



From Out of the Shell

TERRY SNUTCH HAS TURNED A SNAIL'S VENOM INTO A \$500M DEAL WITH MERCK & CO. AND IN THE PROCESS COULD ELIMINATE CHRONIC HUMAN PAIN FOR GOOD

Buried beneath a sea of paperwork, scientific journals and textbooks, UBC Vancouver molecular neurobiology researcher Dr. Terrance Snutch keeps a box of brightly patterned cone snail shells. These are no ordinary shells; their fragile, diminutive structures potentially hold the secret to efficiently alleviating chronic pain in humans.

"Cone snails are these beautiful shells from the South Pacific," reveals Snutch, handling them with delicacy. "This is where the peptide Prialt comes from. It blocks pain receptors and it's very efficacious in easing human pain."

Just how efficacious, no one could have ever dreamed. The peptide in the snail's venom, which even surpasses the potency

of morphine, prompted scientists to frantically investigate the potential for a new category of drugs that lack the addictive side-effects of traditional painkillers. Initial scientific efforts resulted in Prialt, a drug that blocked pain receptors. Although Prialt was effective at alleviating pain, it proved to be an invasive treatment that required injections into the spinal cord through a pump implanted under the skin.

This lack of effective application of the snail's painkilling agent prompted Snutch to take a drastically different approach: "My idea was to develop a drug that you could take as a pill that would work like Prialt," he explains. "NMED-160 is an orally-made available drug that targets the N-type channel."



Photo> Paul Joseph



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The new direction paid off for Snutch in a big way. Last year, his UBC spin-off biotech company – Neuromed Pharmaceuticals – struck a record partnership deal with Merck & Co. to develop and market the painkiller NMED-160. Valued at nearly \$500 million USD, it is the richest collaboration for a drug in development ever in Canadian history.

“It turned out that out of the 22 pharmaceutical companies we talked to, pretty much all of them – 19 out of 22 – were interested,” says Snutch. “It came down to Merck being the best opportunity: absolutely outstanding scientists, great clinical development and a huge interest in pain.”

Human pain comes in two types: acute and chronic. While acute pain serves as a normal response to a noxious stimulus, chronic pain’s necessity is more obscure because there is no real benefit to it. For the more than 50 million people who suffer from chronic pain in North America alone, an effective, long-term treatment of this constant affliction has proved elusive. Although opioids, or derivatives of morphine, have been the most successful method of treating chronic pain, their harmful side-effects have long been documented.

“The opioids are very powerful painkillers but they’re not very good for chronic treatment because there are a lot side effects – addiction, severe constipation, respiratory depression,” Snutch explains. “Even if you’re in pain, you still want to be able to do your job and opioids don’t really allow for that.”

To create a painkiller that was effective and without side-effects, Snutch began

investigating N-type calcium channels – located in the spinal cord – that act as a conduit between the sensory nerve endings that record pain. Understanding the dynamic between the N-type channels and sensory nerves brought Snutch to a remarkable discovery: “If you block the N-type channel in the spinal cord, it blocks the neurotransmitter release in those sensory nerves in the spinal cord before they even reach the brain. If the pain signal doesn’t reach the brain, by default, you don’t feel pain because pain is actually felt in the brain.”

Armed with this knowledge and the discovery of the snail venom’s ability to block the N-type channel, the idea for NMED-160 was born. Now in Phase Two clinical trials, Neuromed has passed NMED-160 to Merck for further testing, a process that generally lasts six or seven years. Because NMED-160 has been used in humans since 2004, Snutch estimates that, if effective, it could be made available to the public by 2011. For chronic pain sufferers, that day could not come sooner.

“The drugs that are out there that treat chronic pain maybe work in about a third of patients. The other 60 to 70 per cent of patients don’t get any significant relief,” Snutch suggests. “So it would be a huge benefit to patients if NMED-160 worked. There is every reason to believe it will but you never know until you do the clinical trials.”

While there are no sure bets in the world of clinical trials, Snutch is cautiously optimistic about the potential for NMED-160. Because the drug is now in the hands of Merck, Neuromed is able to refocus its efforts on developing a whole range of pain

killing drugs: “The Merck collaboration not only pays for NMED-160 to go through clinical trials, but for other new compounds to be developed and go through development. Not having to fund further clinical development of NMED-160 on its own, Neuromed can take some of its money raised from venture capital and put it towards other research so we’re able to build a pipeline in the company. It’s a win-win situation for Neuromed.”

The company’s latest research includes investigations into T-type calcium channels that are implicated in epilepsy, heart disease, certain types of cancer, and pain.

For Snutch, the development of NMED-160 is ultimately a real-world example of how research at the university level can be transformed into something of substantial benefit to the public. His passionate commitment to science continues to drive him towards new, undiscovered frontiers: “I’m intrigued by the notion that every day I wake up, I have something new to do. There’s no such thing as the end of an experiment. You can publish your data but that usually just leads to more experiments, more ideas. It’s a very good way to go through life, never having a point of finality in anything you’ve done.”

Dr. Terrance Snutch’s main research grants are provided by the Canadian Institutes of Health Research (CIHR). In addition to his research in molecular neurobiology at UBC, Dr. Snutch is founder and Chief Scientific Officer of Neuromed Pharmaceuticals Inc., a biopharmaceutical company focusing on drug development in treating chronic and neuropathic pain, epilepsy and cardiovascular disease. ■