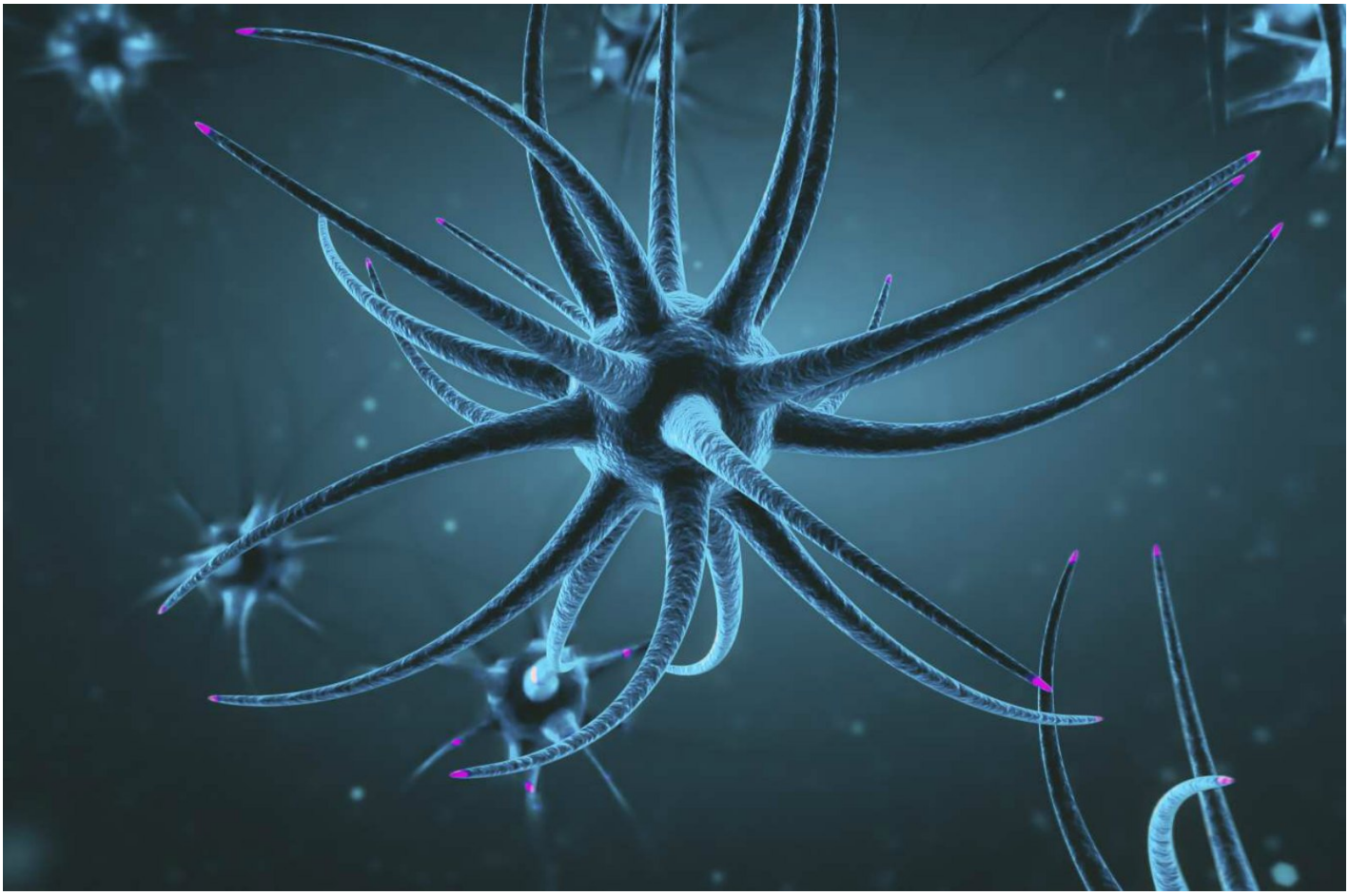
New Protein Therapy Shows Promise For Treating Muscular Dystrophy

University of Nevada, Reno



Prothelia Inc. may be a new company, but the research and relationships supporting it have been decades in the making. Devoted to researching new treatments for muscular diseases, the people at Prothelia are motivated not only by scientific inquiry and business opportunity, but also have motivations that are heartfelt and deeply personal. A laboratory's "What if?" experiment years ago has grown into a new company that is working to validate and market new therapies for muscular dystrophies.

Prothelia has licensed rights to a protein known as Laminin-111 from the University of Nevada, Reno, (UNR), along with several other potential promising treatments. Laminin-111, which is naturally produced by the body, assembles into a matrix around muscle cells and helps promote muscle-cell health and survival.

Prothelia's technology originated from Dean Burkin, Ph.D.,'s exploration into whether Laminin-111 could restore muscle

function after the onset of a disease. Burkin is an associate professor at the university's School of Medicine. He directs a biomedical research program focused on studying the molecular basis of muscular dystrophies to develop potential treatments.

"In Duchenne and other forms of muscular dystrophy, we've been able to show that alpha7beta1 integrin, a laminin receptor in muscle, prevents muscle disease," explains Burkin. Using this knowledge, Burkin established a drug discovery program, developed a novel muscle-cell-based test and identified several molecules that increase alpha7beta1 integrin in muscle. Burkin discovered that these compounds can help repair and prevent muscle damage.

> *"It was really surprising to us that such a large protein could be delivered to muscle and protect the muscle from damage," Burkin says, describing mouse-model experiments that began in 2007 at the university.*

Muscular dystrophy patients experience tears in muscles, usually starting in childhood, that weaken the muscles and limit their use. As the disease progresses, the heart, diaphragm and other organs can atrophy. More than 40 genetic diseases are categorized as muscular dystrophy — some marked by an absence of critical muscle proteins, causing progressive muscle weakening and degeneration.

According to the National Institutes of Health (NIH), the most common variants — Duchenne and Becker muscular dystrophy — effect approximately 1 in every 3,500 to 5,000 boys, or as many as 600 boys born every year in the United States. Most cases are a result of new mutations or a family history of the disease.

Reconnecting at the Right Time

A biochemist and pharmacologist originally from New Zealand, Burkin was pursuing a postdoctoral fellowship at the University of Illinois in the mid-1990s and collaborated with Bradley Hodges, Ph.D., then a doctoral student in neuromuscular biology. Both scientists worked on the alpha7beta1 integrin, a molecule located on the surface of muscle tissue that holds the tissue together. Over the next decade, Burkin continued his research at the UNR Center for Biomedical Research Excellence.

Hodges worked for seven years in the laboratories of Genzyme Corp., a Cambridge, Mass., biotechnology company.

In 2007, he was ready for a new challenge and contacted several university technology transfer offices to ask about research on treating muscular dystrophy. Then he reconnected with Burkin to ask about his research, and both men started down the path to collaboration. Burkin needed a corporate partner to continue development of laminin compounds and had filed a patent.

Longstanding relationships appear to be a major strength for Prothelia. As a graduate student, Jachinta Rooney did the original laminin-111 experiments in Burkin's lab. She is now continuing the work as a post-doctorate researcher studying the effects of protein therapy in mouse models.

"Muscular dystrophy is one of the most common 'rare' diseases, so there is a good market opportunity for a drug that can help some of the 20,000 patients out there," Hodges says. "When I decided to start a company I knew it would address muscular dystrophy because I knew the issues." Hodges also knew that large companies are hesitant about emerging treatments, so he incorporated Prothelia and made his case to UNR officials. Hodges approached the university at the right time.

"In academia, you can only get research so far before you have to get industry to come in," explains Burkin. "Brad's

background, interest and enthusiasm were key to the development of this discovery. The Technology Transfer Office here at the university eased the process toward development by licensing the intellectual property."

As it turns out, the technology office also saw a unique opportunity.

"Protein therapeutics was the area Brad wanted to pursue and I was convinced very quickly that there was a good relationship here," says Richard Bjur, former director of the UNR Technology Transfer Office. "There was a lot of serendipity here since Brad and Dean know each other." Bjur and current Technology Transfer Office Director Ryan Heck say the choice of a licensing deal with a startup instead of a much larger company made sense because of the early stage of laminin research.

"One barrier we see to commercializing our faculty's research is that it can be difficult to find someone who grasps the science well enough to understand and overcome the challenges posed by an early-stage technology," adds Heck, who has a doctorate in chemistry and, as an outside attorney for the university, wrote the initial patent applications. "Brad comes from a scientific background and understands what he's getting into."

Devoting a Company to Muscle Disease Treatment

Armed with the license agreement, Hodges began writing grant applications to the NIH and the Small Business Innovation Research program and was awarded on the third try. He also recruited Richard Cloud to serve as the company's chief executive. They met at a conference Cloud helped organize in Atlanta for parents seeking a cure for congenital muscular dystrophy. Cloud's oldest daughter has MDC1A — one of the variants of muscular dystrophy Prothelia expects to address.

"The research community for muscular diseases including ALS (Lou Gehrig's disease) and muscular dystrophy is a tightknit group," Hodges notes, "with a lot of cooperation between the NIH and the many patient advocacy groups devoted to muscular dystrophy." The diseases have been recognized since the mid-1800s yet have eluded treatment despite a relatively high public profile. The genetic mutation causing Duchenne muscular dystrophy was identified in 1986.

The Challenges and Possibilities of a Young Technology Transfer Office

The state of Nevada's only public medical school is fairly new, founded in 1969, and officials there recognize the need for impact that will draw corporate partners. The laminin technology has great potential, and its partners share a passion needed to reach that potential. The university's Center for Economic Development estimated that $74 million in research expenditures in 2009 meant a regional impact of nearly $300 million for Nevada. The university has more than 30 active business and industry partnerships, and the university technology transfer program is pursuing goals of expanding that local impact, Heck says.

"Our office started small, with just me, and expanded back in 2003 and grew into a full-time office," Bjur adds. "We're trying to bridge the gap between the university and community, and one way is to create economic opportunities." He cautions that in technology transfer, "What you don't want is a situation where there are unrealistic expectations."

Thus far, the UNR Technology Transfer Office has been able to capitalize on such opportunities. As one example, Prothelia, which appears to be well-positioned for success, is pursuing both venture capital funding and strategic relationships.

But for the people who suffer with muscular dystrophy, these opportunities provide something even more valuable:

hope.

This story was originally published in 2010.

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