## The contribution of GTF2I haploinsufficiency to Williams syndrome.

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**Public Summary:**
We review the scientific literature showing that the GTF2I, a gene located in the Williams syndrome deletion region, is implicated in social phenotypes. We also provide potential mechanistic models to explain how this gene might affect the human social brain.

**Scientific Abstract:**
Williams syndrome (WS) is a neurodevelopmental disorder involving hemideletion of as many as 26-28 genes, resulting in a constellation of unique physical, cognitive and behavior phenotypes. The haploinsufficiency effect of each gene has been studied and correlated with phenotype(s) using several models including WS subjects, animal models, and peripheral cell lines. However, links for most of the genes to WS phenotypes remains unclear. Among those genes, general transcription factor 2I (GTF2I) is of particular interest as its haploinsufficiency is possibly associated with hypersociability in WS. Here, we describe studies of atypical WS cases as well as mouse models focusing on GTF2I that support a role for this protein in the neurocognitive and behavioral profiles of WS individuals. We also review collective studies on diverse molecular functions of GTF2I that may provide mechanistic explanation for phenotypes recently reported in our relevant cellular model, namely WS induced pluripotent stem cell (iPSC)-derived neurons. Finally, in light of the progress in gene-manipulating approaches, we suggest their uses in revealing the neural functions of GTF2I in the context of WS.