Gene Array Analysis of Cleidocranial Dysplasia Dental Cells. L. SANTOS*, S. KADAPAKKAM, S. CHEN, and M. MACDOUGALL, University of Texas Health Science Center at San Antonio, USA.

Cleidocranial dysplasia (CCD) is an autosomal dominant disorder characterized by defective bone formation and dental abnormalities including supernumerary teeth and delayed eruption. Mutations in the transcription factor, core binding factor alpha 1(Cbfa1), also known as Runx2, have been shown to cause CCD, however target genes that function as downstreatm mediators of Cbfa1/Runx2 during osteogenesis and odontogenesis are yet to be well defined. The purpose of this study was to use DNA microarray technology to perform a broad survey of potential altered gene expression in CCD versus normal dental pulp cells to define potential Cbfa1/Runx2 target genes during odontogenesis and tooth eruption. An Atlas™ human cytokine/receptor DNA array was used to compare over 200 genes in this study. Dental pulp cultures were established from extracted teeth of a CCD patient with a Cbfa1/Runx2 $R_{225}Q$ mutation and an age-matched control. For each group,RNA was extracted, converted to ^{33}P-cDNA labeled probes, and hybridized to the arrays. Resulting phosphorimages were analyzed using AtlasImage™ software. A signal difference threshold of a 2-fold increase or decrease CCD versus control was established. Among 266 genes analyzed, 24 (9.0%) genes were upregulated including IL-6, IL-8 and bone-derived growth factor-1; 17 (6.4%) genes were downregulated including TGFβ2, IL-1R1 and pleiotrophin. Computer DNA sequence analysis revealed that reported promoter sequences of these genes contain Cbfa1/Runx2 core binding sites (ACCRCA). Some of the altered genes are key factors previously shown to be involved in odontogenesis, while others represent newly identified genes expressed during tooth formation. This study has identified for the first time pulpal gene expression changes associated with CCD as well as key downstream target genes for Cbfa1/Runx2 that will enhance our understanding of the mechanisms leading to the dental findings related to CCD.