Researchers find mechanism behind cleft palate development

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Researchers from Mount Sinai School of Medicine have found a new mechanism that explains why a certain gene mutation causes craniofrontonasal syndrome (CFNS), a disorder that causes cleft palate and other malformations in the face, brain, and skeleton. Cleft palate affects one of every 1,000 newborns. The research is published in the September 15 issue of *Genes & Development.*

Previous research has shown that a mutation in a gene called ephrin-B1 caused abnormalities in facial development, but researchers were uncertain of how. Philipe M. Soriano, PhD, Professor, Developmental and Regenerative Biology, and Jeffrey O. Bush, PhD, Postdoctoral Fellow, Developmental and Regenerative Biology, both at Mount Sinai School of Medicine, studied mice embryos that were genetically engineered to have a mutation in the ephrin-B1 gene. They determined that ephrin-B1 controls craniofacial development by signaling cells to multiply. When there is a mutation in this gene, it causes anomalies in the cell proliferation process.

"Common thinking has been that ephrin-B1 only guided cells in craniofacial development," said Dr. Soriano. "We were surprised to learn that, instead, this gene signals for cells to multiply, providing us with a clear understanding of why craniofacial development is abnormal when a mutation is present."

Drs. Bush and Soriano also wanted to determine why females with one normal copy of the ephrin-B1 gene are more severely malformed than

males who have no copy of the gene at all. They found that female mice embryos with this type of mutation had a so-called "mosaic" cell proliferation, meaning cell multiplication is disrupted in some areas while developing normally in others. This creates abnormal craniofacial development.

"Craniofacial anomalies are among the most common human birth defect," said Dr. Bush. "Our findings represent a critical step forward in understanding how cleft palate and other malformations develop, and will hopefully bring us closer to finding ways to prevent or treat these abnormalities."

Drs. Bush and Soriano plan to study ephrin-B1 further by identifying which molecules work in conjunction with it and how. Gaining a further understanding of the signaling mechanisms of this gene will likely lead to designing prevention and treatment strategies.

Provided by The Mount Sinai Hospital