A new molecule is found to prevent preterm birth

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A new molecule is found to prevent preterm birth. Image does not depict child involved in study. Credit: Sarah Hopkins. BY NC ND 2.0

Premature births are intimately linked with inflammation of the uterine tissue, a biological response which induces contractions and preterm

labor. In their search for a mean to prevent this phenomenon and complications related to deliveries occurring before 37 weeks of gestation, researchers at CHU Sainte-Justine and University of Montreal discovered an agent that shows efficacy in inhibiting inflammation and preventing or delaying uterine contractions and premature delivery in murine models - without adversely affecting the fetus or the mother. This discovery is a giant step towards preventing prematurity, which is the world's leading cause of infant death and the origin of potentially severe, long-lasting physical, intellectual or psychological impairment for the 10% of infants born preterm world-wide.

While examining uterine tissues, the scientists found a messenger, called Interleukin 1, to be responsible for triggering and amplifying inflammation in the uterus, which led them to run preclinical trials in which they tested therapeutic agents known to target that messenger - although they were traditionally never used such an application. However, their effect was found to be negligible on inflammation and contractility of the uterine cells, in addition to causing serious side effects in the fetus. "Interleukin-1's effect is much larger than just amplifying inflammation. Its physiological role is critical in protecting the vulnerable fetus against infections, and ensuring that cells will survive inflammation and other sources of aggression", says Mathieu Nadeau-Vallée, a Ph. D. candidate in pharmacology and the first author of the paper. "Orthosteric antagonists currently available on the market are large molecules. They block most of the signaling pathways of Interleukin 1, including some protective mechanisms critical for the fetus, such as immunesurveillance and cytoprotection."

Looking for a way to get past this problem, scientists have developed another therapeutic agent, which proved much more effective, in addition to being safer than the existing molecules designed for the same target. "The allosteric modulators that we have developed work differently. Our molecule is very small", says enthusiastically Dr. Sylvain

Chemtob, a neonatologist and investigator, and the lead author of the study who developed the molecule in collaboration with his research associate Christiane Quiniou, Ph.D. and Dr William Lubell, professor of chemistry at University of Montreal). "The small size of the molecule allows it to act more selectively on Interleukin 1. It specifically blocks the pathway that controls inflammation without interfering with those which exert a protective effect on the immune system and the cells."

"101.10", as the scientists have named their molecule, now needs to be tested in humans. For the time being, women with a history of prematurity would be candidate for this future treatment, as scientific evidence shows that they are at increased risk of preterm labor. The research team is looking forward for tests to be able in a near future that will be able to predict the preterm delivery risk of a woman, notwithstanding her history of birth or delivery.

The article "Novel Noncompetitive IL-1 Receptor-Biased Ligand Prevents Infection- and Inflammation-Induced Preterm Birth" was published online on August 24, 2015 in the *Journal of Immunology*.

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