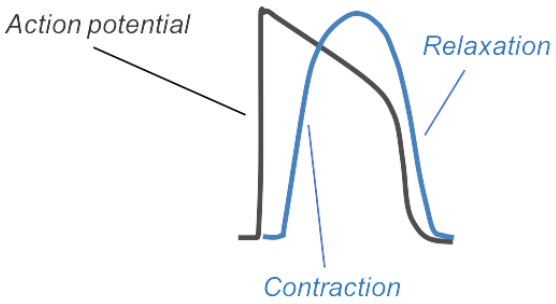
CardioPRIME™

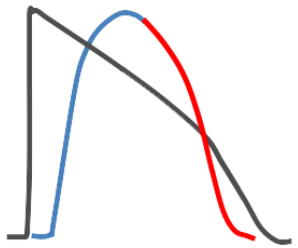
Simultaneous Prediction of Drug-Induced Pro-Arrhythmia and Inotropic Risk

CardioPRIME™ is a human primary cardiomyocyte-based assay designed to simultaneously assess pro-arrhythmia and inotropic risk. **CardioPRIME™** leverages the tight electromechanical coupling that exists in primary cardiomyocytes.

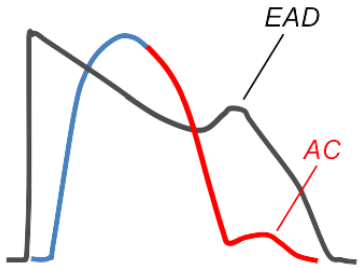
As illustrated in the figure below, any drug-induced alteration of the action potential will result in a modification of the intracellular calcium dynamics, resulting in changes to the contraction/relaxation cycle. Therefore, in contractility assays, drug-induced action potential prolongation is detected as relaxation prolongation while pro-arrhythmic EADs are detected as after-contractions.

We recently validated **CardioPRIME™** using 38 drugs with known human toxicity profiles and reported a 96% predictivity. (Nguyen et al. 2017, published in Frontiers in Physiology)



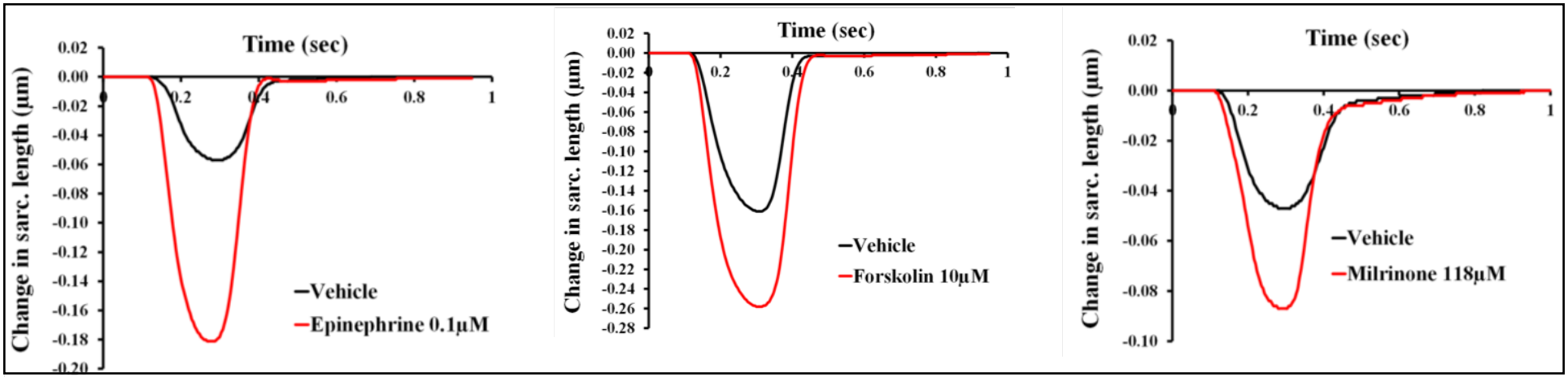


Action potential prolongation / triangulation
Prolongation of the myocyte relaxation phase



Early after-depolarization (EAD)
After-contraction (AC) at the end of relaxation

Detection of Positive Inotropic Effects in Human Primary Cardiomyocytes



CardioPRIME™ detects drug-induced inotropic effects by reporting changes in sarcomere shortening. The human primary cardiomyocytes exhibit the expected positive inotropic effect when exposed to drugs known to increase contractility (as an example, see the effect of epinephrine, milrinone and forskolin in the figures above).

This allows the **CardioPRIME™** assay to reliably identify positive inotropes at early stages of drug discovery. By contrast, stem cell-derived cardiomyocytes do not increase the amplitude of contractions in response to positive inotropes, possibly due to anomalies in the intracellular calcium handling and/or disturbances in the excitation/contraction coupling.

AnaBios
Early Human Insights

Detection of Pro-Arrhythmic Risk in Human Primary Cardiomyocytes

Human primary cardiomyocytes exhibit aftercontractions when incubated with pro-arrhythmic drugs. In the example to the left, the contractility transients induced in adult human cardiomyocytes are recorded in vehicle only (black trace) or in the presence of 0.02µM dofetilide (red trace). The aftercontractions are apparent in the red trace right at the end of each contraction transient. An example of the AC event is highlighted with a pink ellipse.