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# Molecular mechanisms offer hope for new pain treatments

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By working with individuals suffering from a severe disorder that causes sensory neurons to degenerate, researchers at the University of Montreal Hospital and CHU Sainte-Justine Hospital have discovered how a specific genetic mutation causes their patients' condition, which in turn has revealed more information about the mechanisms in our bodies which enable us to sense pain. Genetic mutations are mistakes in our genetic code that can either be passed from parents to their children or created when DNA is replicated. Lead author Dr. Jean-Baptiste Rivière published the team's results in the *American Journal of Human Genetics* today.

The currently untreatable disorder is called "hereditary sensory and autonomic neuropathy type II." It starts during early childhood and is characterized by a loss of perception of pain, touch and heat. Because affected individuals are unable to react to pain and protect themselves, they often develop ulcers that can become infected, leading to amputation of the affected body part. By working with their international colleagues under the direction of the University of Montreal's Dr. Guy Rouleau, the research team was able to pinpoint how the disorder is related to the patients' genetic code.

"After showing that the WNK1/HSN2 protein interacts with the KIF1A gene, we were able to go back to the cohort of patients and identify mutations of the KIF1A gene," Rivière said. "The study results will be of immediate benefit to HSAN2 patients, as the identification of this new gene has made it possible to provide valuable genetic testing to assess the

risk or the cause of the disease in individuals at risk or presenting the disease." While the genetic mutation affects very few people, the knowledge that the researchers have gained is applicable to everyone. Scientists know the different parts of our genetic code, but they don't know how every single specific gene contributes to the functioning of our bodies. When a gene does not function properly due to a mutation, the resulting disorder can provide insight into its normal role. These findings provide clues about the components underlying the transmission of pain signal from sites of injury to the central nervous system

Researchers may be able to use their new knowledge about the KIF1A gene to develop new pain relief drugs. "Our results not only open the door to a better understanding of this disorder," Rouleau explained, "they also give us valuable information about the molecular mechanisms involved in pain perception, which is important for the development of new anti-pain drugs." A future drug might work by modulating interactions between different proteins associated with pain and KIF1A. "Further research could help us to identify other proteins that are transported by KIF1A or that interact with it, and that will help to better refine our understanding of pain mechanisms," noted Dr. Patrick Dion, who also contributed to the research.

Provided by University of Montreal