of uterus/body weight in all NP groups, DES doses of 0.50, 1.00, 2.00, and 4.00 -de-g/kg body weight, and BPA dose of 240 mg/kg body weight were significantly increased (all P < 0.05).	mammalian
pipeline + manual curation	increased uterus weight		The above results revealed significantly increased the uterus/body weight ratio in treated groups, indicating the ratio is the most sensitive parameter to assess the estrogenic effect.	mammalian

Explore species conservation To select appropriate 3R species for testing

geneid	full name	human	rat	mouse	rabbit	zebrafish	nematode	vine mold
ENSG00000292847	argonaute RISC component 1	AG01	1.1	1.1	1.1	1.1	N/A	0
ENSG00000122908	argonaute RISC catalytic component 2	AG02	1.1	1.1	1.1	1.1	1.6	0
ENSG00000126270	argonaute RISC catalytic component 3	AG03	1.1	1.1	1.1	1.6	N/A	0
ENSG00000134898	argonaute RISC component 4	AG04	1.1	1.1	1.1	1.1	N/A	0
ENSG00000196951	adaptor related protein complex 2 subunit alpha 1	AP2A1	1.1	1.1	1.1	1.1	1.6	N/A
ENSG00000182020	adaptor related protein complex 2 subunit alpha 2	AP2A2	1.1	1.1	1.1	0	1.6	N/A
ENSG00000061125	adaptor related protein complex 2 subunit beta 1	AP2B1	1.1	1.1	1.1	1.1	N/A	N/A
ENSG00000161203	adaptor related protein complex 2 subunit mu 1	AP2M1	1.1	1.1	1.1	1.6	0	0
ENSG00000042753	adaptor related protein complex 2 subunit sigma 1	AP2S1	1.1	1.1	0	1.1	1.1	1.1
ENSG00000141480	arrestin beta 2	ARRB2	1.1	1.1	0	1.6	0	0

Predict human adverse outcome pathways Based on integration of *in vitro* and *in vivo* data

Pathway ID	Pathway Name	Filter and re-ranking
0_234	HSP90 chaperone cycle for steroid hormone receptors (SHR)	
0_248	Erythropoietin activates Phosphoinositide 3-kinase (PI3K)	
0_292	Hedgerophylin	
0_187	Hedgehog (Hh) signaling	
0_187	Synthesis of IP3 and IP4 in the cytosol	
0_179	Affector activation and deactivation	
0_179	DAPK2 interactions	
0_179	Transport of vitamins, nucleosides, and related molecules	
0_178	Biosynthesis of specialized proresolving mediators (SPMs)	
0_178	TICR signaling	
0_172	Signaling by FGFR in disease	
0_171	Metabolic disorders of biological oxidation enzymes	
0_145	Genetic Transcription Pathway	
0_143	Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R)	
0_14	GPCR ligand binding	
0_134	Phospholipid metabolism	
0_128	GLM system	
0_127	Signaling by ERBB4	
0_124	Neurotransmitter clearance	

Want to try out the DARTpaths platform? – Contact Vivaltes at: dartpaths@vivaltes.com

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