DARTpaths, an in silico platform to investigate molecular mechanisms of compounds

Commonly used acronym: *DARTpaths*

Created on: 10-06-2022 - Last modified on: 13-06-2022

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Organisation

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Country Belgium
Geographical Area Flemish Region

Partners and collaborations

Open Analytics, Hogeschool Utrecht , Vivaltes

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research, Regulatory use - Routine production
Type of method	In silico

DESCRIPTION

Method keywords

Data analysis
phenotype ontology
pathways
chemoinformatics

Scientific area keywords

computational modelling
data modeling
data integration
bioinformatics

Method description

DARTpaths is an an integrative app to support the prioritisation of chemicals. The Open Source R shiny application allows for the prediction of compound-induced molecular mechanisms of action. The tool integrates phenotypic endpoints of different species induced by compounds and genetic variants, *in vitro* targets, adverse outcomes,

molecular pathways and evolutionary conservation. The toolbox proposes follow-up tests for model organisms to validate the predictions of which molecular pathways are causative for phenotypes.
- All code for the application and a dockerized version are available on https://github.com/Xpaths/dartpaths-app
- Demonstration of use-cases of the application are available on https://www.vivaltes.com/dartpaths/

Lab equipment

Computer.

Method status

Internally validated

PROS, CONS & FUTURE POTENTIAL

Advantages

The application integrates different data sources and combines them to find the most likely underlying molecular pathway for an adverse outcome of a compound. Based on knowledge generated over decades in model organisms, it can also predict expected phenotypes (endpoints) when disturbing this pathway in a non-vertebrate model organism.

Challenges

Phenotypes induced by compounds as well as *in vitro* target data are incomplete and for specific compounds often only available inside companies that develop new compounds. For accurate pathway and phenotype prediction, complete data is ideal.

Modifications

Users can install the application on their own site and connect (private) data to the app to improve pathway and phenotype prediction.

Future & Other applications

- The species conservation of molecular pathways can inform researchers in life sciences research interested in specific pathways if studies in alternative, non-vertebrate model organisms are useful and informative.
- The NLP pipeline for identification of connections between compounds and phenotypes in full-text reports is widely applicable in toxicology and pharmacology.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

DARTpaths, an *in silico* platform to investigate molecular mechanisms of compounds. Diksha Bhalla1*, Marvin N. Steijaert2*, Eefje S. Poppelaars3*, Marc Teunis4*, Monique van der Voet3, Marie Corradi4, Elisabeth Dévière2, Luke Noothout5, Wilco Tomassen5, Martijn Rooseboom6, Richard A. Currie7, Cyrille Krul4, Raymond Pieters4,8, Vera van Noort1,9^, and Marjolein Wildwater3^ Bioinformatics, submitted

Associated documents

Supplement_DARTapplication_20220504_V8.docx
Manuscript_DARTapplication_20220504_V8.docx

Links

GitHub repository
Demo page

Other remarks

A manuscript about the application has been submitted to the journal Bioinformatics.

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Financed by