

In Vivo and In Vitro Cartilage Differentiation from Embryonic Epicardial Progenitor Cells

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The presence of cartilage tissue in embryonic and adult hearts of various vertebrate species is a well-recorded fact. However, while the embryonic neural crest has been historically considered as the main source of cardiac cartilage, recently reported results on the wide connective potential of epicardial lineage cells suggest they could also differentiate into chondrocytes. During heart embryogenesis, the epicardial epithelium forms over the originally bare myocardial surface from epicardial progenitor (proepicardial) cells to then give rise to a large population of mesenchymal Epicardial-Derived Cells (EPDCs) that will crucially contribute to the building, growth, and maturation of the ventricle and atrioventricular cardiac structures. In this work, we describe the formation of cardiac cartilage clusters from proepicardial cells, both *in vivo* and *in vitro*. Our findings report, for the first time, cartilage formation from epicardial progenitor cells in the embryonic heart, and strongly support the concept of proepicardial cells as multipotent connective progenitors. These results are relevant to our understanding of cardiac cell complexity and responses to pathologic stimuli.