

Researchers identify drug that alleviates opioid withdrawal

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Opioid use and abuse is a significant social, health and economic issue in Canada. Researchers at the University of Calgary's Faculty of Veterinary Medicine (UCVM) and Hotchkiss Brain Institute (HBI) have discovered that an existing anti-gout medication is effective in reducing the severity of withdrawal symptoms in opioid-dependent rodents. Their work is leading to the development of a clinical trial at the Calgary Pain Clinic.

Neuroscientist Tuan Trang, PhD and his team, including PhD student Nicole Burma, explored the underlying causes of opioid withdrawal and identified an important target in the spinal cord that is responsible for producing withdrawal symptoms in rats and mice. The target, called pannexin-1, is located throughout the body and importantly, in the brain and [spinal cord](#). The study was published January 30 in the prestigious journal *Nature Medicine*.

Opioids are a potent class of drugs that are used to treat [pain](#). Stopping opioid use can result in severe withdrawal symptoms - a key contributor to continued opioid use. Currently, there are few medications that ameliorate these symptoms. For their study, Trang and Burma looked specifically at two common opioid drugs: morphine and fentanyl.

"Opioid withdrawal is aversive, debilitating and can compel individuals to continue using the drug in order to prevent these symptoms," explains Trang, an assistant professor in the UCVM and the Cumming School of Medicine. "In our study, we effectively alleviated [withdrawal symptoms](#) in rodents, which could have important implications for patients that

may wish to decrease or stop their use of these medications."

Prior to this study, the cellular mechanism of opioid withdrawal was not well understood, hampering the search for therapeutic avenues. Trang explains, "the focus of much of the research so far has been on neurons themselves. Our study looked at key immune cells in the nervous system - and specifically at the pannexin-1 channel on these immune cells, which is something that hasn't been explored before."

The discovery represents a key shift in understanding how withdrawal occurs and it opens the door to treatments that could have tremendous therapeutic potential.

Once they identified the mechanism, the researchers were able to test an existing drug - in this case an anti-gout medication called probenecid that is known to have non-selective pannexin-1 blocking effects. The drug is Health Canada approved, is relatively inexpensive, and has few side effects. Importantly, the researchers were also able to demonstrate that the drug did not affect the ability of the opioid to relieve pain.

"This is an exciting study which reveals a new mechanism and a potential therapeutic target for managing opioid withdrawal, says renowned Canadian pain researcher Dr. Michael Salter, Chief of Research at SickKids Hospital in Toronto. "The findings of Dr. Trang and his team could have important implications for people on [opioid therapy](#) and those attempting to stop opioid use."

With such encouraging preclinical results, the researchers quickly started looking at how to translate this discovery to humans. They are already moving forward with Dr. Lori Montgomery and Dr. Chris Spanswick at the Calgary Pain Clinic to design a clinical trial.

"We now need to look to see if this works with patients as well as ensure

safety," says Spanswick, Medical Leader of the Calgary Pain Program. "We are at the very early stages of organizing clinical research. It will be some time before this research gets off the ground and we look forward to continuing collaboration with the HBI on this and other areas of research."

"Opioids are the pharmacological cornerstone for treating chronic pain in a large variety of diseases," says Trang. "Understanding why opioid withdrawal occurs and how to alleviate it, is of critical importance in improving pain therapy and may have implications for substance abuse in opioid addicts. The potential impact is immense."

More information: Blocking microglial pannexin-1 channels alleviates morphine withdrawal in rodents, *Nature Medicine*
[nature.com/articles/doi:10.1038/nm.4281](https://doi.org/10.1038/nm.4281)

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