A time to heal, abbreviated

Catalyst grant spurs advanced research into the repair and regeneration of damaged tissue

By Ashley WennersHerron

Robert Gourdie thought it might be too good to be true. The tissue samples were healing, and they were healing quickly. The compound he developed with his research team worked.

“I’m a bit of an Eeyore when it comes to good news, especially in the lab,” said Gourdie, director of the newly expanded Center for Heart and Regenerative Medicine Research at the Virginia Tech Carilion Research Institute, referring to the mopey character in the classic Winnie-the-Pooh tales.

Gourdie had reason to worry. He and his team, then located at the Medical University of South Carolina, might have cracked the code to the body’s ability to heal, from skin wounds to cancer to traumatic brain injury. Any misinformation could spark an avalanche of false hope for millions of people, not to mention a public relations nightmare.

“I started thinking of all the issues that could arise,” Gourdie said. “But, then, we replicated the results. And other experiments, independent of my lab, started getting the same results. That’s when my anxieties started to lessen.”

The work was recently recognized with a grant from the Virginia Biosciences Health Research Corporation. The $200,000 Catalyst grant will fund a collaborative three-pronged study to advance this regenerative compound.

The worry still hasn’t disappeared, but Gourdie allows more excitement to creep into his voice when he discusses his research. The implications were and continue to be enormous. It all still seems too much to hope for.

Gourdie hails from New Zealand, and he earned his doctorate degree studying the biophysical properties of wool fibers. It sounds like a bad joke.

“I can get curious about anything,” Gourdie said.
Once he graduated, a postdoctoral position at University College London caught his eye. It was there that Gourdie learned about gap junctions, the electrical connections between heart cells.

His work then led him to the Medical University of South Carolina, where he studied the developmental biology of electrical conduction in the embryonic heart. That research instilled in him a general curiosity about cardiac connections.

“We had this fundamental question — how does electricity flow through the heart?” Gourdie said. “We had no idea the answer would lead to a treatment for healing skin wounds.”

The research team was initially interested in communication between cells, with a specific focus on electrical signals in cardiac muscle. They developed a peptide, ACT1, that prevents a protein called connexin43 from binding another protein, ZO-1. The compound enhanced electrical flow exactly as Gourdie and his team designed it to do. But they weren’t satisfied.

“We knew the peptide had changed the function of connexin43, but when you push one side of the seesaw down, the other side goes up,” Gourdie said. Indeed, while the phone line was cut, the Wi-Fi signal seemed to gather strength.

This result prompted further research in Gourdie’s lab. At the time, other research teams were studying how the connexin43 protein was involved in the healing process. They found that it increased the time it took to heal and the amount of scar tissue.

Gourdie’s group hypothesized that their peptide may decrease the healing time and lessen the amount of scar tissue. The scientists scratched a single layer of skin cells lying on a petri dish, applied the peptide, and waited — but not for long. The cells began mending, and Gourdie got anxious.

He relaxed a little once the results were replicated, in-house and independently. His postdoctoral associate at the time, Gautam Ghatnekar, left the lab to run a company spun off from the wound healing technology — FirstString Research Inc. — to bring the compound to the public.

Shortly after, Gourdie was recruited to the Virginia Tech Carilion Research Institute.

“The research institute is a startup,” Gourdie said. “There is flexibility and creativity. The people are mostly younger and certainly more energetic than I am — it’s an invigorating place to be. We have started exploring what else we could make this peptide do.”

Since it was founded, FirstString Research scientists have worked with clinicians to test the peptide as a treatment for diabetic foot ulcers, a particularly hard-to-heal wound.
“Treating diabetic foot ulcers wasn’t our intention, but 10 percent of people with diabetic foot ulcers will eventually require amputation,” Gourdie said. “The phase 2 clinical trial data indicate that the compound could halve the healing time for these wounds.”

While the early clinical studies showed promise, the treatment needs to progress through phase 3 trials before it can be made available for wider use in the clinic.

These types of trials require implementing strict protocols at several centers all over the world. More than 500 patients will need to match the correct criteria and undergo treatment of their diabetic foot ulcers in these tests.

The Catalyst grant will fund the phase 3 clinical trials for the diabetic foot ulcer treatment, as well as further studies into other potential uses for the peptide beyond healing skin wounds.

Along with Steven Poelzing, an associate professor at the Virginia Tech Carilion Research Institute, Gourdie will develop different variants of the original peptide. He’ll also study the healing mechanism and standardize a system to test the peptide so it can be manufactured safely and accurately as a medical treatment.

“We’re hoping that this will lay the groundwork for using the peptide for other damaged or diseased tissues,” Gourdie said.

If his research team can fully understand the connection between communication and healing, Gourdie said, the implications for treatment are broad.

Cancer cells are one example. Generally these cells don’t communicate well among each other, impeding the effectiveness of chemotherapies. The signal is halted before it reaches all the diseased cells, requiring multiple rounds of treatment or redundant methods.

Scientists could, hypothetically, use the peptide to increase communication between cancer cells. That would allow the signal sent from the chemotherapy to spread further and the message would be unhindered. It would be easier to kill off all the cancer cells in less time.

While the peptide and method might vary, the general idea stays the same. Human cells need to communicate more efficiently in ways that benefit us.

“In the long term, we want to determine if this could heal damage in the heart,” Gourdie said.

In that vein, Jeffrey Holmes, a professor of biomedical engineering and medicine at the University of Virginia and the third recipient of the grant, will use his portion to lead a study designed to study how this compound could treat heart damage.
“Science can be transformative in unexpected ways,” Gourdie said. “In this case, basic research on fundamental cellular processes led to a treatment that will help alleviate suffering. Support of collaborative research is essential to ensure scientists can make such breakthroughs.”