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Refinement of the four-dimensional human heart atlas during the first trimester of gestation with rare and diverse cell states

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Congenital heart defects are frequent and collectively represent a significant burden for human health. Understanding the developmental origins of such anomalies is key to improving diagnoses, prognoses and therapies. The Human Developmental Cell Atlas (HuDeCA) consortium in France gathers as much data and metadata as possible about normal human embryonic and early fetal tissues donated to research, complete with strict quality control procedures and use of standardized annotations, as a complement to the international Human Cell Atlas and a baseline for the scientific community worldwide. Here, we contribute new data about the identities and trajectories of cells in human male and female hearts from 8 to 12 post-conceptual weeks through judicious comparisons of individual hearts assessed through single-nucleus and spatial transcriptomics and advanced imaging approaches. We integrate and validate this information both across our datasets and with existing atlases, using multiple technical platforms to provide four-dimensional analyses at varying levels of resolution. Delineating the gene expression networks deployed within individual cells at specific positions has revealed an unsuspected diversity of cellular states. This data enables new hypotheses about the paracrine influences exerted by and on the many lineages necessary for the complex functions of the first and longest-lived vital organ.