

Discovery may offer new therapeutic approach for kids with Prader-Willi syndrome

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Stem cell researchers at UConn Health have reversed Prader-Willi syndrome in brain cells growing in the lab, findings they recently published in the *Human Molecular Genetics*.

The discovery provides clues that could lead to a treatment for Prader-Willi, a genetic disorder that occurs in about one out of every 15,000 births, and is the most common genetic cause of life-threatening childhood obesity.

Unlike many genetic syndromes that are caused by a mutation in a gene, people with Prader-Willi often have the right gene available—it's simply that it's been silenced.

The gene is silenced because it is on the part of their chromosome they inherited from their mother, and for mysterious reasons our cells use the father's copy of this gene. But if the father's copy is missing, the cells can't express that gene at all.

UConn Health's Maeva Langouet, a post-doctoral fellow; Marc Lalonde, professor of Genetics and Genome Sciences; and their colleagues wondered if it was possible to reverse the silencing of the mother's copy.

The researchers noticed that a certain protein, called ZNF274, was involved in the process. It silences many other genes as well, but in those cases it usually acts with another protein. On the Prader-Willi region of our DNA, the protein seems to act alone, they said.

So Langouet and Lalonde took stem cells donated by Prader-

Willi patients, and carefully deleted ZNF274. They then encouraged the stem cells to grow into neurons, a type of brain cell. And the cells seemed normal. They grew and developed, as expected.

Critically, the new cells also expressed the maternal copy of the Prader-Willi region.

“We still need to figure out if knocking out ZNF274 is doing anything else,” that might be undesirable, says Langouet.

And many other questions still need to be answered: Does this work directly in human brain cells? Will it only work in embryos, or can it help the brain develop normally even after birth?

Currently, there is no cure for Prader-Willi syndrome, and most research has been targeted towards treating specific symptoms. For many individuals affected by the disorder, the elimination of some of the most difficult aspects of the syndrome, such as the insatiable appetite and obesity, would represent a significant improvement in quality of life and the ability to live independently.

But in the future, this new line of research may offer a therapeutic approach for kids with Prader-Willi, Langouet says.

Source:

[*Giving Silenced Genes a Voice*](#)