

THE CURE IS THE FINISH LINE

Brains and brawn: How wheelchair athletes like TIPHANY ADAMS and researchers like STEPHEN STRITTMATTER are teammates in Wings for Life, the global quest to cure spinal cord injuries.

Words CHRISTINE FENNESSY
Photography MATTHEW REAMER



Tiphany Adams, shot for *The Red Bulletin* on March 4, competed in her first World Run on a dare.

A

Am I really doing this right now?

There were 20 minutes to go before the start of the 2015 Wings for Life World Run in Santa Clarita, California, and Tiphany Adams couldn't believe she was pinning on a race bib. Although she regularly hit the gym, she didn't consider herself an athlete, not the racing kind of athlete anyway, and she'd sworn off races after it had rained during her first 5K, several years earlier. She'd been so wet and so cold. She couldn't believe people actually raced in the rain.

It was her dad's fault. She'd called him after her interview with World Run organizers and he'd goaded her into it. She figured she'd done her part, talking about why a run that puts every cent in entry fees toward spinal cord injury research was important. The interview had gone well and now she was tired; she'd stayed up too late with friends watching a Manny Pacquiao fight, slept less than 30 minutes, then driven 50 minutes in the dark from Marina del Rey to make the 3 a.m. interview. She figured she'd watch the start of the race then head home, but her dad began talking smack over the phone, about how tough it must have been to do an interview while everyone else was getting ready to race, and so she'd asked one of the officials if she could still register. And now here she was. Doing something she had sworn she'd never do again. She had no idea what to expect, no clue about the course. All she knew was that she'd have to keep going until the finish line—in the form of a catcher car—caught up to her. She downed a cup of coffee and moved toward the starting line. *Get your head in the game, she told herself. You're doing this.*

The starting area felt like a street party. Music blared, a canopy of lights was strung between trees on either side of the start corral. White vendor tents lined the curb and photographers and videographers were positioning themselves in front of the giant white truss of the starting line. Thousands of participants crowded into the road, bathed in the soft light of the bulbs hanging over them, talking, laughing and loosening up for the 4 a.m. start.

Adams had never seen anything like it, so many people gathered for the singular cause of finding a cure for paralysis. Gratitude washed over her. She said a silent prayer and gave thanks for her life and for the chance to be part of something that may help heal—and even save—other lives.

Then she took her place at the front of the corral with the rest of the wheelchair participants and waited for the gun to go off.

Every year, about 17,500 Americans suffer a traumatic spinal cord injury. They are most often in a car crash or a fall—and the force of the impact breaks, compresses or dislocates one or more of the 33 bones in their spine. Those vertebral bones, which a split second earlier had formed a protective collar around the spinal cord, now crush the spinal cord. Cells die. A bruise of sorts forms on the spinal cord and more cells die. Some of those dead and dying structures are neurons, or nerve cells, and that is bad news, as they form the body's communication highway.

This highway runs from the brain down to the end of the spinal cord. Along the way, 31 pairs of spinal nerves act as on-ramps and off-ramps. Impulses from the brain shoot down the highway and, for example, take the off-ramp that tells your legs to start running. Impulses from your feet take the on-ramp to tell your brain about a blister on your toe.

A traumatic injury can bring all this traffic to a standstill. It can knock down these critical on- and off-ramps, these spinal nerve pairs. When that happens, communication to and from specific areas of the body is lost or greatly diminished.

Losing site-specific function is bad enough. But what makes spinal cord injury truly debilitating is that it essentially breaks up the highway. The bruise or contusion cuts off the healthy spinal cord above the injury from the healthy spinal cord below it. Signals from the brain can't bridge the gap and tell the body what to move, and signals from the body can't bridge the gap and tell the brain what to feel.

Signals can't bridge the gap because the nerve fibers that make up this highway, the nerve fibers

She had never seen anything like it. Gratitude washed over her.



The 4 a.m. start of World Run 2015 in Santa Clarita.

Neurologist Stephen Strittmatter has spent 17 years developing a drug that helps nerve fibers grow.



It's taken Strittmatter 17 years and millions of dollars to get here.

that are broken apart by the injury, simply do not regrow. If they can't regrow, they can't reconnect. And if they can't reconnect, they can't communicate.

To date, no one has solved the puzzle of paralysis. But Stephen Strittmatter may be getting close.

Strittmatter, M.D., Ph.D., is the director of Cellular Neuroscience, Neurodegeneration and Repair at Yale University School of Medicine and a member of the Wings for Life scientific advisory board. He's spent 17 years developing a drug that can stimulate nerve fibers to grow and reconnect. He's hoping to alleviate not only the disability of the injury itself but the cascade of problems that come with spinal cord injury, including blood clots, pressure ulcers and pneumonia. Bladder, bowel and sexual dysfunction. Depression and loss of livelihood.

"People are suffering for decades with a whole range of different disabilities," he says. "Unless we can promote nerve fiber growth, it's unlikely these deficits are going to go away."

Strittmatter's journey toward solving the paralysis puzzle began in 2000, when he and his team were one of three research groups, working independently of each other, who discovered why spinal nerves don't regrow. Molecular inhibitors tell them not to.

Inhibitors aren't saboteurs in the body's greatest time of need; it appears that saying no is their job. They step in after the central nervous system is finally all wired up, sometime in childhood, and stabilize the structure. Once the highway and all its ramps are built, the inhibitors tell the nerve fibers, "You're done." The problem, however, is that after an injury, the message remains the same: "Don't grow."

Just how the inhibitors communicate that message wasn't clear until 2001. That's when Strittmatter's team found a receptor on the nerve fiber, specifically on the long, tubelike structure that protrudes from nerve cells called axons. Axons are a big deal because they're like the tarmac on the highway; they conduct the signals that tell you to start running or put a Band-Aid on your blister.

"Some axons go from the brain to the lower part of the spinal cord, and they can be a meter long in humans," says Strittmatter. "They transmit electrical signals over long distances to create a network."

Signals that go nowhere if the highway gets washed out.

What Strittmatter discovered was that axons had receptors for these molecular inhibitors. Basically, the two were attracted to each other. When axons tried to regrow after being damaged by an injury,

LAUREL GOLIO



Adams, now 35, after winning the 2017 World Run in Santa Clarita.

these inhibitors stuck to them and told them loud and clear to forget about it.

Strittmatter now knew how inhibitors blocked regrowth of nerve fibers. And even back then, he could envision the path to a potential therapy.

That potential therapy is now closer to reality. The Nogo Trap—so named for one of three inhibitors it targets—is a drug that sucks up the inhibitors, which leaves the axons free to grow. Strittmatter developed the drug around 2004 and has since tested it in numerous animal models. In the most recent such study, he used it on rats with chronic spinal cord injury, meaning that three months after their inflicted injury, their bodies had healed naturally to their fullest extent. Compared to injured rats not given the drug, all the rats who got it improved, and a third of the rats improved significantly.

“I wouldn’t say they went from zero function to completely normal function,” says Strittmatter. “But they went from not strong enough to walk to strong enough to walk.”

Strittmatter’s research is that rarest of investigations: the kind that makes it out of the lab and into the clinic. The Nogo Trap is slated to enter human clinical trials later in the year. And it will be the first of its kind—an intervention that promotes nerve fiber growth in the chronically injured, those people who have reached the point where they experience little to no change in their condition.

It has taken Strittmatter 17 years and millions of dollars to get here. It has also taken the resolve,

generosity and compassion of thousands of runners, walkers and rollers around the world. People like Tiphany Adams.

The blister on her left hand was the size of a quarter. Her knuckles ached from the continuous grip-and-release of the metal rims around the wheels of her chair as she propelled herself forward. And she was cold. It was Santa Clarita in early May at 5 in the morning and the temperature was brisk. All she had on was what she’d worn for the interview—a thin Nike top and printed blue tights. No gloves, no hat.

Her foot kept falling off its plate at the base of her chair and that was a little annoying. The downhill brought relief and dread—relief at the momentum, dread over debris in the road that might catch one of her chair’s small front wheels and flip her over.

But none of it mattered. People she passed shouted “Keep up the good work!” and she stayed focused. It didn’t matter that she hadn’t trained for this, she was going to give it her all—that’s what she always did, and she was going to block out the pain because she was good at that, too. After the head-on collision when she was 17—the wreck caused by a drunk driver that killed him and her two friends and left her with a T10 fracture in her thoracic spine, with no movement or sensation below her belly button—she’d gotten good at persevering. Despite being in a coma for three weeks, she’d left the hospital earlier than expected, sooner than the doctors would have liked, determined

to figure out for herself what life in a chair meant. She went to college, taught elementary school for a while, worked in a gym and taught herself how to stay fit. Through it all she dealt with survivor’s guilt and post-traumatic stress and eventually figured all that out, too. She starred in a reality TV series called *Push Girls* about the triumphs and challenges of life in a wheelchair.

She had regained some function below her injury. She could move her abs. She could feel to the tops of her thighs or when someone moved her foot. And she had accepted life in a wheelchair. But she knew that scientists might someday help her and everyone like her learn to walk again. And there was no better way to help them do that than to give this race her all.

The Wings for Life World Run is actually a run, walk or roll event, and it’s arguably unlike any other charity race. Participants around the globe all start at the same time and try to hold off the finish line—an actual or virtual catcher car—for as long as they can. And every euro, peso, pound, mark, rand, real, lek, lira, leu and dollar in entry fees goes to support spinal cord injury research like Strittmatter’s.

Since the inaugural event in 2014, the run has attracted 435,000 participants and raised more than \$25 million. It is the single largest source of funding for the Wings for Life foundation, a nonprofit on a mission to find a cure for spinal cord injury.

The foundation began in 2004, after Red Bull founder Dietrich Mateschitz and his close friend and two-time motocross world champion, Heinz Kinigadner, learned that spinal cord injury fell into the dreaded category of “rare.” Kinigadner’s son Hannes had been paralyzed from the neck down in a motorcycle accident the previous year and the two friends had met with the best researchers in the world, desperate to improve Hannes’s prognosis. They kept hearing the same thing: We believe we will find a cure; there’s just not enough funding.

Despite the debilitation of a spinal cord injury, it’s considered a rare condition. Globally, the World Health Organization estimates that between 250,000 and 500,000 new injuries occur each year. There’s just not enough financial incentive for drug companies to plow resources into a cure. Governmental support is similarly compromised by overwhelming problems like Alzheimer’s and heart disease. Spinal cord injury needed its own benefactor and so Mateschitz and Kinigadner started Wings for Life to fund the research that could find a cure. Red Bull assumed operating costs of the foundation so that all money raised through corporate and private donations goes directly to research.

To date, Wings for Life has helped fund 170 research projects, 59 of which are now under way. The foundation backs an average of 15 to 20 new

projects every year in amounts that range from \$100,000 for lab work into the millions for research entering the clinical trial phase. It covered three of Strittmatter’s preclinical studies over the past decade, and last July committed \$7 million to support his upcoming trial. A unique stipulation of the funding—which is typically granted for a period of two years—is that all investigators must attend a yearly conference in Austria to share their progress, says Verena May, a scientific advisor for Wings for Life.

“This exchange with colleagues and with experts from our scientific advisory board might help overcome hurdles and gain new ideas beyond the current research,” says May. “They can also be the starting point for new collaborations.”

Strittmatter has been on the advisory board since the foundation first got started. “I’d like to see spinal cord injury research move forward and come up with a cure,” he says. “And if I can provide advice and help to make that happen, I’m happy to do it.”

In his advisory role, Strittmatter helps define research criteria and reviews applications for funding. His own work over the years had to meet similar criteria and undergo the same review process. And the support has been crucial. Without it, he says, the clinical trial of the Nogo Trap would not happen.

“Foundations like Wings for Life are critically important,” he says. “They’re filling a gap that commercial and government entities don’t fill. And they’re essential to move this research field forward to overcome a daunting and completely unsolved problem in neurology.”

On May 6 in places like Denver, San Diego and Sunrise, Florida, runners, walkers and rollers will join tens of thousands of participants around the world. Doing what they can to fill that gap.

Adams felt a tap on her shoulder and looked up in surprise at the race official standing beside her. “Excuse me” he said. “I need to talk to you for a second. You registered as a runner.”

Crap, Adams thought. She was in the post-race burrito line, ticket in hand. She’d been obsessing about a burrito since the catcher car caught her eight miles into the event. She was ravenous.

“Listen, I’m sorry,” she began.

“Because you’re a wheelchair user,” the man continued, “and so we need to let Austria know that you took first place.”

Adams was horrified. *Oh my god*, she thought, *this is so cruel. Austria has been training for this. I don’t want to shatter her dreams.*

“Maybe we can give the win to Austria, because honestly I didn’t...”

“No,” the man interrupted, laughing. “Austria as in the country, where Red Bull’s headquarters are!”

Winning had never crossed her mind. All she’d thought about during the race was the reason behind it. That if she was part of it, she, too, could be part of the solution. Part of the movement.

Adams stared up at him. Then she began to cry.

wingsforlifeworldrun.com

Winning had never crossed her mind during the race.

CARLO CRUZ FOR WINGS FOR LIFE WORLD RUN