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

Commonly used acronym: DARTpaths


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Organisation
Name of the organisation: Katholieke Universiteit Leuven (KUL)
Department: Faculty of Bioscience Engineering
Country: Belgium
Geographical Area: Flemish Region

Partners and collaborations
Open Analytics, Hogeschool Utrecht, Vivaltes

SCOPE OF THE METHOD

<table>
<thead>
<tr>
<th>The Method relates to</th>
<th>Human health</th>
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</thead>
<tbody>
<tr>
<td>The Method is situated in</td>
<td>Basic Research, Regulatory use - Routine production</td>
</tr>
<tr>
<td>Type of method</td>
<td>In silico</td>
</tr>
</tbody>
</table>

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.