Cellular Dynamics international

iCell® Cardiomyocytes:
Cytotoxicity Characterization

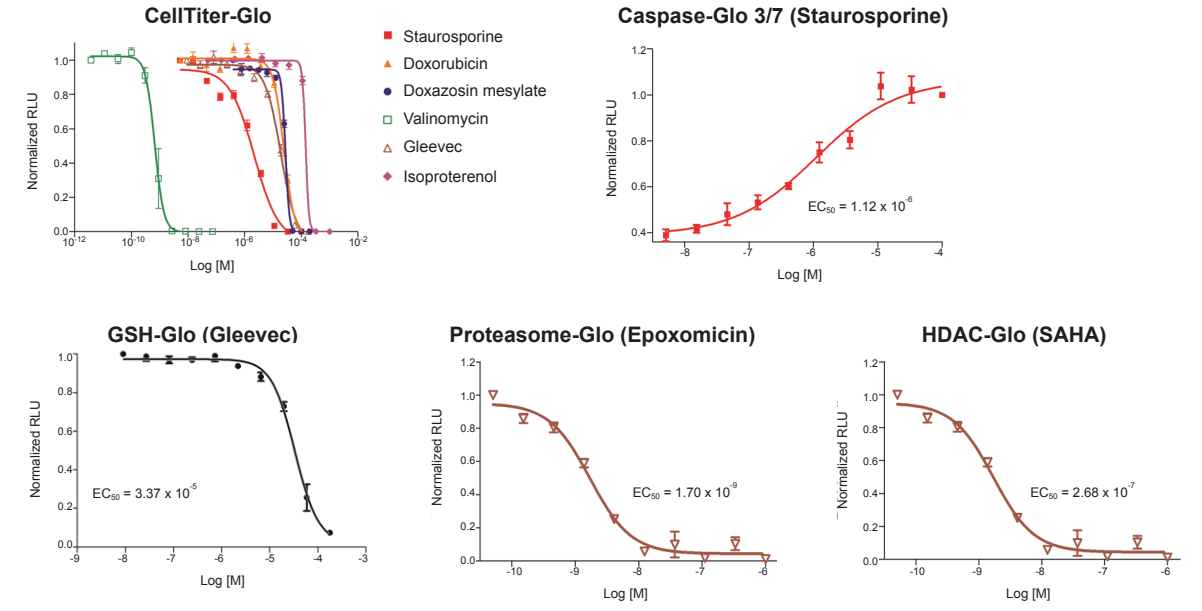
Cellular Dynamics International (CDI) offers iCell® Cardiomyocytes, human induced pluripotent stem cell (hiPSC)-derived cardiomyocytes suitable for a wide variety of applications including cell-based assessment of compound cardiac cytotoxicity.

iCell Cardiomyocytes are differentiated from hiPSCs that were reprogrammed to their pluripotent state from terminally differentiated cells, thus avoiding the controversial and ethical issues surrounding embryonic stem cells. iCell Cardiomyocytes are a human-based test system that exhibit stable transcriptional and phenotypic profiles over weeks and months in culture. Their human origin and long-term functionality overcome the limited potential of cadaveric, transformed cell lines, and non-human primary cell cultures.

Cardiac Cytotoxicity Assays

iCell Cardiomyocytes have demonstrated utility in the following biochemical assays:

- Cell viability
- Apoptosis
- ATP production
- Oxidative stress
- Mitochondrial dysfunction
- Proteasome activity
- Histone deacetylase activity
- Simultaneous multiplexing of multiple assays



▲ **Figure 1: Cytotoxicity Assays Using iCell Cardiomyocytes**
iCell Cardiomyocytes were treated with increasing concentrations of a variety of known toxicants, and general viability was assessed via CellTiter-Glo® (upper left). iCell Cardiomyocytes can also be used to assess specific toxic endpoints, such as apoptosis (Caspase-Glo® 3/7), oxidative stress (GSH-Glo™), proteasome activity (Proteasome-Glo™), and histone deacetylase complex activity (HDAC-Glo™). In all cases, iCell Cardiomyocytes showed a dose-dependent response to toxicological insult. (Data generated with the assistance of Promega Corp.)

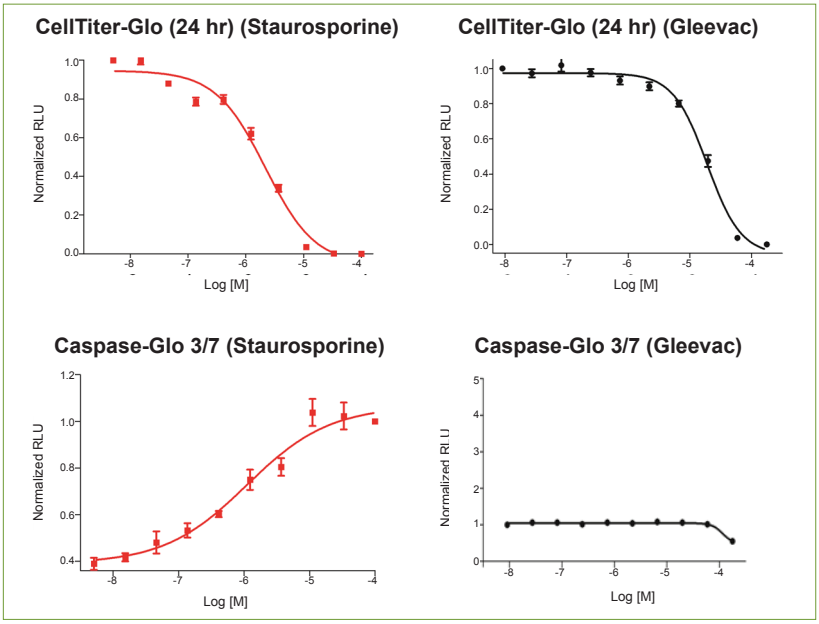


Figure 2: Mechanistic Insights
The effects of staurosporine or Gleevac (imatinib) application on iCell Cardiomyoctyes were monitored using CellTiter-Glo or Caspase-Glo 3/7. Both compounds caused a decrease in iCell Cardiomyocytes viability (CellTiter-Glo), but only staurosporine activated the caspase pathway, indicating that the mechanism of cell death for this compound was apoptosis whereas Gleevac (imatinib) caused a more generalized cell death. (Data generated with the assistance of Promega Corp.)

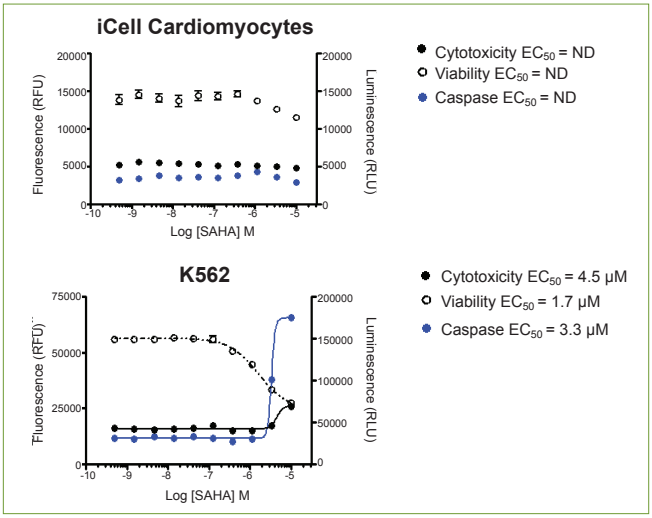


Figure 3: Cell-specific Effects
Inhibiting histone deacetylase (HDAC) activity has emerged as an anti-neoplastic therapy. Ascertaining the potential cardiotoxic side effects of such therapeutics is an essential portion of their development. Figure 3 shows the effect of the HDAC inhibitor Vorinostat (SAHA) on its intended target, the K562 cancer cell line, as well as iCell Cardiomyocytes. Vorinostat had minimal to no effects on iCell Cardiomyocytes viability, cytotoxicity, and caspase activity while it showed clear effects on the target cell line, thus demonstrating the lack of the cardio-specific cell based effects. (Data generated with the assistance of Promega Corp.)

ADVANTAGES

Drug Safety Screening & Discovery

- Human cardiomyocytes are expected to generate more accurate predictions of human physiological response than surrogate animal models.
- Assays can be performed in 96-well plates, requiring small amounts of compound for a cardiac cytotoxicity profile.
- Cells remain viable in culture for several months, enabling acute and long-term toxicity research.

For More Information

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