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Investigating the Development Requirements of Sex Chromosome Genes Affected in Turner Syndrome

Turner Syndrome (TS) is the set of phenotypes associated with the 45, X karyotype, which is the result of a missing second sex chromosome in women. We hypothesized that a precise expression of candidate TS genes located on the sex chromosomes is required for viable human development, implying all living TS patients are mosaic and only some of their cells are missing the second sex chromosome. First, we set out to optimize DNA probes that could specifically bind to the X and Y chromosomes for fluorescent in situ hybridization (FISH). We used a Y chromosome probe in mouse tissue to test the FISH protocol on formalin fixed paraffin embedded tissue sections. We optimized the human X chromosome probe on human embryos to detect mosaicism. Additionally, we analyzed RNA sequencing data on developing embryos for expression of TS candidate genes. The following genes were highly expressed in 46,XX and 46,XY samples and may therefore be haploinsufficient in TS: RPS4X, TMSB4X, DDX3X, EIF1AX, RPS4Y1, DDX3Y, EIF1AY, SLC25A6, and CD99. Through quantitative polymerase chain reaction analysis of samples from lymphoblastoid cells, TS samples (45,X) were found to have lower expression of these genes when compared to controls. The results in this study support the hypothesis that changes in expression level of TS genes are responsible for the TS phenotype. Our analysis of TS candidate gene expression can lead to targets for gene therapy or exogenous replacement of proteins coded for by these genes, resulting in better health care for TS patients.