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Biological properties of cardiac stem cells in normal and pathological conditions - matrix makes a difference

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Cardiac cells and extracellular matrix (ECM) are reciprocally related and their characteristics are modified in response to developmental or pathophysiological cues. Adult human cardiac tissue regeneration mediated by cardiac stem cells (CSCs) is strictly regulated and, hypothetically, impaired by the ECM-CSC signalling in the pathological conditions.

To test this hypothesis, we isolated cardiac fibroblasts (CFs) and CSCs from the atria of age-matched adult human normal (n=9) and pathological hearts (ischemic cardiomyopathy, n=11). The CFs were cultured in order to obtain ECM coating and conditioned medium, which were characterized by immunoblotting and ELISA, respectively. Next, we examined the effects of CF-derived ECM and CF-conditioned medium on normal and pathological CSC proliferation, apoptosis, and migration in vitro.

The ECM produced by CFs from normal heart was composed mainly of fibronectin, laminin α2 and collagen I, while that produced by CFs from hearts with ischemic cardiomyopathy contained also laminin α1 and tenascin X. Compared to the normal CF-conditioned medium, that conditioned by pathological CFs contained twice as much IGF1 and HGF, and it stimulated proliferation and migration, while reducing apoptosis of CSCs. In the presence of pathological CF-derived ECM, there was a nearly 2-fold increase ($p<0.05$) in proliferation of normal and pathological CSCs, when compared to normal CF-derived ECM. Moreover, pathological CF-derived ECM reduced CSC apoptosis, specifically in cells from pathological heart. However, in the same conditions, the migration of pathological CSCs was significantly lower.

These results indicate that the activity of CFs and its modification in chronic ischemic conditions determines biological properties of CSCs. Such an influence should be taken into consideration when attempting ischemic cardiac tissue stem cell-based regeneration.

Keywords: Cardiac stem cells, extracellular matrix, cell-matrix Interaction, cardiac regeneration.