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Title:

Morphological changes during the third month of gestation refine both molecular and anatomical aspects of the human developmental heart cell atlas

Abstract:The heart is the vital organ with the longest functional lifespan. Cardiac malformations can range from asymptomatic to immediately life-threatening and can also predispose to complications many decades after birth. Understanding the origins of congenital heart defects could improve diagnoses, prognoses and therapies. The first gestational trimester in humans corresponds to critical inductive and morphogenetic events in the hearts of animal models. However, a more comprehensive atlas of the human heart during the eight to twelve post-conceptual week window of vulnerability is needed. We establish cellular states, identities and dynamics in this timeframe in prenatal human cardiac tissues from both female and male fetuses, using single-nucleus and spatial transcriptomics as well as light-sheet microscopy to provide a four-dimensional anatomical scaffold with blood vessels and autonomic nerves. By integrating and validating newly identified minority cell populations across the individual hearts represented in our and other datasets, we demonstrate that multiple levels of map resolution are informative. Notably, the transcriptomes of cells at junctional positions in human hearts during the third month of gestation show semi-continuous identities in subclusters that reflect the importance of spatial and temporal context during morphogenesis. This information will be helpful for future revisions of the human cell atlas, not only before birth but also as a baseline for understanding when and how genetics contribute to cardiac health disparities.

Presentation Type: Oral

First choice of session topic: Cardiac Morphogenesis

Second choice of session topic: Other

Role of presenting author: Senior Faculty (Associate or Full Professor or Equivalent)