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Engineered human myocardium for safety and efficacy screens of cardioactive compounds

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We employ engineered human myocardium (EHM) as patient-centric model for preclinical safety and efficacy screens, replacing animal research. Based on the spontaneous and stimulated auxotonic contraction exhibited by EHM we developed a 48 well screening plate for chronic and acute screens of potentially cardio-active compounds. EHM are cast and suspended on fluorescent rubber poles generating a defined restoring force, contractions are recorded at high spatial (20µm) and temporal (20ms) resolution and analyzed in real time using special purpose image recognition hardware. Based on contraction frequency and amplitude we determine, besides others, inotropic, chronotropic, lusotropic and arrhythmogenic responses to treatment. Our video-optical measurements are sterile and non-perturbing allowing successive measurements over weeks and months to follow tissue maturation and chronic effects. Continuous electrical stimulation may be applied for improved maturation and as a tachycardia model. Poles with increasing stiffness simulate pressure overload. The screening platform is validated against reference compounds, comparison to our classical isometric organ bath measurements and clinical data.

Keywords: Engineered Human Myocardium, Drug Screening, Image Analysis, Inotropy, Chronotropy,

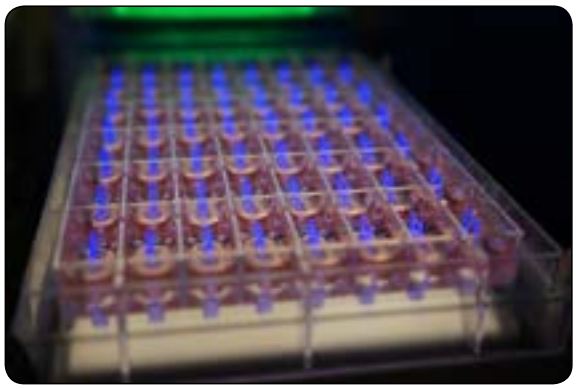

Figure 1: In-house 48 well tissue plates for high throughput screening. Fluorescent elastic poles allow for video-optical live analysis. Contactless, sterile measurements allow for continuous, chronic measurements over prolonged periods of time.

Recent Publications

1. M Tiburcy,.., T Meyer,.., WH Zimmermann (2017) Engineered Human Myocardium With Advanced Maturation for Applications in Heart Failure Modeling and Repair. Clinical Perspective. Circulation 135 (19), 1832-1847
2. J Riegler,.., Meyer T,.., JC Wu (2017) Human engineered heart muscles engraft and survive long-term in a rodent myocardial infarction model. Circulation research, CIRCRESAHA. 115.306985.
3. M Tiburcy, T Meyer, PL Soong, WH Zimmermann (2014) Collagen- based engineered heart muscle. Cardiac Tissue Engineering. Methods in Molecular Biology, 1181. Humana Press, NY

Biography

Tim Meyer has his expertise in tissue engineering of human myocardium and the automation of tissue generation and analysis. Coming from a multidisciplinary, engineering background his focus is on methods development, 3D printing, video analysis and laboratory automation.

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