

In vitro produced cardiac organoids as a novel tool for pharmacological research.

Reference Number: TO 15-00551

Challenge

In vitro produced organoids are 3D-cellular aggregates, which are obtained from human pluripotent stem cells (PSC) and are often referred to as “mini organs”. According to their exceptional ability to resemble organ development, organoids have been used in various pharmacological studies. Unfortunately, all recent approaches to mimic the human embryonic heart failed and genuine cardiac organoids still do not exist. Thus, there is a strong

need for cardiac organoids as an efficient tool in pharmacological research as well as in organ-specific lab-on-a-chip approaches.

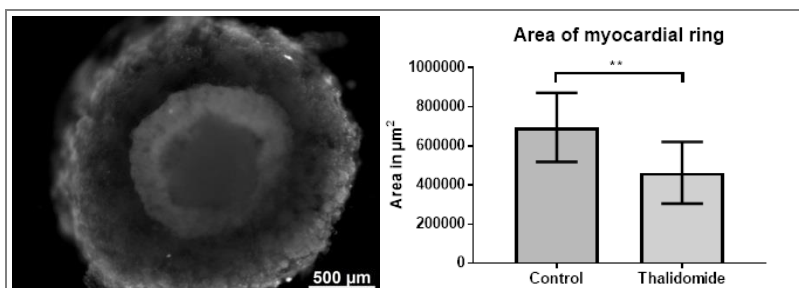


Fig. 1: 3D-Cardiac organoid

Fig. 2: Teratogenicity assay with Thalidomide as a test compound demonstrates the known effect of Thalidomide to cause cardiac malformations during embryo development is also seen in the development of the cardiac organoids.

Technology

The herewith presented technology comprises the production of genuine cardiac organoids from human PSC to

overcome the aforementioned limitations. The novel approach leads to the highly reproducible, screening platform-compatible generation of cardiac organoids in tissue culture, which contain all heart layers in an organized 3D pattern. Of particular importance, in depth analysis revealed that all cell types expected for the generation of the human heart are present in the novel cardiac organoids, including the formation of foregut endoderm and endothelial networks. As a consequence, cardiac organoids can be perfectly used as an *in vitro* model for drug screening on both differentiated organoids and during their development, e.g. in teratogenicity assays and safety pharmacology. Furthermore, the novel cardiac organoids have a significant value for organ-specific lab-on-a-chip approaches, e.g. in combination with genetic disease modeling e.g. by using patient-specific hiPSC lines and directed gene targeting.

Commercial Opportunity

In-licensing or collaboration for further development is possible.

Developmental Status

Well-established protocol for *in vitro* production of cardiac organoids. First teratogenicity test assays performed.

Patent Situation

Patent has been granted in Europe (EP 3765599B1, national validation in DE, CH, FR and GB) with priority of 2018.

Patent applications in US, CA and CN (based on PCT/EP2019/054225) with priority of 2018 are pending. Further EP patent application with priority of 2022 is pending.

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Further Reading

Fatehullah, A; Tan, SH; Barker, N. Organoids as an in vitro model of human development and disease. *Nature cell biology* **18 (3)**, (2016).

Kempf, H; Olmer, R; Haase, A; Franke, A; Bolesani, E; Schwanke, K; Robles-Diaz, D; Coffee, M; Göhring, G; Dräger, G; Pötz, O; Joos, T; Martinez-Hackert, E; Haverich, A; Buettner, F; Martin, U; Zweigerdt, R. Bulk cell density and Wnt/TGFbeta signalling regulate mesendodermal patterning of human pluripotent stem cells. *Nat Commun* **7**, 13602, (2016).

Halloin, C; Schwanke, K; Löbel, W; Franke, A; Szepes, M; Biswanath, S; Wunderlich, S; Merkert, S; Weber, N; Osten, F; de la Roche, J; Polten, F; Wollert, K; Kraft, T; Fischer, M; Martin, U; Gruh, I; Kempf, H; Zweigerdt, R. Continuous WNT Control Enables Advanced hPSC Cardiac Processing and Prognostic Surface Marker Identification in Chemically Defined Suspension Culture. *Stem Cell Reports* **13 (2)**, (2019).