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Content

SPATIAL PROFILE OF ANKRD1A ACTIVATION DURING REGENERATION OF ZEBRAFISH HEART

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Introduction: In contrast to humans, zebrafish have a remarkable ability to regenerate injured heart through a complex and highly orchestrated process involving all cardiac structures. The major source of new myocardial cells are resident cardiomyocytes, which dedifferentiate and reinitiate proliferation, invading the area of injury to replace the lost myocardium. The response of the myocardium and coronary vasculature is preceded by activation of epi- and endocardium, which form active scaffolds to guide regeneration. The aim of this study was to identify cardiac structures in which *ankrd1a* gene is activated during zebrafish heart regeneration.

Methods: We crossed several zebrafish reporter lines: *TgBAC*(*ankrd1a*:*EGFP*) (to identify cells expressing *ankrd1a*), *Tg*(*myl7*:*nls-dsRedExpress*) (for labeling cardiomyocyte nuclei) and *Tg*(*kdrl*:*RAS-mCherry*) (for labeling endocardial/endothelial cells). Zebrafish hearts were cryoinjured and left to regenerate for 3 and 7 days. Dedifferentiating cardiomyocytes and epicardial cells were immunostained with anti-MYH7 and anti-caveolin1 antibody, respectively. Cells labeled with transgenes and immunostaining were visualized on tissue cryosections by fluorescent microscopy.

Results: Zebrafish *ankrd1a* was activated in the injury border zone cardiomyocytes, located between the injured and remote myocardium. Its expression preceded that of a dedifferentiation marker, MYH7. The *TgBAC(ankrd1a:EGFP)* transgene was not detected in epicardial or endocardial cells of regenerating zebrafish heart.

Conclusion: Activation of *ankrd1a* during regeneration of zebrafish heart is restricted to borderzone cardiomyocytes, implicating this gene in dedifferentiation and proliferation of cardiomyocytes. The absence of *ankrd1a* expression in epicardium and endocardium indicates that this gene does not contribute to the regeneration process occuring in these layers of the heart.

Keywords: zebrafish; heart; regeneration; *ankrd1a*

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