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Enhancing the effectiveness of human cardiac stem cell therapy with the HO-1 inducer-Cobalt Protoporphyrin (CoPP)

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The regenerative potential of c-kit+ cardiac stem cells (CSCs) is severely limited by the poor survival of cells after transplantation in the infracted heart. We have previously demonstrated that preconditioning human CSCs (hCSCs) with the HO-1 inducer, CoPP, has significant cytoprotective effects in vitro. Here, we examined whether preconditioning hCSCs with CoPP enhances CSC survival and improves cardiac function after transplantation in a model of myocardial infarction induced by a 45-min coronary occlusion and 35-day reperfusion in immunodeficient mice. At 30 min of reperfusion, CoPP-preconditioned hCSCsGFP+, hCSCsGFP+, or medium were injected into the border zone. Quantitative analysis with real time qPCR for the expression of the human specific gene HLA revealed that the number of survived hCSCs was significantly greater in the preconditioned-hCSC group at 24 hours, 7 and 35 days compared with the hCSC group. Co-immunostaining of tissue sections for both GFP and human nuclear antigen further confirmed greater hCSC numbers at 35 days in the preconditioned-hCSC group. At 35 days, compared with the hCSC group, the preconditioned-hCSC group exhibited increased positive and negative left ventricular (LV) dP/dt, end-systolic elastance and anterior wall/apical strain rate (although ejection fraction was similar), reduced LV remodeling, and increased proliferation of transplanted cells and of cells apparently committed to cardiac lineage. In conclusion, CoPP-preconditioning of hCSCs enhances their survival and/or proliferation, promotes greater proliferation of cells expressing cardiac markers, and results in greater improvement in LV remodeling and in indices of cardiac function after infarction.

Biography

Chuanxi Cai has completed his PhD from the Institute of Biophysics at Chinese Academy of Sciences in Beijing, China and Post-doctoral studies from UMDNJ-Robert Wood Johnson Medical School (RWJMS). Currently, he is the Associate Professor of Cardiovascular Medicine in the Albany Medical College. He has published 17 papers in reputed journals and has been serving as Editorial Board Member of several scientific journals.

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