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Project Title	The role of TGF-B1 and TGF-B3 in calvarial bone cell differentiation
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Summary/Abstract	

THE ROLE OF TRANSFORMING GROWTH FACTOR B1 AND B3 iN CALVARIAL BONE CELL DIFFERENTIATION

A Thesis
Submitted to
The Temple University Graduate Board

In Partial Fulfillment
Of the Requirements for the Degree
MASTER OF SCIENCE IN DENTISTRY

By
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ABSTRACT

The mechanisms Involved in normal cranial suture development and fusion as well as the pathophysiology of craniosynostosis are still not clearly understood. Several studies have related the continual presence of transforming growth factors with sutural fusion. Immunohistochemical studies have revealed a distinct, yet repeatable pattern of expression for TGFB1 and TGFI33 in the fusing and non-fusing sutures.

The purpose of this study was to examine whether the in vitro expression patterns of TGFB1 and TGFB3 mimic those reported to occur in vlvo during sutural morphogenesis. Primary calvarial cells obtained from day 11 chick embryonic frontal bones were treated with TGFf31 and TGFB3 either for two days (transient treatment) or 12 days (continuous treatment) and different concentrations were employed. Expression of osteogenic marker genes, such as osteocalcin, osteopontin, alkaline phosphatase and type I collagen was analyzed by Northern blot hybridization. Cell proliferation assays were performed in order to elucidate the arbitrary role of TGFB's in the proliferation of cells. In addition, mineralization assays and staining for alkaline phosphatase activity and calcium concentration were performed for different treatment times and doses.

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All marker genes tested except type I collagen were downregulated in TGFB1 and TGFB3 treated cells. Type I collagen was not significantly affected.

Cell proliferation was significantly compromised when the untreated and treated samples were compared. Alizarin red S staining and Ca2~ and Pi analysis of the cell layers appeared substantially reduced. Furthermore, specific APase

activity was also reduced in treated cell cultures. In all experiments performed, no significant difference was observed between the effects of TGFI31 and TGFB3 in the cultured cells.

Based on the results obtained from our study we can conclude that there does not appear to be a cause an effect relationship between the presence of TGFB1 and sutural fusion. However, TGFf33 could contribute to the sutural patency. In addition, the unusual inverted relationship observed between proliferation and differentiation indicates complex regulatory mechanisms by TGFt31 and TGF3 in osteogenesis.

We were able to answer a very significant question in suture fusion research. Subsequent lab data holds the promise to the cure for premature cranial sutural fusion.

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