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TETRASPANINS IN ZEBRAFISH DEVELOPMENT

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Introduction: Tetraspanins represent a family of integral membrane proteins involved in cell-cell interaction, including adhesion, fusion, differentiation and proliferation. These basic functions are essential for embryonic development, yet there is little research on the role of tetraspanins in this process. The aim of my project is to pilot zebrafish as a new and sensitive model for assessing tetraspanin function in vertebrate development.

Background: There are approximately 50 tetraspanin genes in zebrafish, representing orthologues of most of the 33 mammalian genes. mRNA expression analysis has shown that at least 22 of these are expressed in zebrafish embryos and thus may regulate developmental processes. CD9 is a well-characterized tetraspanin and we have shown that zebrafish CD9 orthologues are present in the posterior lateral line (pLL), a sensory system comprised of hair-cell containing neuromasts. The development of the pLL coordinates proliferation, deposition and migration simultaneously and thus requires highly regulated cell interactions.

Major findings: We generated CRISPR double knockouts (dKOs) of both zebrafish CD9 paralogues. The dKOs are adult viable and fertile, in contrast to mouse CD9 KO females which are sterile. Inspection of the pLL in the CD9 KOs revealed that there is measurably slower migration of the primordium and fewer hair cells in the posterior neuromasts at 10 dpf. Furthermore we observed a reduced regenerative capacity of the dKO neuromasts, and also upregulation of CD9 paralogues during bone repair.

Conclusions: Our results suggest a role for CD9 in collective cell migration and hair cell development. We will analyse the organisation and migration of the primordium in more detail as well as the development and regeneration of the neuromasts and bone. This will be aided by generating fluorescent transgenic zebrafish to visualise dynamic processes involved. This offers a unique insight into the in vivo function of tetraspanins.