



Spatially resolved multiomics of human cardiac niches

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Abstract

A cell's function is defined by its intrinsic characteristics and its niche. Here, we combine single-cell and spatial transcriptomic data to discover cellular niches of the human heart. We map cells to micro-anatomic locations and integrate knowledge-based and unsupervised structural annotations. For the first time, we profile the cells of the human cardiac conduction system (CCS) and show that the sinoatrial node is compartmentalised, with a core of pacemaker cells, fibroblasts and glial cells. We introduce a druggable target prediction tool, drug2cell, which leverages single-cell profiles and drug-target interactions. In the epicardium, we show enrichment of plasma cells forming immune niches which may contribute to infection defence. We identify a ventricular micropathological niche consisting of activated fibroblasts and stressed cardiomyocytes which are expanded in cardiomyopathy. Overall, we provide new clarity to cardiac electroanatomy and immunology, and our suite of computational approaches can be deployed to other tissues and organs.

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