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Single Cell Transcriptomic for Studying Lineage Identities, relationships and cross-talks during Cardiac development and disease

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Abstract

The heart is the first organ that forms during embryogenesis and its functionality depends onthe proper spatio-temporal assembly and integration of multiple progenitor cell populationsthat ultimately give rise to the diverse cell types within the specialized cardiac structures.Lineage tracing and clonal cell analyses in mice have identified two sources ofcardiac mesoderm progenitors at the beginning of cardiogenesis, known as first and secondheart fields (FHF and SHF), which are specified already at the primitive streak stage and show differential contribution to specific heart compartments later on.The FHF cells differentiate first, forming the primitive heart tube and ultimately the LV, while the SHF progenitors are added later to the heart tube at the anterior and posterior poles: the anterior SHF give rise to the RV, the proximal OFT, while the posterior SHF contribute to the atria. Recent advances in single-celltechnologies now enable to deal with developmental processes that are characterized by rapid dynamic changes in cellular states studying lineage identities, relationships and cross-talks during cardiac development and disease. Indeed, over the past decade cardiomyocytes generated from patient-specific induced pluripotent stem cells (iPSCs) have been shown to recapitulate key features of heritable diseases and provide a promising platform for disease modeling and drug development, in order to identify perturbations in gene programs controlling cardiac lineage.

Here, we took advantage of iPSC disease model and single-cell approaches to predict mechanisms of disrupted cardiac development in hypoplastic left heart syndrome (HLHS)one of the most lethal congenital heart disease (CHD)characterized by underdevelopment of the left-sided cardiac structures at unprecedented resolution.

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