“Breakthrough: The Killer Snail Chemist” Transcript

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MANDË HOLFORD: Cone snails are fascinating because they're so unexpected. It's this gorgeous shell. And it's this little tiny animal that actually moves very slow. Not at all. And can easily be overlooked. But they pack a powerful punch. And what's wonderful is something that kills you can actually then potentially be something that cures you.

It's just amazing, all the snails do. And also, the potential for what they can do for human disease and drug discovery. My name is Mande Holford. And I'm a venomous snail hunter. We work with these killer snails to investigate their venom and look for novel compounds that can be used to treat pain in cancer.

I grew up in Brooklyn. And I'm one of five kids. And my parents came from South America to New York. And decided that this is where they're going to try to make their life. As a kid growing up in New York, you have a couple of places that are really special. And the American Museum of Natural History is one of those for me. We would go to the Museum of Natural History and go on our adventure roaming through the halls.

Each hall was like a new adventure. What I didn't understand as a child then was that that was science. It has a special place in my heart to be a scientist.

Almost every Natural History Museum on the planet has a shell collection. You can learn about biodiversity. You can learn about family trees of the snails. And look at how venom has evolved over time.

The snails that we work with, are they're not garden snails. These are marine snails. They're found in tropical marine environments all over the world. In the whole family of the snails, there are upwards of I would say 20,000 species. Not all snails are venomous. But some of these species of these snails are fatal to humans. I affectionately like to call my snails killers snails because they're very, very lethal. Deadly, actually.

Conus geographus, it's been tagged the cigarette cone, because after you get envenomated you basically have time to smoke a cigarette. And then you're going to drop dead.

My love for killer snails wasn't there originally. As I was finishing my graduate program, there was a seminar from Toto Olivera - I call him the godfather of snails. He came and he gave a talk. And he showed a video of a snail eating a fish. And I was completely, like everyone in the audience, we were blown away. Like how is this possible?

The snail is hidden under the sand. They have a siphon that sticks up. The siphon is kind of like a nose. It can smell. If there is prey in the water, then the proboscis comes out. And it's kind of like a tongue. And on the tip of the tongue is a harpoon, which is filled with venom. And then when they harpoon the prey with the venom, their venom has things in them that will shut down everything basically in the prey. Blood sugar, locomotion. The prey then instantly becomes paralyzed. Its mouth, or rostrum, opens really wide. And it will then engulf a fish or a worm completely whole. So the venom arsenal that nature has developed has worked wonderfully for millions and millions and millions of years. It's kind of been perfected.

Learning from nature is actually something we've been doing for a long time. All cultures. Ancient cultures have traditionally used their natural environment to look for cures to things that ailed them. And so what we've done now is we've gotten a little bit more strategic in how we learn from nature.

You have to be very careful when you collect the snails. Usually we have scuba gloves on. And then you sometimes can use salad tongs. Very high tech. To pick them up, drop them in the bucket, drop them in a bag, and bring them back up to the surface.

After we've collected the snails, we will dissect out the venom gland to then figure out what are the components inside of the venom. Venom is actually a cocktail. I like to call it nature's deadliest cocktail. The venom of the snails that we work with is mostly proteins with peptides.

Peptides are small proteins. Each snail and produce upwards of 200 different peptides in their venom arsenal. But each peptide is very targeted. They come in and they can block specific function of the prey. Since the peptides found in venoms are very specific, very potent, those are sort of the ideal for the drug discovery world. But they're also giving us new pathways for treating old problems. And what we have to do is figure out how they work and where they work in the cell.

Once we have identified which peptide we want to work on, we create it in the lab. The goal then is to identify the molecular target of the channel inside of the cell that they're working on. For example, in the instance of chronic pain there's this constant signal from one neuron to another. Peptides will block the channel that's helping to perpetuate that signal.

Cancer cells, like normal cells, they have these different channels on them that the peptides could target. In cancer, tumor cells or proliferating and there's this signal that's sort of gone crazy. With the group here at Hunter College, we got very excited because we found a peptide. It's called TV1. TV1 was hitting tumor cells at a higher degree than it was hitting normal cells. And so we're trying to identify which channel in the liver tumor cells are being inhibited with TV1.

The first drug from the snails, these killer snails, was ziconotide. The commercial name is Prialt. It's found from Conus magus. Similar to how the venom peptides will target a tumor cell to shut down proliferation, it works in stopping chronic pain signal.

Currently, the way that most drug companies are dealing with pain is through the opioid receptor. And the big major side effect is addiction. With Prialt, you don't have the side effect of addiction. So the snails showed us not only a new drug. But they showed us a new model for how to treat pain.

Prialt is wonderful, but it doesn't cross the blood brain barrier. You have to take a spinal tap, which is a very painful and invasive way of doing it. So we're looking for ways in which we can deliver the Prialt drug without delivering it through a spinal tap. We have what we call a Trojan horse strategy, in which we are encapsulating the peptide inside of a nano container. And trying to shuttle it across the blood brain barrier. And then releasing it.

What we're trying to do is learn from how the cells are giving us new drugs, but also giving us new pathways and new models for looking at diseases and disorders, particularly around pain and cancer. Cells are really fascinating because it's always like the little package with the big surprise.

And the more you learn about nature, you find out that there are lots of twists. And some of them are good. And some of them are not so good. But this a really, really surprising twist of nature that's possible when you study the venom.