Exploring cell signaling in zebrafish tooth development

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Intercellular signaling pathways are necessary for directing proper gene expression and influencing the resulting cell phenotypes and organ development. The model vertebrate zebrafish (Danio rerio) has been used to study these signaling pathways due to their close genetic relationships to other vertebrates (including humans), their fast development, and the ease with which they can be genetically manipulated. By studying the roles of cell signaling pathways in specific organs and structures, such as the teeth, we can gain new information about how these structures develop and take form.

Many studies have been conducted altering the expression of cell signaling pathways and looking at the resulting changes to phenotypes and gene expression. The Jackman Lab focuses the interactions between cell signaling pathways known to be involved in zebrafish tooth development. Two of these signal transduction pathways are the Hedgehog and Retinoic Acid pathways. Both Hedgehog and Retinoic Acid signaling have been individually manipulated in zebrafish and resulting changes to dentition and gene expression have been observed (Yu et al. 2015, Seritrakul et al. 2010). However, cell signaling pathways often interact and regulate one another, which suggests that combined manipulation of cell signaling pathways simultaneously could result in novel dental phenotypes and gene expression. A previous in vivo study in mice has shown that this combinatorial treatment method can lead to non-additive increases in dental complexity (Harjunmaa et al. 2012).

This summer, my goal as a member of the Jackman Lab was to recreate the results found in Seritrakul et al. 2012 where overactivation of retinoic acid signaling led to anterior supernumerary teeth. From there we wanted to explore the results of the honors project done by Sienna Mitman ’15 where combined overexpression of Hedgehog and Retinoic Acid led to tooth phenotypes distinct from Retinoic Acid overactivation. Ultimately, the main goal for this summer was to begin combinatorial treatments starting with Hedgehog and Retinoic Acid and then to prepare for more treatments involving other signaling pathways during the school year.

Our results were consistent with Seritrakul et al. 2012 where overactivation of Retinoic Acid signaling led to ectopic teeth anterior of the pharynx. In contrast, Hedgehog overactivation by two different methods had no changes to the tooth phenotype. When combined Retinoic Acid and Hedgehog overactivation led to distinct tooth phenotypes not observed in Seritrakul et al. 2012 or any of our previous studies. These results lead the Jackman Lab to believe there is increased credibility in combinatorial treatments as a way to explore cell signaling and their interactions during tooth development. Furthermore, these resulting phenotypes are only a part of the story, as changes to gene expression are also expected with this treatment. Moving forward we would like to explore these expected changes to gene expression as well as try new combinatorial experiments with other cell signaling pathways known to be involved in zebrafish tooth development.

Faculty Mentor: Bill Jackman

Funded by the Maine IDeA Network of Biomedical Research Excellence and the National Institute of Health
References:

