Transcriptome Atlases of the Craniofacial Sutures: 1 U01 DE024448-01, FaceBase2 Spoke Project

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The skull is made up of the calvaria (roof of the skull), facial skeleton, and skull base. Intramembranous bones, differentiating directly from mesenchymal condensations, form the calvaria and the facial skeleton. These bones develop sutures with their neighbors, at which growth occurs along the bone margins (osteogenic fronts). Pathological obliteration of these sutures occurs in craniosynostosis (CS) and has adverse consequences for the continued development of the face and skull, requiring surgical and clinical management. Mutations in many genes have been found to underlie various forms of syndromic and non-syndromic CS and the sutures affected can vary depending on the gene mutated, but in the majority of non-syndromic CS cases the underlying genetic cause is not known. Knowledge of the gene expression particular or common to the various sutures and their subregions (osteogenic fronts and suture mesenchyme) is crucial to obtain a better understanding of the formation and maintenance of craniofacial bones and sutures, and is of wider importance to an explanation of craniofacial development in terms of both embryology and evolution, and may aid in the development of better clinical management of CS. The mouse provides an excellent model of human craniofacial skeletal development, having a similar arrangement of skull bones and sutures, as demonstrated by the large variety of human CS mutations successfully modeled by targeted mutation in mice. The creation of murine suture expression atlases will be a powerful resource for hypothesis-driven research into the etiology of CS and the developmental and evolutionary biology of the vertebrate skull. The specific aims of the FaceBase2 project, "Transcriptional Atlases of Craniofacial Sutures" are:

Aim 1. To isolate the subregions of multiple murine craniofacial sutures at progressive embryological ages using laser capture microdissection.

Aim 2. To use next-generation sequencing to create a time course of gene expression atlases for murine wild-type craniofacial suture subregions.

Aim 3. To use next-generation sequencing to create a time course of gene expression atlases for craniofacial suture subregions in two representative CS mouse models.