Pharmacogenetic insights into the treatment of Angelman syndrome

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Research Summary: Angelman syndrome is a severe neurodevelopmental disorder characterized by lack of speech, intellectual disability, and seizures. The disorder is caused by a loss of the maternal UBE3A allele; because the paternal allele is epigenetically silenced in neurons, loss of the maternal allele practically eliminates UBE3A protein from the brain. My lab strives to understand the basic pathophysiology underlying Angelman syndrome, and our research has provided synaptic and circuit insights into the basis for hyperexcitability in the Angelman syndrome brain. Simultaneous to our basic research studies, we have performed drug discovery that identified small molecules that can unsilence the paternal UBE3A allele and, hence, provide a treatment approach. Our research and that of others suggests that clinical trials are looming on the horizon. Given the increased interest in performing clinical trials, we have recently turned our attention towards identifying potential biomarkers in Angelman syndrome, including EEG recordings and MRI-DTI measurements of white matter integrity. In this talk, I will provide an overview of our understanding of Angelman syndrome pathophysiology and possible outcome measures that might be used in upcoming clinical trials.

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