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Hypoxia activates stem cells in myocardial tissue

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On behalf: Laboratory of Molecular Cardiology

Topic(s):
Stem Cells, Cell Cycle, Cell Senescence, Cell Death

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S66

Background. Regeneration of the myocardium after ischemic damage is an actual problem of current regenerative medicine. Endogenous stem cells of the heart have been described. These cells retain their regenerative potential in the postnatal period. Cardiac stem cells are a heterogeneous group of cells. Populations of these cells have been identified in the atria, ventricles, epicardium or pericardium of the heart. The discovery of these cells is an important step towards regenerative medicine, but the mechanism of activation of cardiac stem cells remains little known.

Purpose. Our aim was to compare cardiac stem cells from peri-infarction area to cardiac stem cells from healthy area of the myocardium in the experimental model of acute hypoxic damage. We compared cells by functional properties, such as growth rate, migration and differentiation abilities.

Methods. Myocardial infarction of the left ventricle was induced in Wistar rats by a permanent ligation of the left coronary artery. After 3 days cardiac stem cells were isolated from the ischemic area by enzymatic dissociation of the tissue healthy myocardial tissue was used as control. The cells were immunophenotyped by flow cytometric analysis. Proliferation rate was evaluated using growth curve method. Migration rate was estimated using scratch method. The cells were differentiated in cardiogenic, adipogenic and osteogenic directions by addition of specific inducers to the cell culture medium. Differentiation efficiency was estimated by qPCR for specific markers of differentiation. Differentiated cells were stained for the specific markers by immunocytochemistry.

Results. Peri-infarct cells possessed a higher proliferative potential than the cells from healthy area of the myocardium. They also had a greater propensity to migrate to the area of a "scratch". According to a PCR experiment, the level of activation of specific differentiation markers (TNNT2, BMP2, Runx2 and Fabp4) was higher in peri-infarct cells.

Conclusion. Ischemic damage of the myocardium leads to activation of the internal regenerative potential of cardiac stem cells in vivo, which is most pronounced in the peri-infarction zone.