WELCOME TO THE NATURE LAB

WHAT DOES A TASSIE DEVIL HAVE TO DO WITH YOUR HEALTH?

FROM CANCER-FIGHTING SUNFLOWER SEEDS TO PAIN-EASING SNAILS AND SUPERBUG-BATTLING MARSUPIALS, THE SOLUTIONS TO OUR GREATEST HEALTH CHALLENGES COULD LIE IN THE NATURAL WORLD. TIME TO GO BACK TO THE WILD

By Alex Davies

HUNTING THE WATERS OFF THE QUEENSLAND COAST IS A DEADLY CREATURE. IT DOESN'T HAVE FINS AND IT'S ONLY A FEW CENTIMETRES LONG. BUT TO A FISH, THE CONE SNAIL CAN BE PROBLEMATIC. THE MOLLUSC USES A SORT OF TOOTH TO HARPOON THE FISH AND DELIVER A SHOT OF VENOM, SO IT CAN PARALYSE THEN DEVOUR ITS PREY. WONDERING WHY WE'RE GOING ALL DAVID ATTENBOROUGH ON YOU? BECAUSE THIS VENOM – OR RATHER, AN INGREDIENT IN IT – COULD PAVE THE WAY FOR A GROUNDBREAKING METHOD OF TREATING PAIN IN HUMANS.

"If you like, snails invented the hypodermic needle 60 million years ago," jokes Professor David Craik, a structural biologist at the University of Queensland's Institute for Molecular Bioscience. After another Australian scientist discovered that cone snail venom actually contains a pain-relieving peptide molecule (probably evolution's bright idea to stop the fish struggling), Craik set about trying to harness it. "We sort of re-engineered [the molecule] to make it more stable and more drug-like," he explains. It's very early days in research terms, but it's thought this potential drug could be about 100 times more potent than morphine.

Craik isn't alone in his efforts to take what nature has created and run with it. Researchers nationwide are now joining forces to investigate molecules found in plants and animals, and their potential in areas including healthcare. Later this year, The ARC Centre of Excellence for Innovations in Peptide and Protein Science (CIPPS) will officially open, directed by Craik and backed by $35 million of government funding over seven years. Welcome to the new frontier of medicine – one that gives a whole new meaning to the word 'natural'.

HIDING IN PLAIN SIGHT

The superstars in this story are really proteins and peptides. Essentially, these are strings of amino acids (peptides are just shorter than proteins) which are "the building blocks of all life," says Kate Jolliffe, a professor of chemistry who heads up the CIPPS branch at the University of Sydney.

"Your fingernails are peptides, the antibodies your body produces to fight off attacks [are peptides]," she adds. "[Peptides] are what plants [make] to try and stop insects eating them, and they're present in spider venoms and things like that. Peptides are everywhere. And they have all these amazing activities. We want to try to use what nature has provided us with and ... maybe modify what it can do to [benefit] mankind."

These omnipresent gems have traditionally been underexplored as drugs because – much like that steak or tofu you just chowed down on – our bodies digest peptides and proteins. So, the risk is we'd just break them down before they could get to work. But, thanks to advances in technology and researchers collaborating on such a big scale, the hope is we can finally maximise their potential.

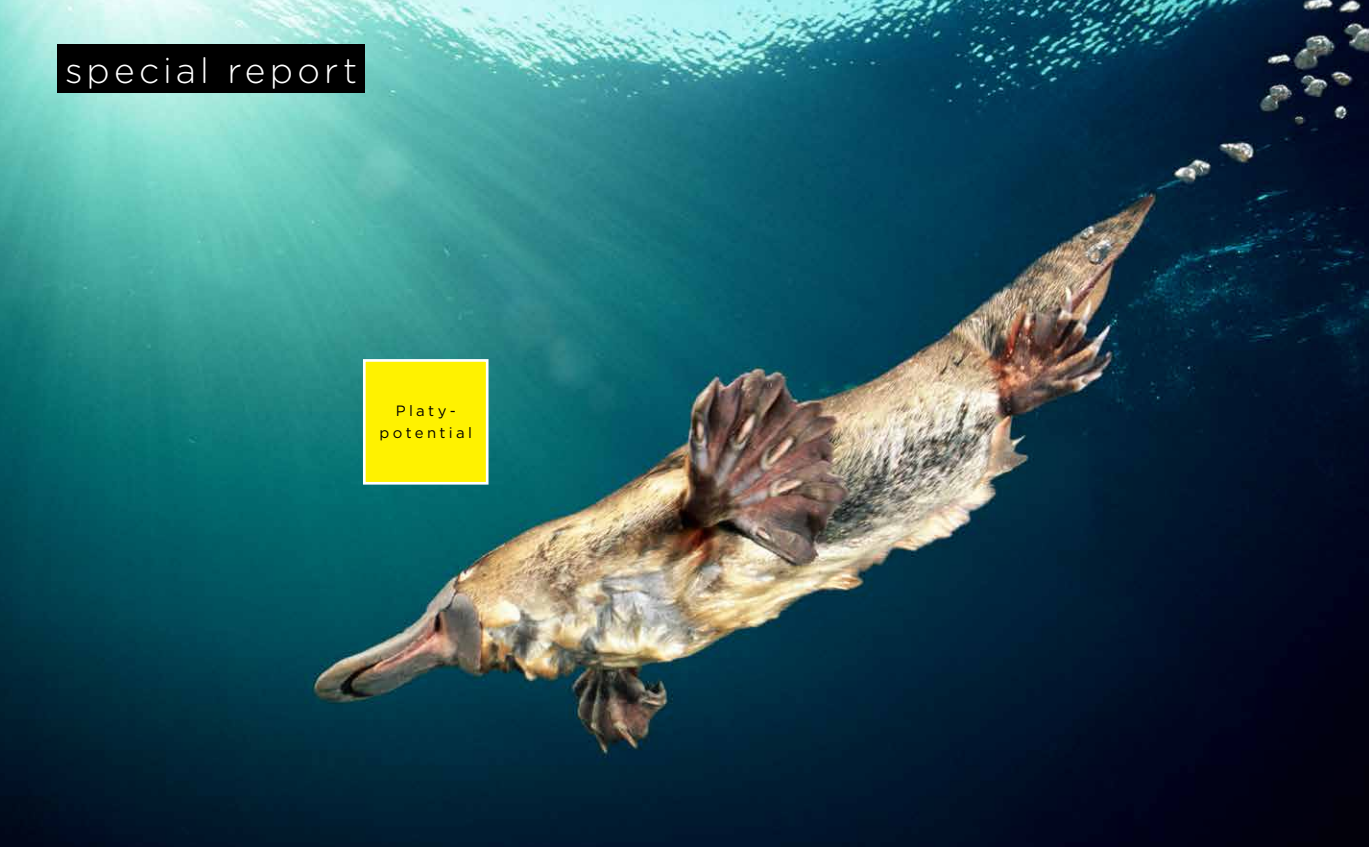
Craik adds, "The current generation of medicines has been fantastic. But many have side effects and a lot aren't all that effective. So for example, many painkillers only work in about a third of patients and there's a crisis with opioid [addiction and abuse] in most countries. We'd like to use peptides and proteins as next-generation medicines because, in theory, they should have fewer side effects because they're more natural molecules."

WHERE THE WILD THINGS ARE

Chronic pain is one area this work could impact, but we're also talking about other global health challenges, such as diabetes, cancer and cardiovascular disease. One example that'll make you look at creepy crawlies in a new way? A peptide in the venom of funnel-web spiders could drastically reduce brain damage after a stroke, according to work by Queensland and Monash Universities. During preclinical studies, it made a difference even when administered eight hours after the event – a huge deal, since most patients don't reach the ER straight away.

Not so into the spider chat? No worries. Let's move onto Tasmanian devils, which could hold the surprise weapon needed to fight deadly superbugs. Full disclaimer here: these researchers rarely work with animals (snails, spiders, devils and co) directly. Once an intriguing peptide or protein is discovered in nature, small samples are whisked off to a lab so chemists such as Jolliffe can re-create its structure. These replicated versions are the ones used in further research. So sadly, laughs Professor Kathy Belov, there aren't Tassie devils running about the oval at her University of Sydney base.

The world-renowned geneticist and marsupial researcher was part of a team that discovered antimicrobial peptides in devils' milk and pouches, most likely there to protect growing babies. "The joey [matures] in an amazing soup of these antimicrobials that protects it until it's old enough to develop its own immune system," she explains. Similar peptides have



been found in koala and other marsupial milk. What's more, Belov's team has seen these peptides kill deadly bacterial and fungal infections, including multidrug-resistant golden staph, which can cause skin infections and worse. "We've also started testing the peptides against the facial tumour ... and they seem to have activity there," she says. "Our work is very crude. We say 'OK, [the peptides] don't kill normal cells but they kill these tumour cells' but I couldn't tell you why. So that's where we need different expertise to try to understand what's [going on]." That's why, she says, the collaboration that comes with the Centre of Excellence is so exciting.

FLOWER POWER

The animal kingdom can't take all the glory here. Remember the sunflowers you grew as a kid? Craik's team has already modified a peptide found in the seeds so it can bind to an enzyme involved in prostate cancer. Then there's *momordica cochinchinensis*, or gac melon to its mates. This spiky tropical fruit is home to a peptide that scientists have again re-engineered to potentially carry cancer-fighting properties into cells. Another plant contains a molecule they've modified to target a brain receptor that reduces appetite – could this be a future tool in the obesity fight?

The goal is to put some of these modified peptides back into plants (whether it's a sunflower or even a potato), which can then grow with the new health-boosting properties. "It sounds far-fetched," Craik acknowledges. "But already the United States Department of Agriculture has approved a modified potato with a lower amount of [a suspected carcinogen, which occurs] when you fry the potato. Regulatory bodies are starting to see that we can think about making our foods safer and add novel properties to devise an anti-obesity drug, for example. It's going to be an interesting time over the next 10 years or so."

Another dream is to make therapies for malaria and HIV/AIDS more accessible in developing countries. "It'd be ideal to have an anti-malarial peptide that's produced in a plant, so that people could basically grow a medicine to protect themselves," Craik explains. "Those are the sorts of things we're trying to do."

A BRIGHT HEALTH FUTURE

The overall vibe from scientists involved in the centre is cautiously optimistic. The road from research to drug is a long, challenging and expensive one but, as Jolliffe says, "We've got the centre for seven years, which is actually a really long time in terms of funding for a scientific project. It will give us time to develop things to a point where a pharmaceutical company might say, 'we're going to buy this one'. To be able to actually do something, have a product – whether it's a drug or a tool that biological researchers would use to investigate diseases – that's really the outcome that I think all of us would like to see."

Professor Frank Grutzner works at the Department of Molecular and Biomedical Science at the University of Adelaide. His research stars one of the most iconic Aussie mammals: the platypus. During breeding season, males deliver venom from the spurs on their hind legs, probably to fight off competition. Grutzner is investigating a peptide in this venom (called GLP-1) with the hope of eventually finding a more effective treatment for type 2 diabetes. "Diabetes, obesity and cardiovascular disease are probably the greatest health challenges of our time," he says. "Using the platypus to find something that could ultimately be helpful, that'd be amazing. I would be so thrilled." *wh*

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