

IDENTIFICATION OF TRANSCRIPTION FACTORS ASSOCIATED WITH DOWN SYNDROME SKELETAL ABNORMALITIES

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Individuals with Down syndrome (DS) exhibit a variety of phenotypes, including craniofacial and skeletal dysmorphologies. It is believed that trisomic genes initiate phenotypes associated with Down syndrome, though specific gene-phenotype relationships for DS are largely unknown. We hypothesize that the altered expression of genes in three copies will also affect the expression of downstream genes, including non-trisomic genes and play an important role in DS phenotypes. Transcription factors, which encode proteins that bind to specific DNA sequences controlling the flow of transcription, are among the genes that may be affected by trisomy. We have identified genetic and phenotypic alterations in craniofacial precursors as early as embryonic day E9.5 of the Ts65Dn mouse model of human DS. This mouse model is trisomic for orthologs of approximately half of the genes on human chromosome 21. Previous microarray data from the developing mandible have shown dysregulation of multiple non-trisomic genes. We will test the expression of the *Six2*, *Gata3*, *Gata6*, *Pth*, *Hoxb4*, *Runx2*, *Ets2*, and *Osterix* transcription factors at two developmental time points, E9.5 and E13.5, to determine which are dysregulated in the Ts65Dn DS mouse model. Understanding the effect of trisomy on non-trisomic transcription factors will help identify links between trisomy and specific DS phenotypes.

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