Analysis of spider venom reveals seven promising compounds with potential to relieve chronic pain

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New research shows that seven compounds of the countless found in spider venom block a key step in the body's ability to pass pain signals to the brain. The hunt for a medicine based on just one of these compounds, which would open up a new class of potent painkillers, is now a step closer according to new research published in the *British Journal of Pharmacology*.

Pain that cannot be controlled can ruin people's lives. One in five people worldwide currently suffer from chronic pain, and existing pain treatments often fail to provide relief. The economic burden is huge, with chronic pain in the USA alone estimated to cost around $600 billion a year, greater than the combined economic cost of cancer, diabetes and stroke.

People sense that part of their body is hurting when nerves from the affected area send signals to the brain through what is called the pain pathway. "A compound that blocks Nav1.7 channels is of particular interest for us. Previous research shows indifference to pain among people who lack Nav1.7 channels due to a naturally-occurring genetic mutation - so blocking these channels has the potential of turning off pain in people with normal pain pathways," says research team leader Professor Glenn King from The University of Queensland's Institute for Molecular Bioscience, Australia.

Part of the search for new medicines has focused on the world's 45,000 species of spiders, many of which kill their prey with venoms that contain hundreds - or even thousands - of protein molecules. Some of these molecules block nerve activity. "A conservative estimate indicates that there are nine million spider-venom peptides, and only 0.01% of this vast pharmacological landscape has been explored so far," says researcher Dr Julie Kaae Klint. The challenge was to build a research method that could search through this huge number of peptides, looking for the ones that could be useful.

Taking up this challenge, the research team built a system that could rapidly analyse the compounds in spider venoms. Using their novel approach, venoms from 206 species of spider were screened, revealing that 40% of the venoms contained at least one compound that blocked human Nav1.7 channels. Of the seven promising compounds identified, they discovered one that was particularly potent, and also had a chemical structure that suggested it would have high levels of chemical, thermal, and biological stability, which would be essential for administering a new medicine. Together these properties make it particularly exciting as a potential painkiller.

"Untapping this natural source of new medicines brings a distinct hope of accelerating the development of a new class of painkillers that can help people who suffer from chronic pain that cannot be treated with current treatment options," says Dr Klint. The novel screening approach used to isolate the protein molecules from spider venoms could also be applied to other compounds, opening up hope more widely for new and better medicines.

More information: Seven novel modulators of the analgesic target Nav1.7 uncovered using a high-throughput venoms-based discovery approach. Julie K. Klint, Jennifer J. Smith, Irina Vetter, Darshani B. Rupasinghe, Sing Yan Er1, Sebastian Senff, Volker Herzig, Mehdi

Mobli, Richard J. Lewis, Bosmans F, & King GF. *BJP*. DOI: 10.1111/bph.13081