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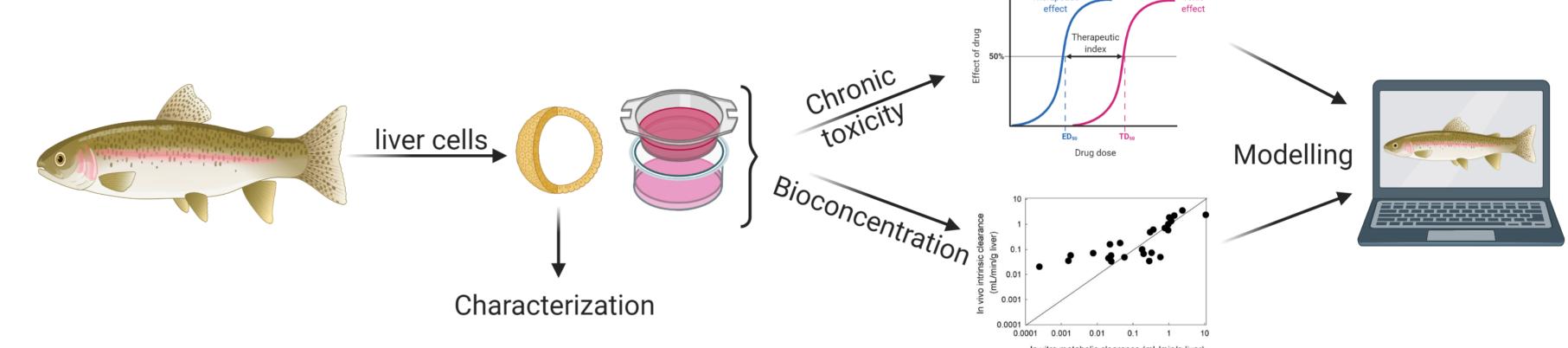
Hepatic 3D Spheroids: The Next Generation of Testing in Toxicology (SPHERTOX)

Background

- Traditional animal testing methods for risk assessment of chemicals have many ethical and economical concerns
- **❖** Alternative: non-animal methods implementing the 3Rs (refinement, reduction, and replacement)
- ❖ BUT currently no non-animal bioassays suitable for investigating long-term toxicity in fish are available
- ❖ The 3-dimensional (D) hepatic spheroid model appears to be a promising model as they preserve morphological, physiological and biochemical properties for weeks after their formation^{[1][2]}



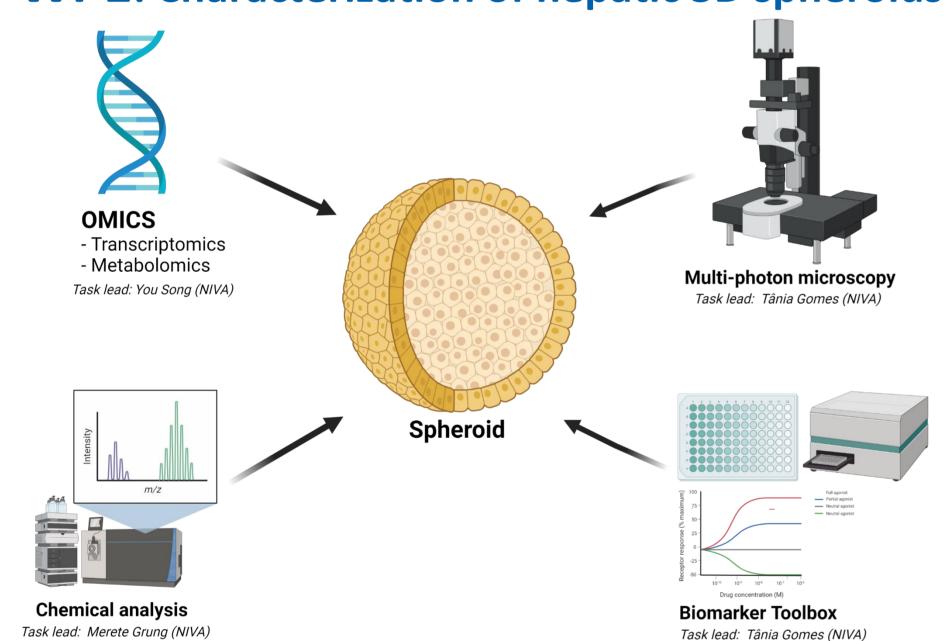
Assess the performance of hepatic 3D spheroids of rainbow trout as an alternative chronic toxicity and bioconcentration (BC) model, alone and in co-culture with other cell types, as an alternative and advanced in vitro model with increased comparability toward in vivo test systems.



Workplan

SPHERTOX project is organized into 6 work packages (WPs) that are highly interlinked and interdisciplinary. (WP1→WP2→WP3→WP4→WP5→WP6)

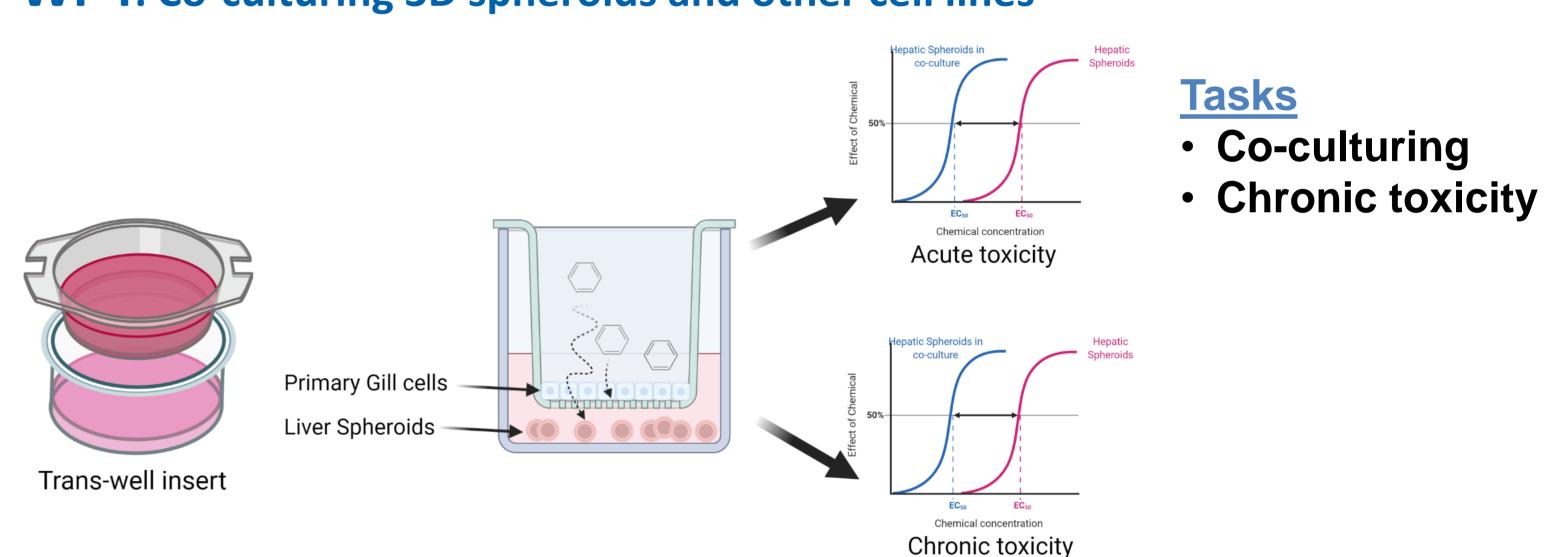
WP1: Characterization of hepatic 3D spheroids



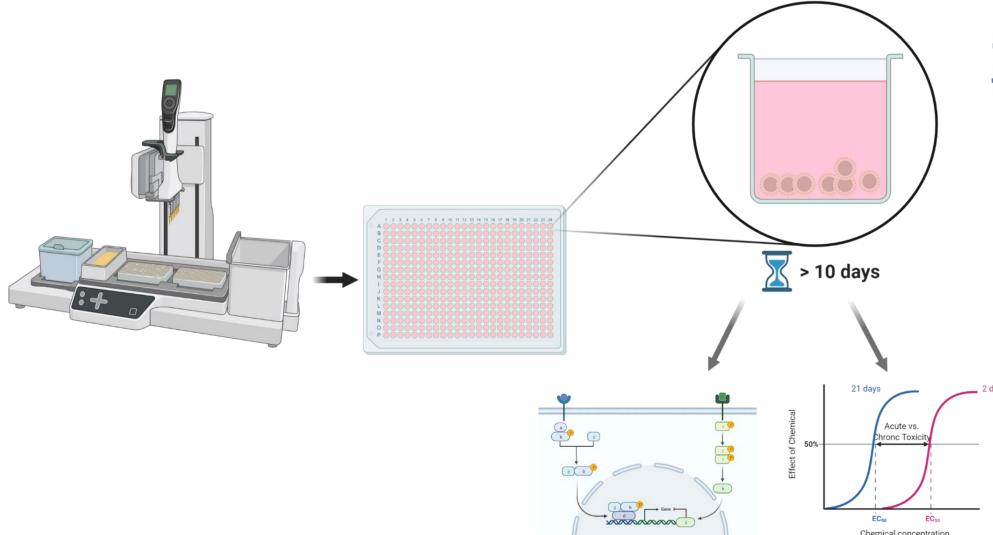
Tasks

- State-of-the-art imaging
- MultiOMICS screening
- Develop Biomarker Toolbox
- Chemical analysis

WP4: Co-culturing 3D spheroids and other cell lines



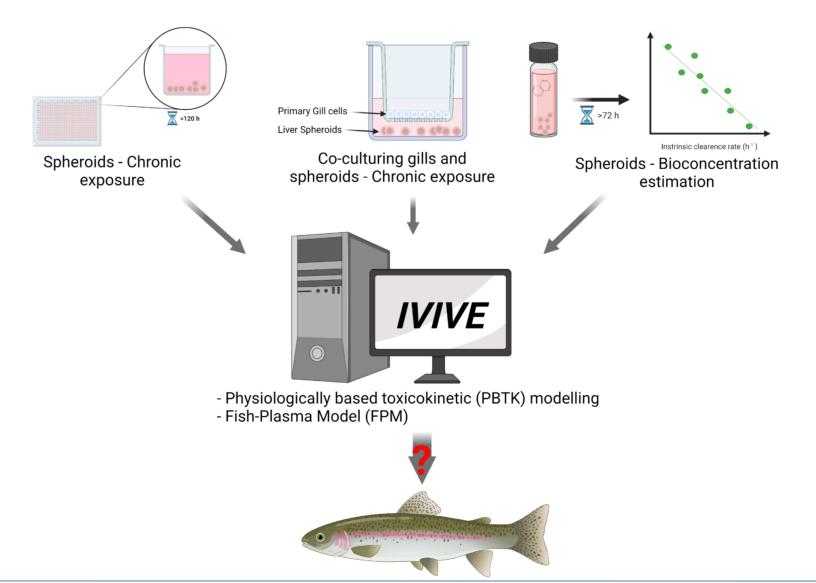
WP2: Chronic low-dose exposure with a high throughput screening approach



Tasks

- HTS approach
- **Baseline toxicity testing**
- Compound specific MoA

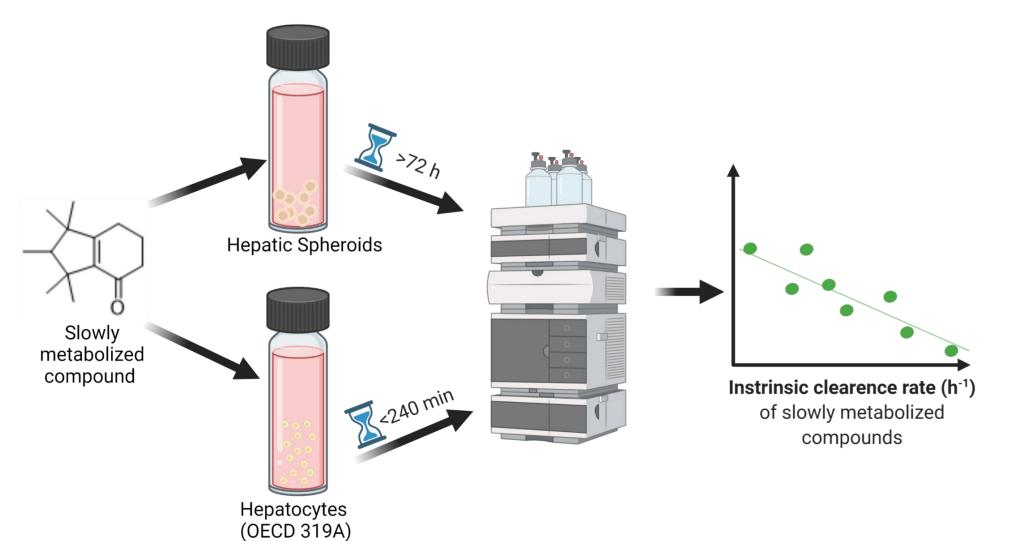
WP5: In vitro to in vivo extrapolation modelling



Tasks

- Physiologically based toxicokinetic modelling
- Fish plasma model prediction

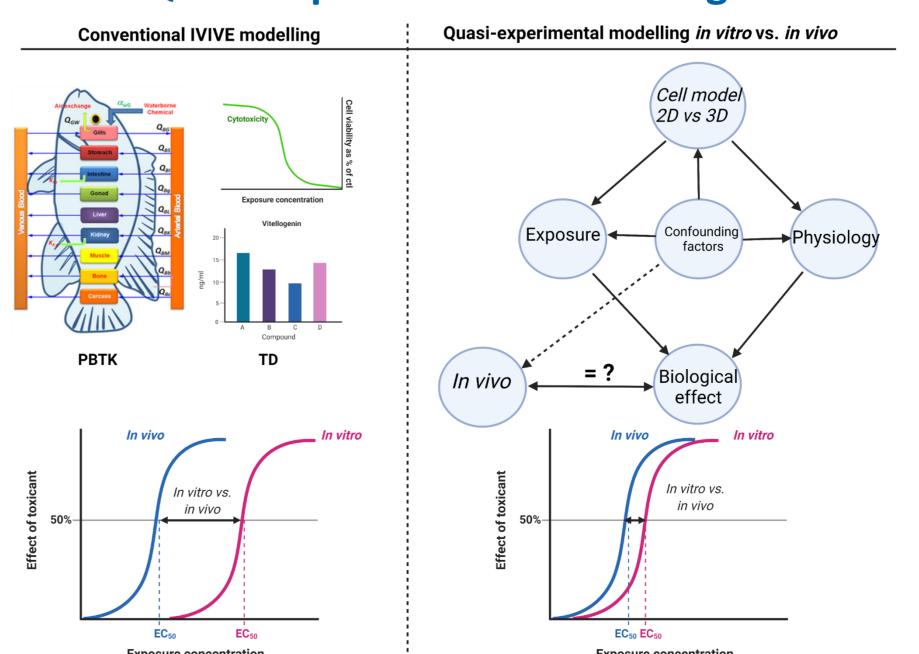
WP3: Biotransformation of chemicals using 3D spheroids for *in vitro* to *in* vivo extrapolation



Tasks

- Compound bioavailability
- Prolonged duration of incubation
- Comparative study of three bioassays

WP6: Quasi-experimental modelling



Tasks

- Causal inference model
- Application of quasiexperimental model

References:

[1]. Baron, M.G., *Ecotox.* 21, 2419-2429 (2012); [2]. Hultman, M.T., *Enivron. Toxicol. Chem.* 38,1738-1747 (2019)

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