Major discovery in the genetics of Down syndrome

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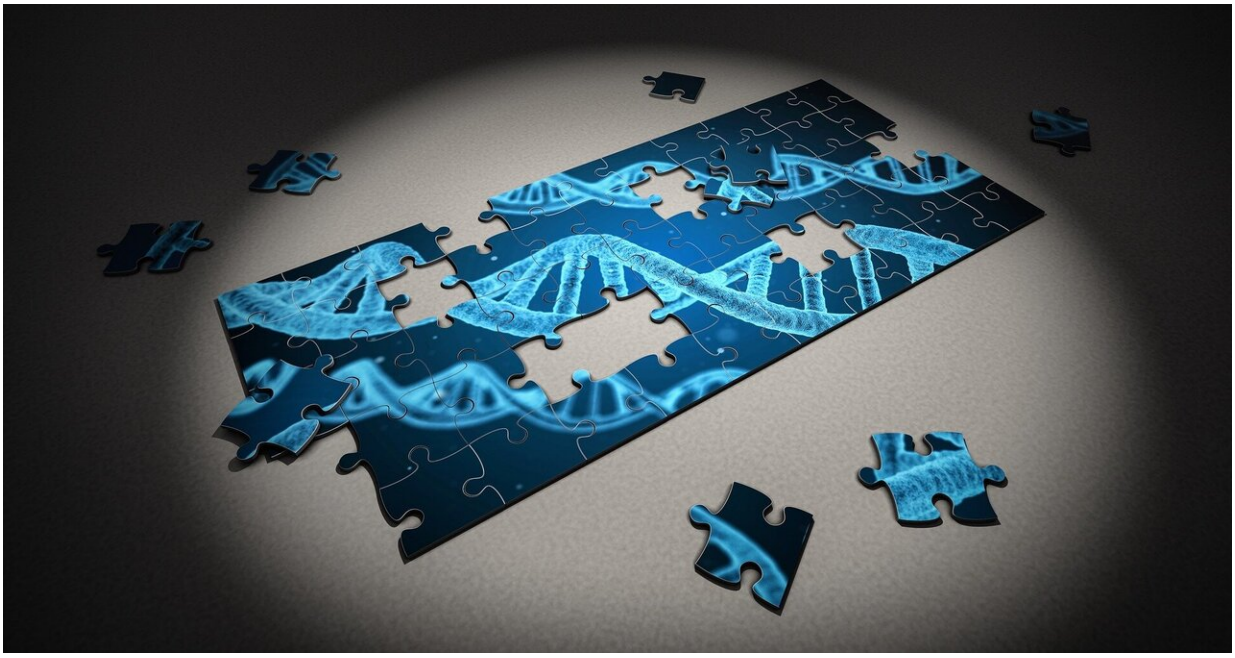

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Researchers at CHU Sainte-Justine and Université de Montréal have discovered a new mechanism involved in the expression of Down syndrome, one of the main causes of intellectual disability and congenital heart defects in children. The study's findings were published today in *Current Biology*.

Down syndrome (SD), also called trisomy 21 syndrome, is a genetic condition that affects approximately one in every 800 children born in Canada. In these individuals, many genes are expressed abnormally at the same time, making it difficult to determine which genes contribute to which differences.

Professor Jannic Boehm's research team focused on RCAN1, a gene that is overexpressed in the brains of fetuses with Down syndrome. The team's work provides insights into how the gene influences the way the condition manifests itself.

Synaptic plasticity, memory and learning

The human brain is made up of hundreds of billions of cells known as neurons. They communicate with each other through synapses, which are small gaps between neurons. The ability of synapses to strengthen or weaken over time is known as "synaptic plasticity." It's an important biological phenomenon because it's essential for memory and learning.

"There are two kinds of synaptic plasticity: long-term potentiation, which strengthens synapses and improves interaction between neurons, and long-term depression, which weakens synapses," said Boehm, a professor at Université de Montréal and researcher at CHU Sainte-Justine.

"We already knew that synaptic plasticity is influenced by certain proteins," added Anthony Dudilot, one of the study's first authors. "For example, calcineurin is inhibited when long-term potentiation is induced, but it's activated when long-term depression begins. But the molecular mechanism underlying calcineurin regulation was less clear."

The research team found that the various signalling pathways that trigger synaptic potentiation or depression converge on RCAN1. They also

determined that the gene regulates calcineurin activity by inhibiting or facilitating it.

Given its dual role as an inhibitor/facilitator, the researchers deduced that RCAN1 works as a "switch" that regulates synaptic plasticity, thereby affecting learning and memory.

A better future for all patients

"This is the first time that the molecular mechanism for calcineurin regulation in bidirectional synaptic plasticity has been determined," said Boehm. "This breakthrough explains how overexpression of the RCAN1 gene could cause intellectual disabilities in individuals with Down syndrome. It also opens up the possibility of developing innovative treatments for affected patients."

"RCAN1 regulates bidirectional synaptic plasticity" was published in *Current Biology* in February 2020.

More information: Anthony Dudilot et al. RCAN1 Regulates Bidirectional Synaptic Plasticity, *Current Biology* (2020). DOI: 10.1016/j.cub.2020.01.041

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