

Pericardium: What We Still Do Not Know?

Epicardium in Cardiac Development and Disease

Jung-Sun Kim, MD, PhD

Department of Pathology Samsung Medical Center

Sungkyunkwan University School of Medicine, Seoul, Korea

The heart tube of the early embryo is composed of an inner endocardial layer and an outer myocardial layer, which is covered by the epicardium later. The epicardium originates from the proepicardial organ, which is located near the venous pole of the heart. A proportion of epicardial cells undergo epithelial-to-mesenchymal transition to populate the subepicardial space, which are called epicardium derived cells (EPDC). EPDCs are distinguished through the expression of WT1, Tbx18, Tcf21 and Raldh2. They migrate into the myocardium to give rise to cardiac interstitial fibroblasts and smooth muscle cells of the coronary arteries. Paracrine signals of EPDCs influence myocardial maturation and development of the coronary vasculature, which include retinoic acid and fibroblast growth factors. Impairment of epicardial developmental process in animal models results in a variety of cardiac anomalies such as non-compaction cardiomyopathy, deficient annulus fibrosis, valve formation, and coronary artery abnormalities. The epicardium in the normal adult heart is quiescent, but it reactivates an embryonic gene program in the injured heart. Cellular contribution to the injured heart by EPDC is still controversial. Reactivation of epicardial signaling in response to injury influences cardiac remodeling (fibrosis) and immune response. Heart regeneration models in lower vertebrates and neonatal mice show organ-wide epicardial activation, epicardial-myocardial interaction and proliferation of pre-existing cardiomyocytes. However, the proliferating population in the adult mouse model is cardiac fibroblasts instead of myocytes in spite of epicardial activation. Further understanding of epicardial contribution in the developing heart and in the injured heart may provide a key clue for the treatment of heart failure.