OASIS Consortium: A strategy for comparing *in vitro* imaging and 'omic technologies to existing rat and human *in vivo* hepatotoxicity data and beyond

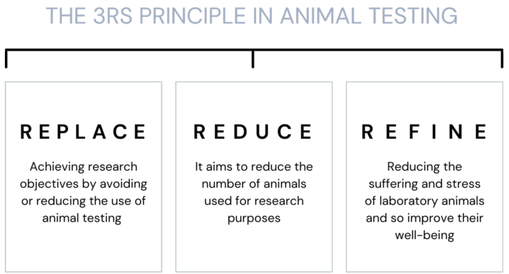
SOT 5054/P155

Christine E Crute[1], Srijit Seal[2], Jessica Ewald[2], Joshua Harrill[3], Jessica LaRocca[4], Jaime Cheah[2], Deidre Dalmas[5], Andreas Bender[6], Sabah Kadri[7], Connie Mitchell[1], Shantanu Singh[2], David Rouquie[8], Anne Carpenter[2] on behalf of the OASIS Consortium.

[1] Health and Environmental Sciences Institute (HESI), Washington, DC, USA. [2] Broad Institute of Harvard and MIT, Cambridge, MA, USA. [3]US Environmental Protection Agency (EPA), Durham, NC, USA. [4]Corteva Argiscience, Indianapolis, IN, USA [5] GlaxoSmithKline, Collegeville, PA, USA. [6] University of Cambridge, Cambridge, United Kingdom. [7]Abbvie, Chicago, IL, USA. [8]Bayer Crop Science, Sophia Antipolis, France.

Introduction

- Animal testing is still considered the "gold standard" for pre-clinical safety testing, but it is costly, time-consuming, and in some cases inadequate in predicting human impacts.
- Many global regulatory agencies are now advocating for the Replacement, Reduction, and Refinement (3Rs) animal testing methods.
- New Approach Methodologies (NAMs) hold promise for high-throughput screening and assessment with the added benefit of reducing dependence on traditional animal tests.
- There is a pressing need for efficient and reliable novel approaches that can replace or reduce animal testing while simultaneously enhancing the safety and effectiveness of new pharmaceutical and agrochemical products.



--- Mission ---

Gain confidence in the combination of Cell Painting, transcriptomics and proteomics for safety assessment using hepatotoxicity as a use-case.

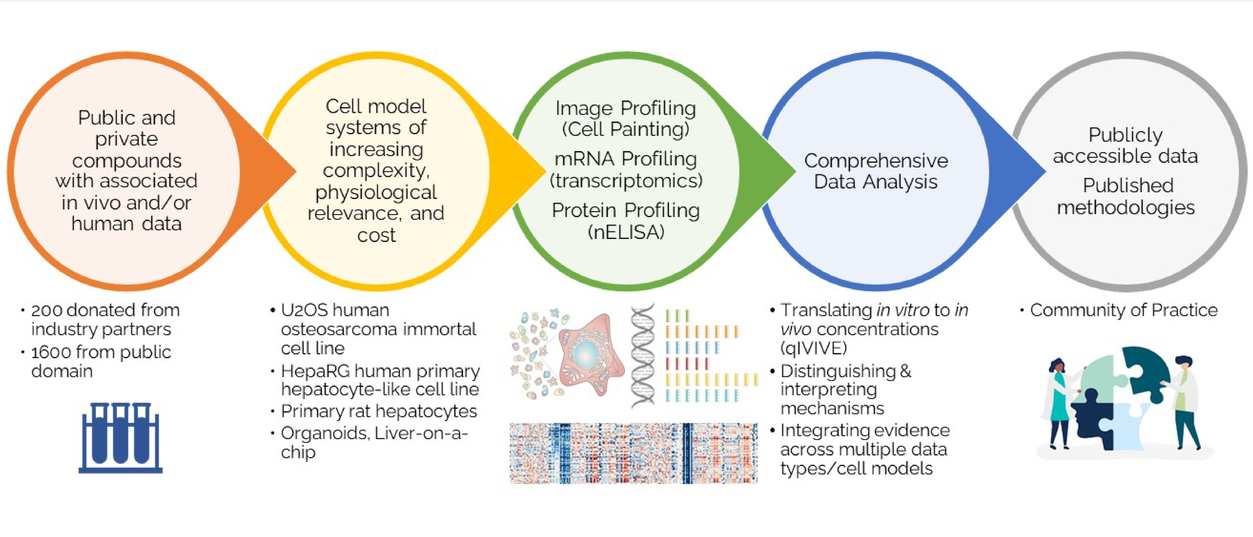
--- Objective ---

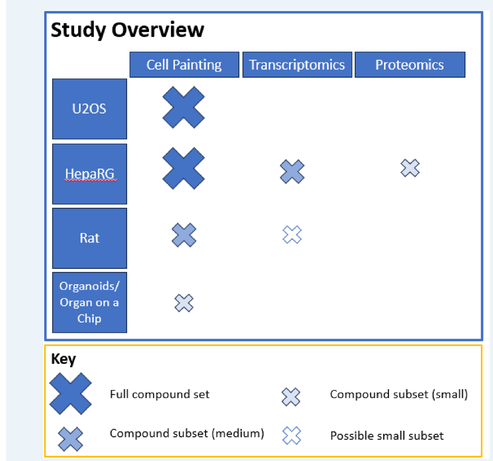
Benchmark in vivo hepatotoxicity (from rodent or clinical trial data) induced by a series of compounds against informatically aligned molecular & phenotypic cell-based assays.

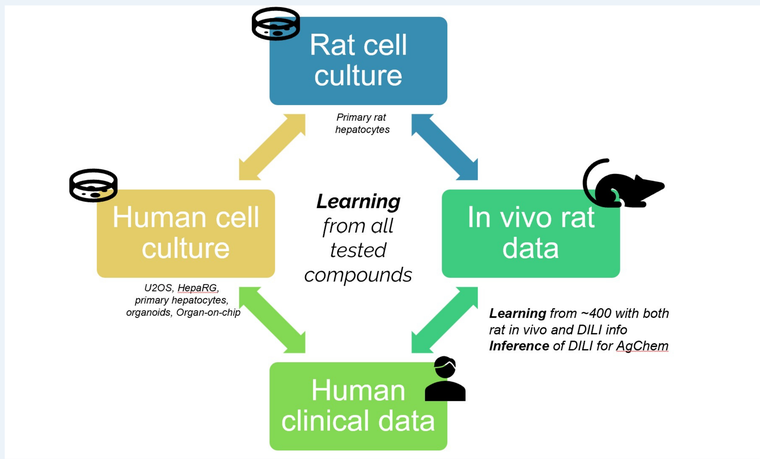
DISCLAIMER

The views, conclusions and recommendations expressed in this poster are those of the authors and do not necessarily represent the policies or positions of their organizations.

Study Approach







Compound Selection

1. Data from 29 databases were crosschecked with the following requirements:

- In vivo repeat dose rat studies with 28 or 90 days duration
- Dosing
- Gender
- Study duration
- Liver histopathology
- Liver weight
- Body weight
- Clinical observations
- Relevant non-liver pathology
- Data on group averages

2. Compounds were selected from the following databases:

- Public databases where compounds have associated rat in vivo data:
  - TG-Gates (Japan NIBIO)
  - ToxRefDB (U.S. EPA/NTP)
  - DrugMatrix (U.S. NIEHS)
  - ICE Datasets (U.S. NTP)
  - RepDoseDB (Fraunhofer ITEM)
- Public databases where compounds have associated with human clinical data: DIList

3. The final compound list contains:

- ~400 compounds with associated rat in vivo data, selected from public databases
- ~200 compounds with associated rat in vivo data, donated from industry partners (may be deidentified)
- ~1000 compounds with human data only, selected from publicly available DILIst

Anticipated Outcomes

- Publicly-available, novel dataset in human and rat cells that informs use of Cell Painting and -omics as non-animal alternative test systems for regulatory decision-making.
- Development of predictive algorithms that integrate novel Cell Painting and transcriptomic data with existing in vivo animal/human data for hundreds of compounds.
- Multi-disciplinary/ Multi-sector team of scientists establishing a community of practice.

Team & Support

The OASIS Consortium is supported by public grant funding in synergy with partnered resources and expertise from industry partners and in-kind contributions from academic, government, NGO, and biotech partners.

This exciting effort engages >60 global experts in toxicology, cell biology, bioinformatics, risk assessment, and assay development from more than:

- 14 academic institutes
- 7 government agencies
- 16 industry organizations
- 2 non-government organizations

*** We are recruiting additional partners from academia, government, and industry ***

If you would are interested in joining our team or getting additional information, please contact HESI Project Managers:
Chrissy Crute (ccrute@hesiglobal.org)
Connie Mitchell (cmitchell@hesiglobal.org)

Commitment to 3Rs

Authors are committed to the replacement, reduction and refinement of animal studies (3Rs). Non-animal models and alternative technologies are part of our strategy and employed where possible. When animals are required, application of robust study design principles and peer review minimizes animal use, reduces harm and improves benefit in studies.