Native New Zealand tree puts the sting on pain

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Credit: Institute for Molecular Bioscience, University of Queensland

Researchers at The University of Queensland (UQ) have found that a native New Zealand stinging tree produces toxins that could hold clues for future pain medication.

In a quest to find new molecules that affect pain pathways, Dr. Thomas Durek, Dr. Sam Robinson and a team from UQ's Institute for Molecular

Bioscience (IMB) studied toxins from the tree nettle known as ongaonga, one of New Zealand's most poisonous plants that can cause painful stings that last for days, and in severe cases can even be fatal.

Dr. Robinson and a team from UQ previously investigated toxins found in an Australian gympie-gympie stinging tree but found the New Zealand tree nettle toxins activated pain receptors in a new way.

"We discovered that the New Zealand nettle tree toxins target the same receptor as their Australian counterparts, but they cause pain in a different way," Dr. Robinson said.

"The Australian stinging tree and New Zealand tree nettle are both members of the nettle family, but separated millions of years ago and have evolved differently.

"The New Zealand tree nettle can grow up to four meters tall and its leaves and stems are covered with stinging hairs that pierce the skin and deliver venom which causes long-lasting pain."

Fossil remains show that the large flightless bird, the Moa, had a liking for eating the tree nettle and it's likely the strong toxins evolved to fend off the now-extinct bird.

The team faced challenges during the study due to international COVID travel restrictions.

"COVID made it difficult to source nettles, but to keep our research going through the pandemic, we managed to source seeds from the New Zealand tree nettle and grow the plant under quarantine in the lab," Dr. Robinson said.

Professor Irina Vetter, Director of IMB's Center for Pain Research, said

understanding pain pathways was key to finding new ways to treat chronic pain.

"Animal venoms have been studied for decades but plants have evolved toxins differently, and this gives us a chance to find molecules that work in a unique way," Professor Vetter said.

"Our goal is to tackle pain more effectively without side effects and addiction."

The research team included IMB's Dr. Edward Gilding and Ms. Jing Xie.

With travel bans lifting, Dr. Gilding plans to go to Vietnam later this year to experience "anything that stings" and is applying for funding to also visit Madagascar and South America to widen the net.

"There are several hundred nettles in the Urticaceae family with stinging hairs around the world—we're keen to compare how they have evolved and whether they all use the same toxins," Dr. Gilding said.

The research is published in the *Journal of Biological Chemistry*.

More information: Jing Xie et al, Neurotoxic and cytotoxic peptides underlie the painful stings of the tree nettle Urtica ferox, *Journal of Biological Chemistry* (2022). DOI: 10.1016/j.jbc.2022.102218

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