REPLIGUT® PLANAR (STEMSCREEN)

A HUMAN HTS PLATFORM FOR ASSESSING GASTROINTESTINAL TOXICITY (GIT) RISK IN EARLY DEVELOPMENT

CHALLENGES

- GI tract represents the most common target organ of adverse drug reactions[1] (35% of clinical AEs)
- Clinical safety failures are only predicted by nonclinical studies 25% of the time.[2,3] Why?
  - Lack of predictable in vitro models
  - Rodents show low concordance (42%) with human clinical outcomes[4]
  - Non-human primates are more predictive, but limited by cost, throughput, and ethics (reserved for lead)[4]
- There is a significant unmet need for human models of GI risk assessment that can be utilized for drug optimization in early development.

ALTIS SOLUTION: REPLIGUT® PLANAR

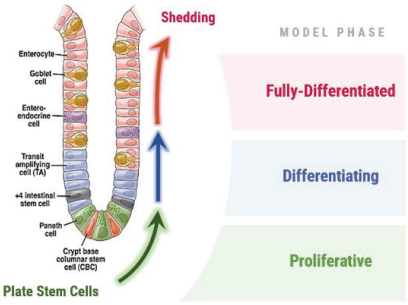
Intestinal Stem Cell Biobank

- High quality *Human* GI stem cell platform (all GI regions)
- *Diverse* donor demographics (age, race, sex)
- Rigorous *Quality Control* of all cell lots

Highthroughput and Flexible Planar Cultures

- Maximizes throughput using *96-well plate* Transwell format
- *Apical and Basal* dosing and sampling
- Sequentially models *Entire GI Life-Cycle*

RepliGut® Planar Overview



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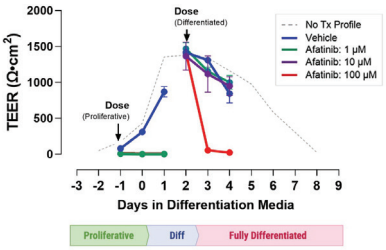
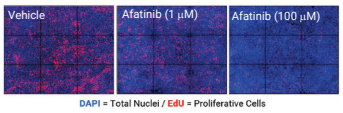
Barrier Formation/ Retention Assay (TEER)



Proliferation/ Viability Assay



Data correctly demonstrates that Afatinib is more toxic to stem vs differentiated cells

- *Top: Simple assay using TEER/Barrier Function*
- *Bottom: EdU vs DAPI to index proliferation vs viability*

Capitalizes on Unique Aspects of RepliGut® Planar

- *Highthroughput* assay for human drug toxicity
- Ability to dose *Stem vs Differentiated* Cells
- *Cell-Specific* toxicological evaluation

Utilizes Relevant/Functional Assays for Toxicity

- Barrier Formation/Retention utilizing *TEER*
- *EdU/DAPI* can be used to assess proliferation/viability
- Assay provide *Rapid* readouts for compound screening

Altis Offers Services and Kits with our Clients

- *Consultative* client approach
- Assays are *Customizable* based on client needs

References

1. J Toxicol Sci. 2013; 38(4):581-98
2. Nat Rev Drug Discov. 2014 Jun;13(6):419-31.
3. Toxicol Appl Pharmacol. 2017; 334(1):100-109
4. Reg. Toxicol. and Pharma. 2000; 32(1):56-67

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