A ROLE FOR MICROPHTHALMIA TRANSCRIPTION FACTOR (MITF) IN CARDIAC PROGENITOR CELL PROLIFERATION AND DIFFERENTIATION

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Background: Microphthalmia transcription factor (MITF) is critical in differentiation and proliferation of several cell types, including neural crest and mast cells. We have previously shown that MITF is expressed in the adult heart, with a prominent role in hypertrophy and stress response. We grew, defined and differentiated cardiac progenitor cells (CPCs) from the left atrial appendages of adult mice and explored the role of MITF in CPC proliferation and differentiation.

Methods: Cells were grown from the atrial appendages of adult wild type (WT) and MITF-mutated mice. Differentiation was induced with dexamethasone. CPC abundance and differentiation was investigated with immunostaining. MITF was detected using RT-PCR.

Results: CPCs expressed MITF-a instead of the adult MITF-h isoform. Ki-67 staining showed a reduced number of proliferating cells from the MITF-mutated mice as compared to WT (figure). WT and MITF-mutated cells expressed specific CPC markers Nkx2.5 and Gata-4. After dexamethasone treatment, WT cells expressed organized sarcomeric proteins, myosin heavy chain (MHC), sarcomeric actinin, and atrial natriuretic factor (ANF). In contrast, expression of MHC and sarcomeric actinin in MITF-mutated cells was undetectable.

Conclusion: MITF is expressed in CPCs and may have an important role in both CPC proliferation and differentiation in the adult heart. This could represent a potential explanation for the role of MITF in cardiac stress responses.