Fibroblast growth factor 2 induces increased calvarial osteoblast proliferation and cranial suture fusion

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Objectives: Craniosynostosis has been associated with fibroblast growth factors (FGF) and their receptors. The purpose of this study was to quantitatively determine the effect of FGF2 on rat calvarial osteoblasts and a rat cranial suture formation model. Methods: Fetal rat calvarial osteoblasts were cultured with and without FGF2. Cell attachment and proliferation was determined by alamarBlue dye assay and cell morphology by toluidine-blue staining. In rat calvarial organ culture, postnatal day 15 rat calvariae with dura mater were placed in serum-free media with and without FGF2. A unique quantitative analysis of suture fusion was developed by obtaining measurements of suture bridging in histological serial sections at progressive stages of fusion. Results: Attachment for cells treated with FGF2 was similar to control. In contrast, proliferation was higher for cells treated with FGF2 while maintaining an osteoblastic morphology. After 5 days in organ culture, FGF2-treated posterior frontal sutures showed a dramatic increase in fusion compared to untreated controls. This increased fusion was maintained throughout days 7 and 10 in culture. Also, fusion was enhanced on the dural side of the suture, as is normally observed *in vivo*, and the normal tissue architecture was maintained. Conclusions: These results indicate that FGF2 can promote rat osteoblast attachment and normal cell morphology as well as induce cell proliferation. In calvarial organ culture, FGF2 treatment produced an enhanced suture fusion. These results provide further support for a critical role for FGF2 in cranial suture development. These studies also present a new quantitative approach to evaluating the effect of suture-perturbing growth factors on cranial suture fusion.