HOW CURIOISITY KILLED THE CRAMP.

This is the origin story of a major breakthrough for athletic performance invented by a Nobel Prize-winning neuroscientist/endurance athlete.
OFF THE COAST OF CAPE COD, TWO NEUROSCIENTISTS WERE DEEP SEA KAYAKING IN THE WINTER WHEN THEY WERE BOTH SEIZED WITH LIFE-THREATENING MUSCLE CRAMPS.

Dr. Rod MacKinnon and his friend, Dr. Bruce Bean, had an incapacitating experience. “We’re going to die,” thought Rod. Almost simultaneously, in their separate kayaks, their bodies were seized by one of the most baffling conditions an athlete can face: muscle cramps. They were experiencing such debilitating pain that neither could steady their kayaks. This would not be a good time to capsize.

Rod and Bruce felt fear mixed with confusion. These two fitness-obsessed geniuses – Rod, a Nobel Prize winning neuroscientist, and Bruce, a neurobiology professor at Harvard – had checked all the boxes of nutrition and hydration before their launch. But what they discovered the hard way was that the familiar preventative measures (bananas, magnesium tablets and sports drinks) were based on wild guesses, not science.

Rod and Bruce survived the onslaught of cramps but that excruciating moment in the kayak flipped the switch on the trait that has defined MacKinnon’s scientific career: curiosity. He asked questions: Why do we cramp? What is the cause? What is the cure?

Over a period of five years, Rod worked to unravel the mystery, to separate misguided assumptions from scientific reality and discovered this surprising truth: When it comes to preventing muscle cramps, it’s not about treating the muscle, it’s about treating the nerve.
THE TRUTH ABOUT MUSCLE CRAMPS

Rod’s conclusion was rooted in his research on the structure of potassium ion channels, work for which he won the Nobel Prize in 2003. Ions carry information through the nervous system via cellular stop-and-go switches. Nerve cells are called into action by the opening and closing of ion channels which trigger action potentials to move from the nerve cells along the axons to their targets. Motor neurons send their signals along their axons in peripheral nerves to the muscles.

Simply put, cramps are caused by an excessive firing of motor neurons in the spinal cord, not by the muscle. Under normal circumstances, motor neurons control muscle contractions without incident. But when the nerves are destabilized, painful cramps can occur.

Rod heard stories about bicyclists and some athletic teams using pickle juice to treat muscle cramps. He also heard about marathon runners who used mustard stirred into warm water to relieve their cramps. How could it possibly work? What did pickle juice and mustard have in common? All of a sudden it occurred to him that maybe it was the activating effect of pickle juice and mustard on TRP channels in the mouth. Rod made the connection that no one else had: It’s the stimulation of the sensory nerves in the mouth, esophagus and stomach that triggers a response from the nervous system and calms down the motor neurons in the spinal cord.

This was Rod’s “Aha!” moment: The nervous system could be prodded, using those very receptors, to cue a cascade of nerve stimulation, also involving pathways from the mouth, esophagus and stomach, projecting signals to the motor neurons of the spinal cord.

The anecdotal stories of pickle juice and mustard drove Rod into the lab to develop a formula that would work.

It was a challenge. It took five years of research to identify and calibrate a balance of natural ingredients to effectively activate TRP ion channels in the mouth, esophagus and stomach.

The result of Rod’s persistence is a 1.7 fl oz breakthrough sports shot called HOTSHOT – the first scientifically proven formula to prevent and treat muscle cramps by stopping them where they start – at the nerve.

Focused on the body’s neural wiring, Rod’s innovative formulation is the foundation of a revolutionary new category in sports nutrition: Neuro Muscular Performance™. NMP is how an athlete’s nerves and muscles work in an optimal way. HOTSHOT boosts an athlete’s NMP to stop cramps, so the athlete can push harder, train longer and finish stronger.

Our scientists, in partnerships with leading sports science institutes, are continuing to study other ways that HOTSHOT impacts an athlete’s NMP.
THERE’S NO SUCH THING AS A HAPPY CRAMPER.

For even the most supremely fit athletes, cramping can bring them to their knees.

Cramps forced LeBron James to the sidelines in Game One of the 2014 NBA Finals. Tennis great Rafael Nadal writhed in pain after an intense match in 2011. Even the ultimate endurance athletes aren’t immune. Two-time world champion triathlete Chris McCormack collapsed twice from muscle cramping in separate world championship races.

For alpha athletes, training, competing and succeeding are a way of life. It’s frustrating and bewildering when their will cannot overcome their bodies.

As Rod’s research underscores, criticisms questioning a cramping athlete’s preparation or dedication are unfair and not based on science. Cramping is not the fault of athletes. But throughout history, athletes have been targets of scrutiny and helpless to control cramps – until now.

Rod’s proprietary formulation helps restore control and create the best ally an athlete can have – the ultimate confidence in their bodies.
**BREAKTHROUGH SCIENCE**

**HOTSHOT** is precisely calibrated to activate TRP ion channels. You can feel it work from the first kick to the warm afterglow. By drinking a 1.7 FL oz **HOTSHOT** 15-30 minutes before and after working out, the proprietary formulation of organic ingredients can become part of an athlete’s toolkit for performance. **HOTSHOT** has received NSF’s “Certified for Sport®” certification – the gold standard in sports banned substance testing chosen by professional sports leagues (including MLB, NFL and PGA) – so you know the proprietary formulation includes the ingredients listed on the label and does not contain banned or prohibited substances. **HOTSHOT** is a game-changer for the 68 million Americans who experience muscle cramps related to exercise. Unlike other existing remedies – that target the muscle - **HOTSHOT** is the first and only scientifically proven solution to prevent and treat exercise-associated cramps.

Stopping cramps is just the beginning. **HOTSHOT** is the cornerstone of a new category in sports nutrition, Neuro Muscular Performance (NMP). We’re just starting to understand the full power of NMP.

**HOW HOTSHOT WORKS:**

- Receptors on nerves in the mouth, esophagus and stomach are activated by the proprietary formulation, resulting in signals that flow to the spinal cord.
- These neuronal signals prompt the spinal cord to send what are essentially stabilizing messages to other parts of the body.
- Because cramps are the expression of destabilized, over-excited nerves, biological relaxing cues naturally reduce that input, causing motor neurons to normalize and cramped muscles to relax.

1. Product, taken orally, stimulates sensory neurons in the mouth, esophagus, and stomach.
2. Stimulated neurons send impulses to the spinal cord.
3. These impulses overpower and inhibit repetitive signals coming to and from the cramped muscle.
4. This stops repetitive signals and prevents and/or treats the cramp.
Rod’s insight forms the basis of Flex Pharma, a Boston-based biotechnology company co-founded by MacKinnon in 2014 and HOTSHOT’s parent company. The company’s medical researchers are pursuing treatments for athletes and pharmaceutical products to treat major muscle issues for patients with ALS, MS and nocturnal cramps.

Dr. Christoph Westphal MD, Ph.D., a Harvard medical doctor, brought together a scientific dream team. To build on Rod’s Neuro Muscular Performance platform, he immediately turned to some of the best minds in forming the Scientific Advisory Board, including neurobiologist and Flex Pharma co-founder, Dr. Bruce Bean, Ph.D., who has worked with Rod on research since their kayak journey, and Chris Walsh, Ph.D., Professor Emeritus at Harvard Medical School.

Rod and the Flex Pharma scientists began using a laboratory model to electrically induce cramping. They conducted multiple studies of TRP activator beverages monitored by an Institutional Review Board in the United States that, in aggregate, showed a statistically significant reduction in participants’ muscle cramping, as measured by surface EMG.

Another series of five studies used healthy, but cramp-prone athletes, who consumed a TRP activator beverage within 30 minutes of their normal training session. The outcome revealed a significant reduction in the frequency of exercise-related cramping frequency compared to baseline measures (i.e., cramps were prevented in some subjects.).

Dovetailing with these findings, researchers at Penn State University presented results showing consumption of HOTSHOT significantly reduced muscle cramp intensity-duration compared to placebo and was associated with lower post-cramp muscle soreness.

In field studies, the majority of athletes reported reduced post-exercise muscle soreness.

Flex Pharma is now working with leading exercise physiologists and sports science institutions to study how boosting an athlete’s Neuro Muscular Performance may translate to additional benefits for athletes.