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MicroRNA let-7c regulates heart regeneration after cryoinjury in adult zebrafish

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Introduction: Micro-RNAs are short, noncoding RNA molecules that regulate gene expression. Micro-RNA let-7c has an important role in cardiac regeneration and remodelling after myocardial infarction in mice. Understanding the role of let-7c in regeneration of zebrafish heart remains incomplete.

Methods: Antagomir injections were used to knockdown Let-7c, while injections of scramble RNA were used as control in adult zebrafish. The apex of the ventricle was cooled with a metal probe dipped in liquid nitrogen, this procedure kills cardiomyocytes and mimics myocardial infarction. Knockdown of let-7c was confirmed with qPCR. Cardiac function was followed with cardiac ultrasound before the cryoinjury and after the cryoinjury at day 1, 1 week, 2 weeks, 3 weeks and 4 weeks. Fractional volume shortening (FVS) of the ventricle was found to be the most reliable and repeatable method to quantify cardiac function. Heart, liver and kidney samples were collected at 2 weeks and 4 weeks for qPCR, Acid Fuchsin Orange G staining and immunohistochemistry with proliferating cell nuclear antigen (PCNA).

Results: Let-7c antagomir treatment resulted in faster recovery of cardiac function and improved regeneration after cryoinjury compared to control treatment. FVS returned to pre-cryoinjury levels ($35.74\% \pm 1.01\%$) in let-7c antagomir fish three weeks after cryoinjury ($29.92\% \pm 1.9\%$, $P=0.053$), whereas, FVS was comparable to pre-cryoinjury levels at 4 weeks ($29.18\% \pm 0.63\%$, $P=0.052$) in the control fish. Let-7c antagomir fish had lower fibrin% ($8.64\% \pm 2.20$, $P=0.039$) in the injured area at four weeks compared to control fish ($19.67\% \pm 4.26$). Collagen accumulation started earlier in the let-7c antagomir fish indicating a faster recovery. At 2 weeks fibrin/collagen% was greater in let-7c antagomir fish compared to control fish ($43.16\% \pm 4.87$ vs. $29.98\% \pm 3.97$, $P=0.05$). Immunohistochemistry with PCNA revealed a trend of higher proliferating cardiomyocytes in the antagomir group at two weeks.

Conclusion: Inhibition of Let-7c improved cardiac regeneration after cryoinjury in adult zebrafish.

Biography

Suneeta Narumanchi is currently a PhD student in Ilkka Tikkanen's Group, Minerva, Biomedicum 2U, from December 2013. She has worked as a Researcher at Department of Biochemistry, University Of Helsinki, Carl Gahrberg's lab in Feb 2010 – May 2012. She also published many articles some of them are sept7b is required for the subcellular organization of cardiomyocytes and cardiac function in zebra fish (* in thesis), Microbes in the Treatment of Diabetes and Its Complications etc.

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