Osteogenic effect of neonatal dura on critical sized defects
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The pediatric population is the one that most requires cranial protection due to their high activity levels and increased potential for injury to the developing brain. However, it is this very population that is least suited for alloplastic reconstruction of large skull defects, and in which morbidity from autogenous bone graft donor sites is greatest and the amount of available donor bone is the most scarce. Large-scale calvarial defects in children between the ages of 2 and 10 years of age are especially difficult to manage. Large defects in this age group tend to heal as nonunion since the osteogenic potential of the underlying dura decreases rapidly after the first year of life. Furthermore, the surgical option of split calvarial grafts cannot be explored because the diploic space is not developed until after 10 years of age. Therefore, there is an intense need for improved treatments of cranial defects in the pediatric population. In order to develop these treatments, accurate animal models must be developed to incorporate the key biological aspects that define the clinical situation. Protein- and cell-based therapies are a possible answer to the problem.

We will utilize a rat critical sized defect model to test the bone regeneration capacity of dura mater depending on the age of the donor and the region of the dura that is used. Bone defects made in juvenile rats have been shown to heal better than defects made in adult rats presumably due to the effects of age on the osteogenic potential of the dura mater. We have developed a model in which we will test the osteogenic potential of transplanted dura mater in vivo. We will use this model to test dura mater collected from rats of different ages (neonatal to adult). This dura will be transplanted into adult rats with critical sized defects. Dura mater samples that are shown to induce defect healing will undergo molecular analysis using qPCR and microarray. Comparison of the gene expression profile between regenerating and non-regenerating calvariae will assist in identifying growth factors and cytokines that positively or negatively regulate bone healing. Growth factors and cytokines identified in these molecular analyses will be bio-printed onto human allograft scaffolds. Using an inlay technique, these scaffolds will be placed into critical sized defects to recreate the osteogenic environment of native neonatal dura.