From human physiology to toxicity prediction: Working on the ONTOX project

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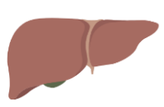
ONTOX (*ontology-driven and artificial intelligence-based repeated dose toxicity testing of chemicals for next generation risk assessment*) is an international project aiming to provide a strategy for developing innovative new approach methodologies (NAMs) to predict systemic repeated dose toxicity effects, which can improve the human risk assessment when combined with personalized exposure assessment, relying mainly on human data [1].

The initiative focuses on predicting toxicity for six particular conditions:

(i) neural tube closure defects;
(ii) cognitive function defects;



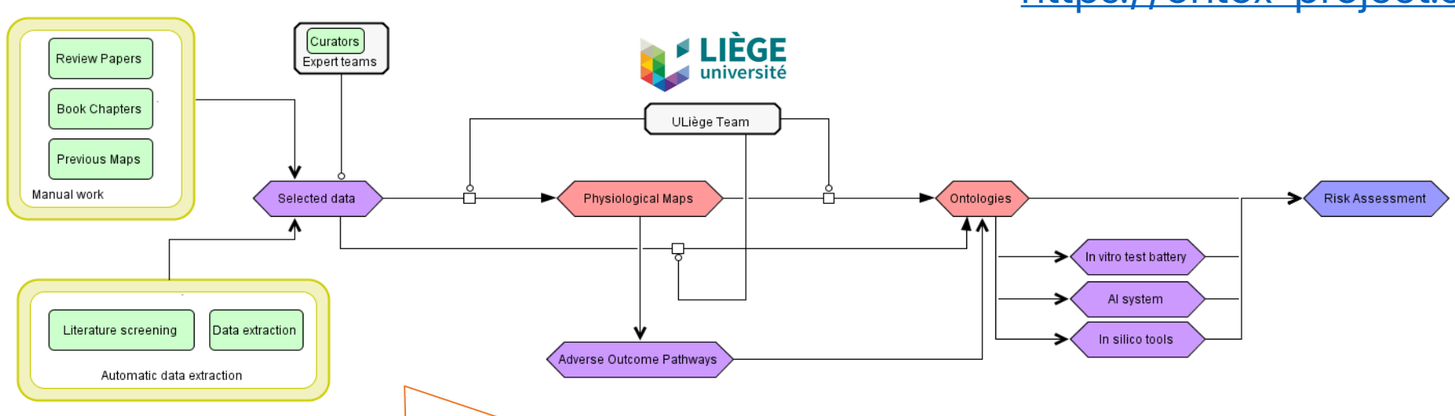
(iii) steatosis;
(iv) cholestasis;

(v) tubular necrosis;
(vi) crystallopathy.

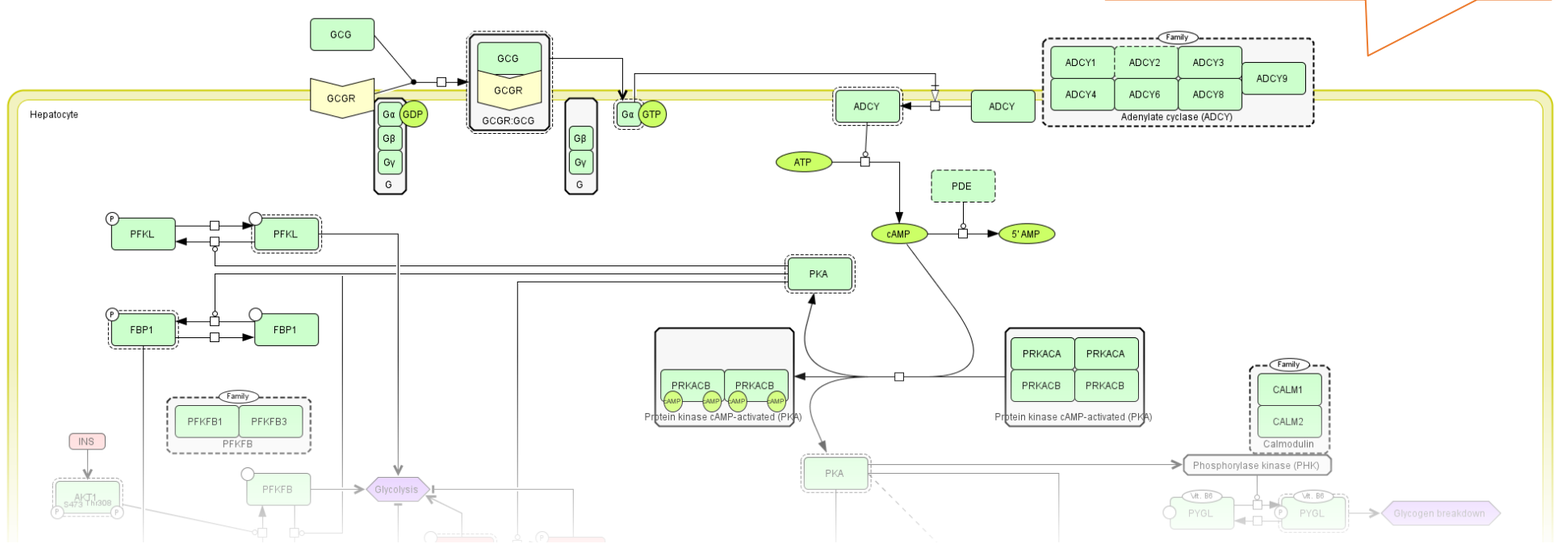
Within ONTOX, the ULiège team, led by Prof. Liesbet Geris, is responsible for producing **Physiological Maps** for the different case studies, which serve as a foundation for the development and refinement of Adverse Outcome Pathways (AOPs), improvement of in vitro test batteries, and computational models for toxicity prediction.

From these physiological maps, my team will also drive the creation of chemical-induced disease **Ontologies**, by adding several layers of information such as pathological, toxicological, chemical and kinetic data.

More information can be found on the project's webpage: https://ontox-project.eu/



A summary of ONTOX workflow focusing on the ULiège tasks.



An example of a physiological map for glucagon signaling in hepatocytes.

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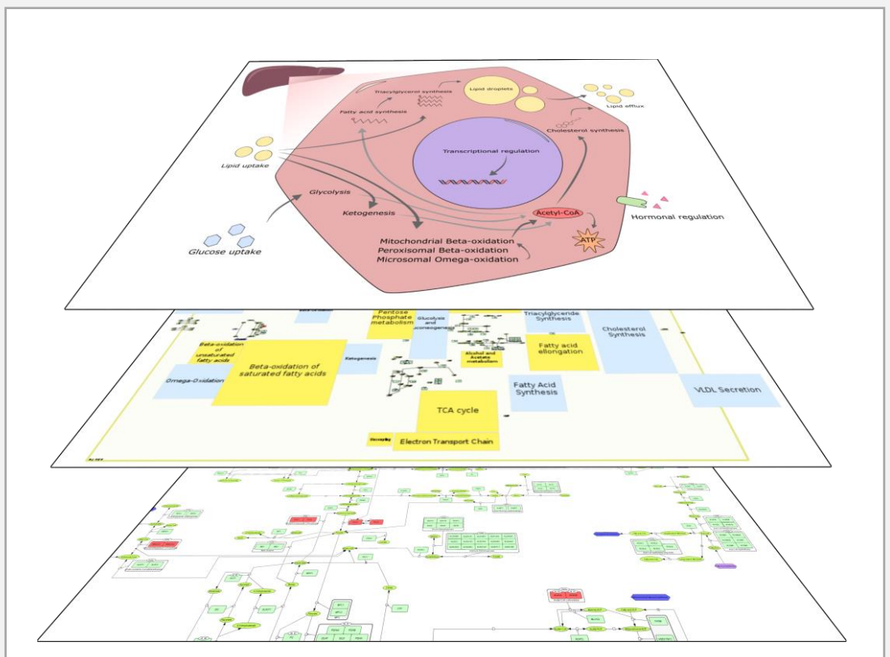
Hi there! My name is Luiz, and I am a Brazilian scientist working as a postdoctoral researcher at the Biomechanics Research Unit, GIGA In Silico Medicine, at the University of Liège (Belgium). I have experience in toxicological and pre-clinical research using animal models, and I am very interested in New Approach Methods (NAMs) to reduce animal use in science, including in silico modelling and network analysis. My work currently focuses on supporting NAMs development by setting the physiological grounds for Adverse Outcome Pathways (AOPs) improvement and refinement, computational modelling rationale, and Ontologies construction.



Graphic concept of the ONTOX ontology for liver lipid metabolism.

The next step is to use the Physiological Maps as a cornerstone to create the **Ontologies,** integrating different layers of pathological & toxicological information chemical information, and quantitative kinetic data. The developed ontologies will contribute to: (1) better understand organ- and disease-specific pathways in response to various chemicals, (2) visualize omics datasets, (3) develop quantitative methods for disease modelling and for predicting toxicity, (4) set up an in vitro & in silico test battery to detect a specific type of toxicity, (5) develop new animal-free approaches for next generation risk assessment. Like the Disease Maps Project [2], it is intended that these tools should be dynamic, and continuously updated, resulting from expert curation and revision in an open community effort.

References:

[1] Vinken, M. *et al.* Safer chemicals using less animals: kick-off of the European ONTOX project. *Toxicology* 458, 1–7 (2021).

[2] Mazein, A. *et al.* Systems medicine disease maps: community-driven comprehensive representation of disease mechanisms. *npj Syst. Biol. Appl.* 4, (2018).

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Funded by: Horizon2020 European Union Funding for Research & Innovation