

VIDEO-OPTICAL ANALYSIS OF ENGINEERED HUMAN MYOCARDIUM IN A 48 WELL FORMAT

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Keywords: Engineered Human Myocardium, Video-optical Analysis, high throughput screening, drug screening, pharmaceuticals

Summary: Engineered human myocardium (EHM) was recently developed is used as an advanced patient-centric model for preclinical safety and efficacy screens, replacing animal research. To address the need for

We have developed a high-throughput in drug screening applications, we have developed a 48-well screening platform for automated handling and analysis using video-optic devices. In this platform, for chronic and acute screens of potentially cardioactive compounds based on the auxotonic contraction exhibited by EHM. EHM are suspended on fluorescent rubber flexible poles, generating a defined restoring force. , Contractions are recorded at high spatial (20 µm) and temporal (20 ms) resolution and analyzed in real time using special purpose hardware (Silicon Software VQ8-CXP6D). Based on contraction facilitated pole movement frequency and amplitude we determine, besides others, inotropic, chronotropic, lusitropic and arrhythmogenic effects after acute (after seconds to minutes) or chronic (up to several months) treatment of EHM responses to treatment. Controlled electrical stimulation is integrated into the screening platform to condition EHM development and assess contractile performance at defined beating frequencies. Optical analysis are sterile and non-perturbing allowing multiple measurements to follow tissue maturation and chronic effects over several weeks of treatment. Continuous electrical stimulation may be applied for improved maturation and as a tachycardia model.

The platform is validated against reference compounds, comparison to our classical isometric organ bath measurements and clinical data. Taken together, we have developed a novel screening platform to analyse cardioactive compounds using dedicated special-purpose hard and software.