Abstract: P139

Human cardiac progenitor analysis in dystrophin cardiomyopathy after cardiac transplantation

Authors:
M Pesl1, S Jelinkova2, G Caluori3, M Holicka4, V Zampachova5, P Nemec6, P Dvorak2, V Rotrek1, 1St. Anne's University Hospital, Center of Biomolecular and Cellular Engineering and dep. of Cardiovascular diseases - Brno - Czech Republic, 2Masaryk University, Biology dep., Faculty of Medicine - Brno - Czech Republic, 3St. Anne's University Hospital, ICRC and CEITEC, Masaryk University, - Brno - Czech Republic, 4Masaryk University, Department of Cardiology, University hospital Brno and Faculty of Medicine - Brno - Czech Republic, 5Masaryk University, St. Anne's University Hospital, Ist Department of Pathology, Faculty of Medicine - Brno - Czech Republic, 6Center for Cardiovascular Surgery and Transplantation - Brno - Czech Republic,

Topic(s):
Basic Science - Cardiac Diseases: Cardiomyopathies

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S36

Funding Acknowledgements:
The research has been funded by the Grant Agency of the Czech Republic no. GBP302/12/G157 and by the NPU projects LQ1601 CEITEC and LQ1605 FNUSA-ICRC

We report for the first time human dystrophy (Becker type, BMD) cardiac progenitor analysis. Following rare cardiac transplantation in case of a symptomatic BMD samples were obtained and compared to healthy control samples. Heart failure is a frequent cause of death in muscle dystrophy patients. We hypothesized lower repair capacity of myocardium, possibly due to decreased percentage of reparative c-Kit+ cells and their impaired migration capacity.

BMD patient has been diagnosed with exon 25 deletion in the dystrophin gene. During late 30’s of patient heart failure progressed, and he was enrolled to heart transplantation waiting list and recently transplanted. With informed consent of patient, explanted organ was dissociated to single cells and progenitors evaluation and cultivation took place. Donor organ atrial myocardium (WT) samples were analyzed as control samples (triplicates from consecutive six following donors). There was no significant age difference between acceptor and donors.

Methods: Gross histopathological evaluation and dystrophin immunostaining was performed, as well as flow cytometry analysis of c-Kit+/CD45- cells. The explanted cells were further propagated in vitro and evaluated for cell migration at 9 and 28 days, 4 different WT samples with at last eleven outgrowths were evaluated.

Results: Dystrophic heart presented irregular fibrosis, thinned or absent myocardial layer and prevalent adipose tissue in both ventricles. Optical microscopy showed non-specific myocardial changes of dilated cardiomyopathy with hypertrophic cardiomyocytes and interstitial fibrosis. Gross samples showed mosaic pattern with subtotal absence of membranous dystrophin staining and only sporadic isolated myocytes. Percentage of BMD c-Kit+/CD45- cells was in atria 0.28% right and 0.35% left; in ventricles 0.42% right, 0.58% left and 0.12% in septum. In WT left atrial samples was c-Kit+ percentage 1.69%. In order to confirm further WT atria were sampled with corresponding values of 1.61% and 1.49% respectively. Outgrowth cell migration distance was 546±298μm in BMD and 1198±90μm in WT (p<0.001). c-Kit+ cells were still detectable in BMD and WT at day 28 (15% of explants vs 30% of WT explants showing phase bright cells), after 6 weeks phase bright cell were still present in in WT, but none were detected in in dystrophin outgrowths, where fibroblast flourished.

Conclusion: Failing dystrophy heart has depleted pool of c-Kit+ cells with reduced mobility and outgrowth survival. This may be caused by previous increase in cardiomyocyte turnover. Process of progenitor depletion may be responsible for genetic as well as non-genetic heart failure, and represents new therapeutically relevant target.
may be responsible for genetic as well as non-genetic heart failure, and represents new therapeutically relevant target.