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Caudal fin regeneration in adult zebrafish: small molecules, cell adhesion molecules and extracellular matrix

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Zebrafish, a small fresh water fish, is a popular model organism for regeneration. Indeed, it has the extraordinary ability to restore many of its organs after injury. These organs include the heart, the spinal cord, the retina, the pancreas and the fins. Fin regeneration occurs through the formation of a specialized proliferative tissue, the blastema, which arises from dedifferentiated cells of the stump. The roles of classical signaling pathways have been extensively studied during fin regeneration. In my thesis, I focused instead on players of regeneration which had garnered less attention so far, namely small molecules, extracellular matrix components and adhesion molecules.

The first project revealed the presence of the neurotransmitter serotonin in two cell populations of the zebrafish fin. The first population of cells, present both in uninjured and regenerative fins, were solitary chemosensory cells located in the epidermis. The second population of serotonin-positive cells were mesenchymal cells of the proximal blastema. Serotonin was present in these cells at the vicinity of the amputation site from 1 dpa to 5 dpa. However, inhibition of serotonin production did not cause any defects in regeneration.

The second projects investigated the reestablishment of actinotrichia after amputation. Actinotrichia are flexible collagenous fibers, present at the distal tip of the uninjured fins, where they act as a scaffold in the absence of bone. We showed that actinotrichia were deposited in the regenerate already at 2 dpa and that their dynamics during the regenerative process were complementary to bone regeneration. We also demonstrated the role of multiple signaling pathway in inducing actinotrichia deposition.

In the third project, the function of Bone Morphogenetic Protein signaling was studied during fin regeneration. This pathway was required for the regeneration of actinotrichia and bones, for the refining of blood vessels and for the organization of the basal wound epidermis.

Finally, in the fourth project, we initiated an investigation into the role of Activated Leucocyte Cell Adhesion Molecule (Alcam) during regeneration. This protein is expressed in the basal wound epidermis and in osteoblasts of regenerating fins. We generated transgenic fish lines for the tissue specific, inducible and reversible expression of different *alcam* versions (full length, transmembrane and secreted). These lines will allow the investigation of the role of Alcam during bone regeneration in zebrafish fins.

Overall, mechanisms of fin regeneration still retain many mysteries, which will continue to occupy scientists for decades. In this work, I contributed to the elucidation of some of them.

Jury:
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