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Researchers make breakthrough in understanding white matter development

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Through the identification of a gene's impact on a signaling pathway, scientists at Children's National Medical Center continue to make progress in understanding the mechanics of a key brain developmental process: growth and repair of white matter, known as myelination. The study, published online in the September 2011 online edition of The *Journal of Neuroscience*, identified Sox17 as the gene that helps regulate the Wnt/beta-catenin signaling pathway during the transition of oligodendrocyte progenitor cells, or immature brain cells, to a more mature, differentiated state where they generate myelin.

"This is the first time the Sox17 gene has been identified as a regulator of the Wnt/beta-catenin pathway during myelination," said Li-Jin Chew, PhD, lead author of the study. "Our findings indicate that loss of Sox17 over-stimulates the Wnt/beta-catenin pathway and keeps oligodendrocyte progenitor cells from maturing and producing myelin, potentially causing developmental disabilities in developing babies and children."

Myelin is the protective material around the axons of neurons; in mass these types of ensheathed neurons are collectively called white matter. White matter serves as the primary messaging "network" that conducts signals rapidly between gray matter areas. Without it, the brain does not function properly. Myelination, or growth of white matter, in humans begins in utero at around 5 months of gestation and continues throughout the first two decades of life. Myelination can be impaired for a number of reasons, most commonly intrauterine infection, reduced or interrupted

blood flow (which carries oxygen and nutrients) to the forming infant brain, or perinatal injury. As a result, white matter doesn't develop the way that it should or is somehow damaged, resulting in mental retardation and developmental disabilities. "From here we plan to look more closely at the parts of the pathway that Sox17 regulates. We'll be able to understand the crucial molecular events that occur during oligodendrocyte development and disease," stated Vittorio Gallo, PhD, director of the Center for Neuroscience Research. "This is an incredibly exciting discovery that puts us closer to figuring out the underlying cause of white matter diseases. It also means that we may eventually understand how we could influence these pathways and possibly ease white matter damage or deficiency in our patients."

Myelination, white matter growth and repair, and the study of complex mechanisms of prenatal brain development are a key focus of the Center for Neuroscience Research at Children's National, which also houses the White Matter Diseases Program, one of the largest clinical programs in the country for treating children with disorders that cause the brain's white matter to degenerate.

Provided by Children's National Medical Center