EPICURE

Programming the EPIcardium to CURE broken hearts

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Summary:
Cardiac diseases are the leading cause of death worldwide, making human cardiac regeneration one of the most critical unmet clinical needs. The epicardium, the mesothelial envelope of the heart, is the source of several cardiac cells and provides signals that are essential for myocardial growth and vessel formation during development. Extensive animal research has indicated that the reactivation of these embryonic epicardial programs is the key to adult tissue repair in regenerative species such as the zebrafish, as well as in rodents up until a few days after birth, before the heart's capacity for regeneration is lost. How the human epicardium develops and responds to injury is largely unknown. We recently established the first human pluripotent stem cell-based cardiac organoids showing the self-organization of epicardium and myocardium into a functionally patterned structure resembling the embryonic ventricular wall. These 'epicardioids' offer unique possibilities to study the dynamics of human epicardium development and function at a single-cell resolution. EPICURE aims at decoding and harnessing these programs as potentially transformative means for human heart regeneration. State-of-the-art lineage recordings, 3D imaging, and spatial multiomics in epicardioids will be used to dissect the fate acquisition mechanisms of the human embryonic epicardium and identify critical signalling pathways in health and disease. This *in vitro* approach will be complemented by charting a spatiotemporal, cross-species single-cell atlas of the cardiac injury response *ex vivo* and *in vivo*, including the first genetic lineage tracing of the adult epicardium in a large animal model. Finally, we will capitalize on the novel concept that CRISPR-mediated, temporal programming of the epicardium could drive meaningful heart regeneration in adulthood. Clearly, EPICURE will yield a wealth of new insights into human epicardial biology while breaking new ground in cardiac regenerative medicine.

Additional information available on CORDIS
https://cordis.europa.eu/project/id/101141820

Project details

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