A Role for MITF in Cardiac Progenitor Cell Proliferation and Differentiation

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Background: There is growing evidence that cardiac progenitor cells (CPCs) exist in the adult heart, but mechanisms of CPC differentiation and proliferation are poorly defined.We recently grew, defined and differentiated CPC's from left atrial appendages of adult mice. Microphthalmia transcriptionfactor (MITF) is critical in differentiation and proliferation of several cell types, including neural crest and mast cells. We recently showed that MITF is expressed in the adult heart, and has a prominent role in cardiac hypertrophy. Here we explored the potential role of MITF in CPC proliferation and differentiation.
Methods: Cells were grown from atrial appendages of adult wild-type and MITF mutated mice. Cardiomyogenic differentiation was induced by dexamethasone. CPC presence and differentiation capability was investigated by immunostaining with CPC and adult cardiomyocyte markers. MITF transcript was detected using PCR.
Results: CPC's expressed MITF-a instead of the adult MITF-h isoform. Ki-67 staining showed that there was a reduced number of proliferating cells from the MITF mutated mice when compared towild-type mice. Both wild-type and MITF mutated cells expressed the specific CPC markers Nkx2.5 and Gata-4. Three weeks after dexamethasone treatment, normal cells expressed organized sarcomeric proteins (myosin heavy chain (MHC) and actinin) and atrial natriuretic factor (ANF). In contrast, the expression of MHC and sarcomeric actinin in MITF mutated cells was undetectable, although expression of ANF and Nkx2.5 was not affected.
Conclusion: Our preliminary results demonstrate that MITF is expressed in CPCs, and suggest a novel role for MITF in both CPC proliferation and differentiation.