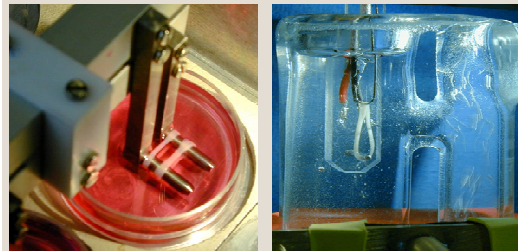
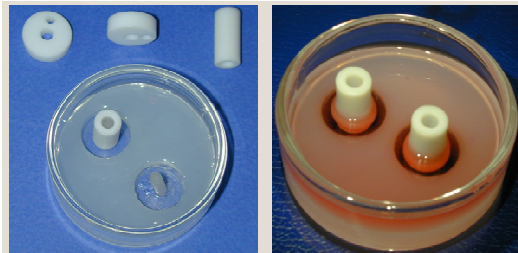


Functional target validation for cardiac insufficiency based on the Engineered Heart Tissue (EHT) technique

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Challenge

Cardiac insufficiency is a major cause of morbidity and mortality in the western world. Current therapeutic efforts aim essentially at relieving the hemodynamic load on the diseased heart. Novel approaches to the treatment strive towards



Freshly isolated mouse embryonic stem cells are mixed with collagen I and growth factors and pipetted into circular wells of silicone coated dishes. During cultivation (day 0-7), the cell-populated hydrogel condenses around the cylinder and forms a 3D EHT ring. For conditioning the rings can be transferred to a stretching device. After 12-14 days, the EHT rings can be transferred to organ bathes to record isometric force of contraction.

identifying specific targets in the heart. Whereas conventional cell cultures of cardiac myocytes allow for simple biochemical and molecular biology tests they are not well suited for evaluating the function of cardiac muscle, namely contractile force, contraction kinetics and rhythm. There is thus a great need for methods which allow a fast and efficient target validation based on functional data.

Technology

A new 3-dimensional culture format for cardiac myocytes has been developed that results in spontaneously, rhythmically and synchronously contracting heart tissue rings which allow both molecular and functional evaluations. The employed ring form is simple, exposes the cardiac myocytes to a continuous and even mechanical load which leads to good

tissue development and can be easily produced in large series. The resulting EHT can be used to determine the impact of prolonged (up to 4 weeks) pharmacological, toxic, genetic and mechanical manipulation on force of contraction and tissue development. A multi-well format has been developed to allow automatization and miniaturization. The test system is especially well suited for assessing proarrhythmic effects of non-cardiac drugs and target validation.

Commercial Opportunity

The technology is offered for co-development or licensing.

Developmental Status

A functional prototype has been developed and tested.

Patent Situation

EU (EP 1250 416 B1) issued in 2006, US pending, JP applied

Further Reading

Zimmermann WH, Fink C, Kralisch D, Remmers U, Weil J, Eschenhagen T (2000) Three-dimensional engineered heart tissue from neonatal rat cardiac myocytes. *Biotechnol Bioeng* 68:106-114



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