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Preconditioning and extracellular matrix analysis in adult zebrafish heart regeneration and characterisation of skeletal muscle regeneration

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Zebrafish are excellent models for regenerative studies, considering their abilities to replace a number of organs and employment of different regenerative strategies.

A new cryoinjury model for massive skeletal muscle injuries has been established, leading to the destruction of four to five myomeres, which will be cleared and replaced in the following ten days. Complete restitution of the tissue is achieved after thirty days. During this process new markers for muscle identities were discovered, revealing a previously undescribed subdivision of the slow-twitch muscle. Such a division is not yet described in mammals. After satellite-like stem cell division, dynamics of myoblast differentiation as well as early myotube formation could be visualised and described. A gene specific for the slow-twitch muscle fibers, called *smyhc1*, seems to be highly expressed during this early stage of muscle regeneration. Completion of regeneration was observed, with the loss of previously sharp boundaries between different muscle fibre types.

The *Tnca/b* as well as *col12a1a/b* genes produce extracellular matrix proteins expressed during regeneration. A double transheterozygous *tnc* mutant displayed no impairment during fin or heart regeneration. The viability of a *col12a1a/b* double homozygous mutant has yet to be confirmed. However, preliminary experiments indicate a function during the reabsorption of the transient scar in the context of heart regeneration for *col12a1a*.

At different time points after cryoinjury serum of zebrafish was pooled and analysed. A high-performance liquid chromatography allowed for a high yield of unique protein numbers and revealed potential candidate genes responsible for a preconditioning effect. The serum of cryoinjured zebrafish was shown to elicit an immune system stimulating effect if injected into the pericardial cavity in advance to a following injury of the recipient fish.

Concluding, the presented work contributes to the understanding of different regenerative principles in the adult zebrafish.

Jury:

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