cyprotex
AN EVOTEC COMPANY

Cardiotoxicity

Cardiotoxicity is one of the main reasons for drug withdrawals, accounting for 45% of all drugs taken off the market between 1994 and 2006. Incorporating in vitro screens at the early phases of drug development is critical in preventing late stage failure.

Cyprotex is Your Partner in Cardiotoxicity Prediction

- **Extensive Experience:** Our team of experienced scientists and toxicologists are dedicated to ensuring the safety of your test articles and have decades of experience in cardiotoxicity research.
- **State-of-the-Art Technologies:** Cutting-edge 3D triculture models formed from cardiomyocytes (iPSC-derived) and transcriptomics services.
- **Wide Range of Services:** We offer both standardized and novel approaches for assessing cardiotoxicity. Screening and investigative services (non-GLP) and regulatory services (GLP) are available.

The Future of Safety Prediction is Omics-driven

HT omics and organ specific models:

- Improve sensitivity and specificity of safety prediction
- Confer understanding of the mechanism of toxicity

Our comprehensive safety database comprises of:

- Known toxic compounds
- FDA CiPA listed drugs
- Confer understanding of the mechanism of toxicity
- Marketed drugs
- Mechanistic compunds & drug properties

Safety liability modeling provides:

- AI/ML predictions of safety liability risk
- Mechanism of action & point-of-departure safe dose prediction
- Compound matching to determine safety profile

Assessing Drug-Induced Cardiotoxicity:

Functional Toxicity

Acute alteration in the heart function

Ion Channel Panel

- CiPA panel and other key ion channels (including hERG)
- Single ion recording
- Uses automated patch clamp

eCiphr Cardio (Microelectrode Array)

- Human iPSC-derived cardiomyocytes
- Viability maintained for extended periods (up to 2 weeks), allowing for acute and chronic studies
- Measures beat rate, field potential duration, sodium amplitude and QT conduction velocity

Structural Toxicity

Damage to cell and tissue morphology

3D Structural Cardiotoxicity Assay

- 3D triculture: human iPSC-derived cardiomyocytes, cardiac endothelial cells, and cardiac fibroblasts
- Detects cardiotoxicity through high content screening (HCS)
- Monitors cell health parameters using HCS & ATP content

3D Hypertrophy Assay

- 3D culture of human iPSC-derived cardiomyocytes
- Detects hypertrophic cardiotoxicity potential combined with structural cardiotoxicity using brightfield and confocal microscopy
- Measured endpoints: nuclear features, mitochondrial potential, calcium, ATP
- Monitors cell health parameters using HCS & ATP with additional spheroid size information at multiple time points

Functional and Structural Toxicity

Cardiotox Screen: Cardiac Safety Liability Assessment

- Human iPSC-derived cardiomyocytes
- Assesses calcium transients, cellular morphology and cytotoxicity through kinetic screening and HCS
- Acute and 24 time points
- Data delivery; minimum effective concentration (MEC) and AC_{50} value for each measured parameter:
  - Frequency
  - Amplitude
  - Peak width
  - Decay time
  - Rise time
  - Cell count
  - Nuclear size
  - DNA structure (DNA)
  - Calcium homeostasis (Ca^{2+})
  - Mitochondrial mass (Mito mass)
  - Mitochondrial membrane potential (MMP)
  - Cellular ATP content (ATP)

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