



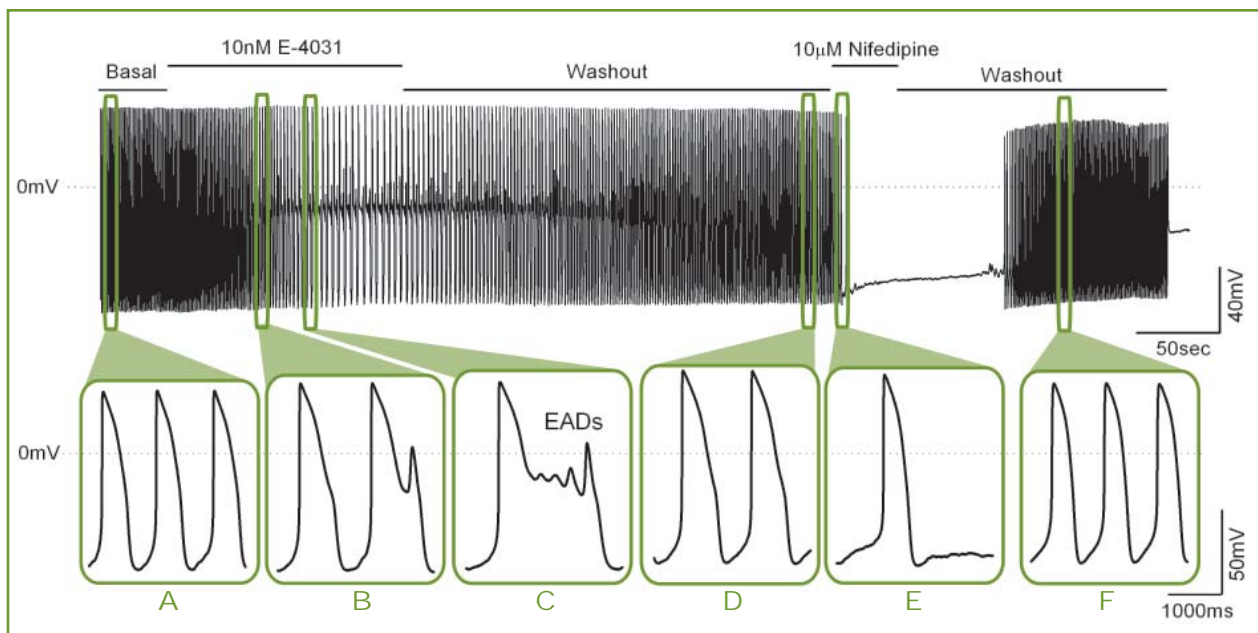
## iCell™ Cardiomyocytes: Electrophysiological Characterization

Cellular Dynamics International (CDI) introduces iCell™ Cardiomyocytes, human induced pluripotent stem (iPS) cell-derived cardiomyocytes that are maintained in vitro and exhibit characteristics and electrophysiological responses of native human cardiac tissue. The electrical activity and controllable environmental conditions of these cardiomyocytes provide an ideal model for arrhythmia testing.

### Determining Adverse Drug Reactions Early

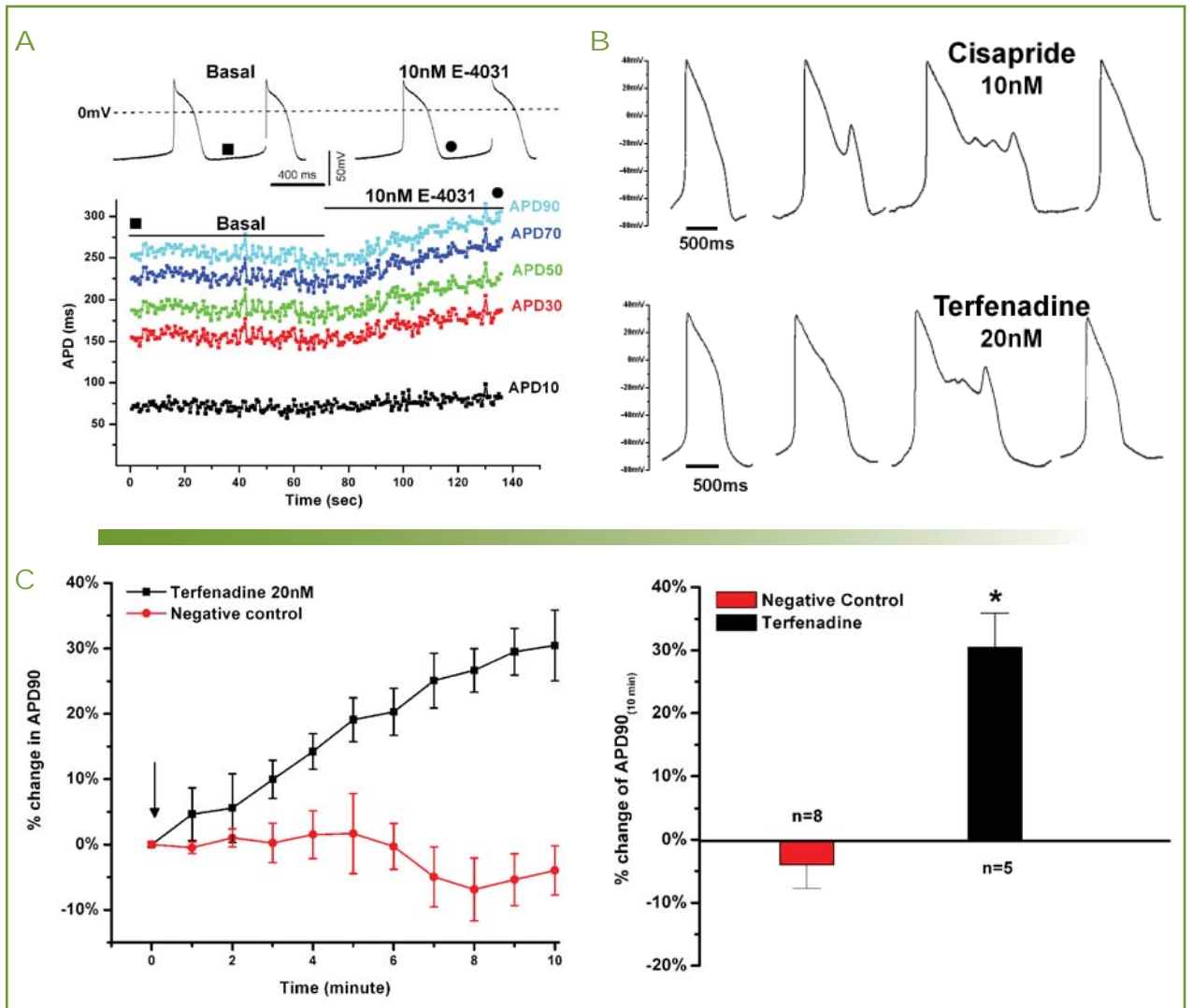
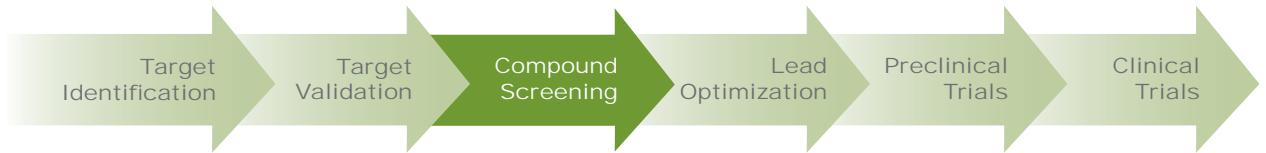
Cardiac action potentials are the rhythmic electrical oscillation of the cardiomyocyte membrane potential. Action potentials underlie basic cardiac function and arise through the precise activity of ion channels located in the plasma membrane. Small molecule compounds can disrupt the functionality of these ion channels, particularly the human ether a' go-go (hERG) channel, which carries the rapidly activating delayed rectifier potassium current ( $I_{Kr}$ ). Cardiac ion channel dysfunction can lead to prolonged action potential duration, ventricular arrhythmias, and even sudden death.

The potential for such adverse cardiac events should be determined as early as feasible during drug development. Because cardiac tissue shows species-specific expression patterns in both ion channel type and level, inaccurate impact assessments can be drawn from the use of expensive surrogate animal models. iCell Cardiomyocytes are differentiated from human pluripotent stem cells, maintained in vitro, and thus provide an easily accessible and physiologically relevant model system for assessing compound effects on human cardiac cellular electrophysiology.



▲ **Figure 1: Example Action Potential Recording and Pharmacological Responses of Isolated iCell Cardiomyocytes**

Spontaneous action potentials were recorded from an iCell Cardiomyocyte using the whole-cell, current clamp technique. The upper tracing illustrates an action potential train recorded while being perfused with Tyrodes saline (Basal), 10nM of the  $I_{Kr}$  blocker E-4031, or 10µM of the calcium channel blocker Nifedipine. The lower groups of tracings illustrate A) normal action potentials during exposure to Tyrodes saline; B and C) prolonged action potentials and early after depolarizations (EADs) in the presence of 10nM E-4031; D and E) recovery following washout; and F) the resumption of spontaneous activity following Nifedipine washout.



### ▲ Figure 2. Action Potential Prolongation by $I_{Kr}$ Blockers

Spontaneous action potentials were recorded, as in Figure 1. *i*Cell Cardiomyocytes were exposed to E-4031, Cisapride, or Terfenadine. All three drugs block  $I_{Kr}$  and show a strong cardiac liability, which either prevented movement into (E-4031) or instigated withdrawal from (Cisapride and Terfenadine) the marketplace. A) Action potential duration (APD) measurements taken at 10, 30, 50, 70, and 90% repolarization. B) Example action potentials during exposure to physiologically relevant levels of Cisapride and Terfenadine. C) APD 90 measurements during Terfenadine application.

## ADVANTAGES

### Drug Safety Screening & Discovery

- Virtually unlimited supply.
- Derived from single (isogenic) or multiple (genetically diverse) cell lines.
- Physiologically relevant ion channel complement.
- Suitable for intracellular, voltage or patch clamp, and microelectrode array recording techniques.
- *in vitro* maintenance amenable to acute and chronic testing.

### For More Information

Cellular Dynamics International, Inc.  
525 Science Drive  
Madison, WI 53711 USA

T (608) 310 - 5100 | Toll-free US (877) 310-6688  
E sales@cellulardynamics.com  
W www.cellulardynamics.com