

## Poster Abstract

P89

### Identification of genes regulated by PTH and gp130 cytokines in differentiating osteoblasts

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Accumulating evidence suggests PTH works co-operatively with the gp130 signalling pathway in its actions on bone. This research aims to understand how PTH interacts with gp130 cytokines in osteoblasts and their precursors, by identifying transcriptional regulators responding to both classes of ligand. Mouse marrow stromal cells, Kusa 4b10, differentiated through 16 days of culture to the time the cells developed functional PTH receptor, were treated with PTH (1-34) and the RNA used to probe Affymetrix whole mouse genome micro-arrays. Of twelve transcription factors differentially expressed in response to PTH, Zinc-finger protein-467 (Zfp467) was chosen for further investigation as it trans-activates STAT3, a gp130 signalling molecule. Zfp467 mRNA was significantly repressed in Kusa 4b10 cells and primary mouse calvarial osteoblasts when treated with either PTH (1-34) or gp130 cytokines (OSM, LIF, CT-1 and IL-11). To investigate whether Zfp467 regulates osteoblast differentiation, it was over-expressed using a retroviral system in Kusa 4b10 cells. Over-expression significantly decreased the rate of mineralization and increased adipocyte formation. The reverse effect was observed when anti-sense Zfp467 was introduced. In addition, real-time PCR analysis of the over-expression studies demonstrated reduced mRNA levels relative to control for the osteoblast markers osterix, ALP and osteocalcin and elevated levels of the adipogenic markers C/EBP $\alpha$ , adiponectin and resistin, throughout the differentiation process. Zfp467 therefore appears to modulate cellular differentiation towards adipogenesis rather than osteoblastogenesis. Future studies will aim to elucidate the role of Zfp467 in the interactions between PTH and gp130 cytokine signalling pathways.