Genomic Analysis of Gene Dysregulation Sites Related to Craniofacial Development in Ts65Dn Down Syndrome Mouse Embryos

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Down syndrome (DS) is caused by a nondisjunction event called Trisomy 21 and is known to effect every system of the body. While it is thought that select genes on chromosome 21 are responsible for specific DS phenotypes, we are unsure of the overall effect the extra genetic information poses across the genome. The presence of an extra chromosome 21 is suspected to cause dysregulation in gene expression across the genome of individuals with DS. These dysregulation sites may vary between individuals due to genetic variability and according to tissue type. Previous studies have shown that genomic regions of gene up regulation and down regulation exist in individuals with DS. Ts65Dn mice have an extra marker chromosome that accounts for approximately fifty percent of the genes that are triplicated in DS. We are using the Ts65Dn DS mouse model to study the variability in the genomic sites of dysregulation caused by trisomy and to determine whether genomic dysregulation is tissue specific. We are comparing the gene expression from genes associated with the neural tube and 1st pharyngeal arch from trisomic and euploid e9.5 embryos. This comparison may provide insight behind the effect trisomy has on genomic dysregulation that causes the small 1st pharyngeal arch and leads to a small mandible in individuals with DS. Significantly dysregulated mRNA expression levels have been collected from embryos of trisomic and euploid mice and have been characterized by next-generation sequencing. We are identifying genomic locations with the most genetic dysregulation and comparing any variability within these sites based on the spatial as well as temporal differences in mRNA expression from tissues of trisomic and euploid samples. We hypothesize that genomic gene dysregulation sites will be tissue specific. Our study aims to explain how these perturbations in gene expression may affect certain DS phenotypes such as craniofacial abnormalities.

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