# Investigating the Relationship Between Ciliogenesis and MED12 Expression in Hardikar Syndrome

Sridhar, Sindura (School: Wilson High School )

Hardikar Syndrome (HS) is a rare genetic disorder characterized by cleft lip/palate, pigmentary retinopathy, intestinal malrotation, and hepatobiliary disease. The disease is known to be caused by a mutation in the gene MED12. It was hypothesized that symptoms of HS are caused by a dysfunction in the primary cilium (a cellular organelle), as the symptoms of the disease are similar to those of ciliopathies. To test this, experiments were conducted to study the correlation between MED12 expression and ciliogenesis. In the first experiment, retinal pigment epithelial (RPE) cells were serum-starved, causing the cells to grow cilia. Through qPCR analysis, it was found that the serum-starved cells had a greater MED12 expression than control cells. In the second experiment, RPE cells were transfected with MED12 siRNA, which lowers the expression of the gene in the cells. They were then imaged under a scanning electron microscope to visualize the amount of ciliated cells. Results showed that cells with MED12 siRNA (less MED12 expression) had fewer percent-ciliated cells. In the last experiment, cells were again transfected with MED12 siRNA, but then put through qPCR to measure GLI1 expression. GLI1 is a transcription factor in the hedgehog signaling pathway, a mechanism that depends on the cilium to activate. Data proved that cells with less MED12 expression had less GLI1 expression. All experiments proved a positive correlation between the expression of MED12 and ciliogenesis. Overall, it was concluded that MED12 expression is consistent with ciliogenesis; therefore, HS is possibly related to a dysfunction in the primary cilium. In the future, this novel research will be essential in successfully treating patients with HS by targeting the primary cilium.

**Awards Won:**