Cardiotoxicity Screening

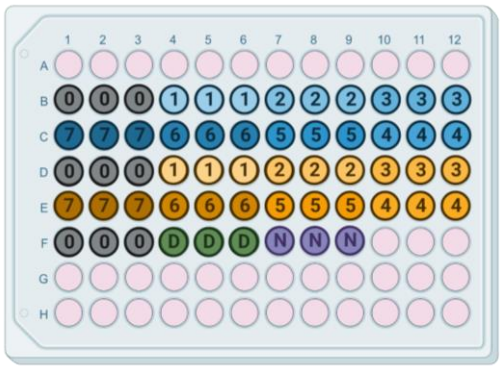
High content imaging to predict proarrhythmia

Vala's Kinetic Image Cytometry® is the first and only *in vitro* screening platform to exceed animal models in predicting drug-induced cardiac arrythmias. Our cardiac biology team uses this platform for routine cardiotoxicity screening services for our pharmaceutical partners. We have screened 1,200 compounds and counting, including data in four FDA IND applications. Learn more below!

1. hiPSC-cardiomyocyte drug treatment

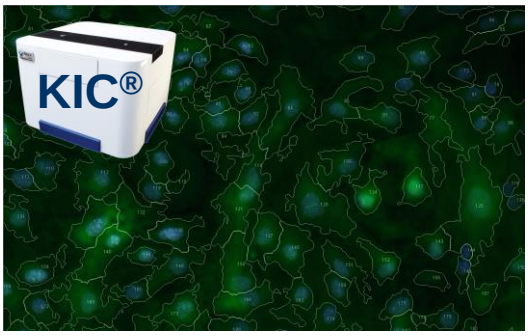
We begin by culturing hiPSC-cardiomyocytes in 96-well plates, following the plate map below. The cardiomyocytes soon begin to beat synchronously. After 12 days in culture, we expose them to DMSO alone, test compounds, or positive controls for 20 minutes before imaging.

Seven-concentration dose response format



1. **DMSO vehicle control**
2. **Test compound 1: 3 wells each of 7 doses**
3. **Test compound 2: 3 wells each of 7 doses**
4. **Dofetilide: hERG blocker that prolongs action potentials**
5. **Nifedipine: $Ca_v1.2$ blocker that shortens action potentials**

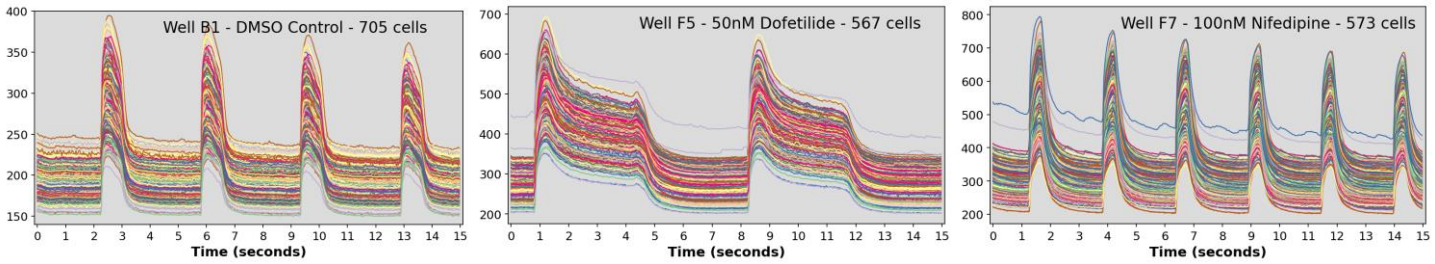
2. Kinetic Image Cytometry® single cell calcium imaging



hiPSC-cardiomyocytes exhibit action potential-induced calcium transients. Kinetic Image Cytometry® captures 15-second movies at 33 frames per second of a fluorescent calcium indicator dye in the drug-treated cardiomyocytes.

CyteSeer®, our image analysis platform, uses nucleus and calcium staining to identify hundreds of cells in each movie. It then reports the calcium fluorescence in each cell in each frame.

Single-cell calcium measurements to detect drug-induced kinetic changes



Vala Sciences Inc.
6370 Nancy Ridge Dr. #106
San Diego, CA 92121, USA

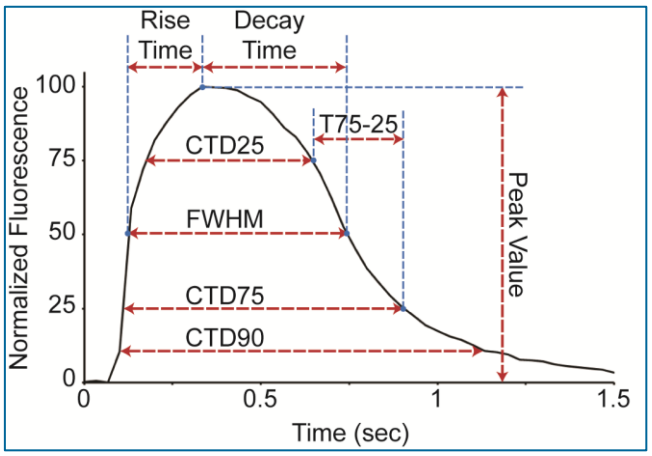
valasciences.com
linkedin.com/company/vala-sciences
twitter.com/ValaSci

Contact us
info@valasciences.com
(858) 742 – VALA (8252)

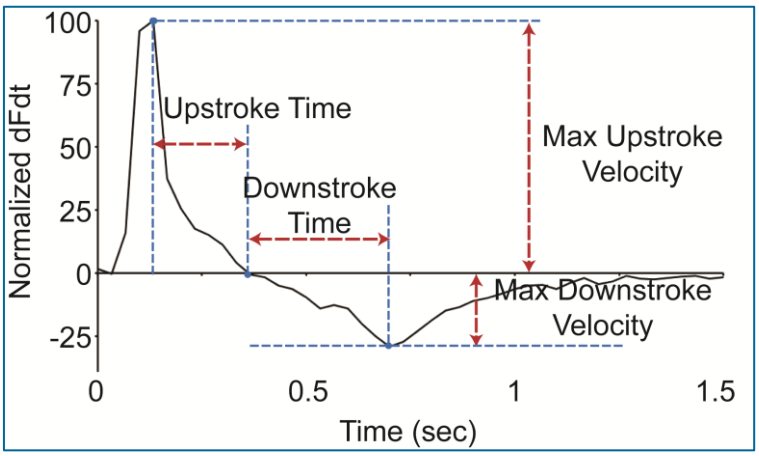
3. Automated readouts of single-transient kinetics

CyteSeer® detects individual calcium transient peaks from each single-cell trace of calcium fluorescence over time. It then reports dozens of kinetic readouts from each peak and its first derivative. We describe several readouts that can detect drug-induced changes in calcium kinetics below.

Cardiac calcium transient



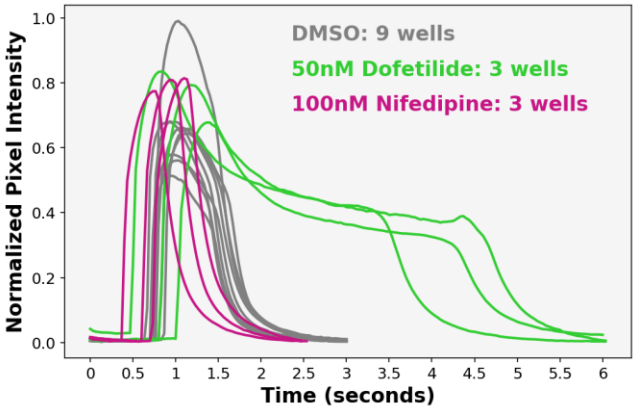
Calcium transient derivative

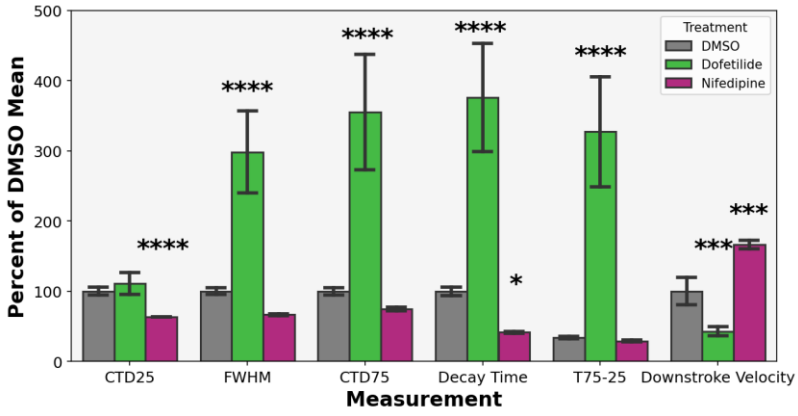


Readout	Description
CTD25	Calcium transient duration in milliseconds at 25% below the peak.
FWHM	Calcium transient duration in milliseconds at 50% below the peak.
CTD75	Calcium transient duration in milliseconds at 75% below the peak.
Decay Time	Time in milliseconds from the Peak Value to the 50% point of the transient downstroke.
T75-25	Time elapsed on the transient downstroke from the 75% point of the peak maximum to the 25% point of the peak maximum.
Max Downstroke Velocity	Maximum negative slope of the transient downstroke, as calculated from the transient 1st derivative.

4. Standardized reports of drug effects

CyteSeer® uses its data-rich readouts to generate automated reports quantifying drug-induced changes in cardiomyocyte calcium transient kinetics. Vala's pharmaceutical partners use these reports to evaluate the proarrhythmia risk for each drug candidate.





Vala Sciences Inc.
6370 Nancy Ridge Dr. #106
San Diego, CA 92121, USA

valasciences.com
linkedin.com/company/vala-sciences
twitter.com/ValaSci

Contact us
info@valasciences.com
(858) 742 – VALA (8252)