

## Jellyfish for Your Health

By Nicole Resnick

As marine creatures, jellyfish fascinate us. Their rather freakish forms tossing about the ocean waves serve as warnings to beware, for as anyone ever unlucky enough to feel the sting of a jellyfish can attest, their toxin can pack a punch.

What few do realize is the rich history behind the application of jellyfish in biological sciences research. Certain species actually glow or light up, an ability that was first harnessed by scientists in the 1960s. Osamu Shimomura, a researcher at Princeton University, discovered the protein responsible for the luminescence, aequorin, in a species of jellyfish called *Aequoria victoria*, and further research demonstrated that the protein binds calcium ions.

The role of calcium in transmitting signals between nerve cells made aequorin a valuable tool in neuroscience research, but for the next three decades, aequorin was used primarily as laboratory reagent, or marker, to study the movement of calcium inside cells.

And then along came Mark Underwood.

Underwood is a believer. Spend an hour talking shop with him, and the strength of his belief in what he is doing, and what he plans to do, makes those around him believe in it, too. He exudes an unshakeable confidence as he tells his story – a calm certainty in himself and his business comes through as he explains his vision.

His company, Quincy Bioscience, based in Madison, Wisconsin, has been built on that same confident foundation. Extending beyond his own capabilities, Underwood clearly believes in the team he has so far gathered to ensure that Quincy achieves its goals. Not quite a conventional crew of bioscientists, technicians and business managers, Quincy employees have landed in the company's Madison headquarters in University Research Park from a wide range of backgrounds and former places of employment. Yet each

seems to fit like a piece of a larger puzzle, as if each was meant to be working at Quincy all along.

And then most important of all is Underwood's belief in the one molecule – the protein called aequorin – on which he founded Quincy Bioscience and propelled Quincy to increasing prominence in the world of bioscience and health. Just last year, *BusinessWeek* featured Quincy Bioscience in a story headlined “Can Jellyfish Help Fight Alzheimer's?”

The critical link between calcium and a host of neurodegenerative diseases such as Alzheimer's, Parkinson's and stroke is what Underwood chose to focus on when entering college at the University of Wisconsin-Milwaukee. A psychology major with an emphasis on neurosciences, the Knoxville, Tennessee native was particularly intrigued by the impact of deficiencies in calcium homeostasis as we age and become more prone to diseases that affect the brain.

In the brain, calcium molecules play a ubiquitous role in regulating virtually all types of cellular communications. Calcium enters brain cells through specific receptors and once gaining entry attach to other specialized proteins called calcium binding proteins (CaBPs). Without the presence of CaBPs to essentially act as calcium sponges and sop up excess calcium, brain cells are destroyed and brain cell function starts to deteriorate. In the case of a stroke for example, neurons are flooded with excess calcium that will destroy them if enough CaBPs aren't there to rescue them. And that is where aequorin, a natural calcium binding protein, enters the picture.

Underwood seized on this particular ability of aequorin and decided he wanted to develop it as a therapeutic drug. He believed that this would work from the time he first began research studies on the therapeutic potential of aequorin, and he did not give up even when his research path grew bumpy.

His plan to pursue graduate work at UWM and continue studying aequorin was stymied when the professor and scientist he intended to work with left the University for another academic opportunity. Underwood instead took a job at a Milwaukee area packaging company as he was “forced to find a job in the real world.” Yet the real world experience may have been the turning point as Underwood met several future business partners and honed his business and management skills in preparation for what would eventually allow him to pursue his mission.

One key business contact was Michael Beaman, a client of Underwood’s employer and owner of Quincy Resource Group, a packaging and fulfillment company in Jackson, WI. Underwood and Beaman to work together as equal partners and start a biotech company based on the therapeutic uses of aequorin. Quincy Resource Group provided the necessary capital and an incubator atmosphere for Quincy Bioscience to begin its work and allow Underwood to focus on the business and technical development required. Together they formed Quincy Bioscience in June, 2004. They filed a patent on aequorin at that time as well.

Again, the pieces seemed to fall into place – in almost uncanny fashion – when Dr. James Moyer arrived around that time at UWM with the skills, tools and knowledge to help accelerate Underwood’s plan.

Hired as an assistant professor in the Department of Psychology from a fellowship post at Yale University, Moyer was the ideal individual to pursue studies on aequorin and develop key trials in laboratory rats demonstrating aequorin’s neuroprotective effects.

Already an established player in the field of age-related learning and memory deficits, Moyer was naturally interested in the role that calcium plays in aging and dementia. He intended to focus on the hippocampus which is responsible for forming new memories and whose capabilities deteriorate and become impaired by aging. Although it is known that calcium is necessary for communication between neurons in the brain, too much calcium leads to neuron death.

According to Underwood, Moyer's lab was the perfect environment for the key studies that still needed to be conducted on the ability of aequorin to inhibit cell death, and in animal trials, to measure enhancement in learning of memory in animals exposed to aequorin. As chief scientific advisor for Quincy, Moyer has provided critical data to support Underwood's belief in the molecule.

In data released last year, they showed that by injecting aequorin into the brains of rats and then inducing the equivalent of a stroke, between 28 and 45 percent more brain cells survived the trauma compared to rats that didn't receive any of the jellyfish protein. As important was the demonstration that aequorin caused no ill effects, no toxicity and is safe.

As Underwood is quick to point out, he never expected there to be any ill effects whatsoever. "We didn't have to establish that aequorin doesn't kill or interfere or cause bad side effects – we have 40 years of data that already show that," he says. "And since aequorin is a natural protein and very similar to proteins that we lose in the aging process, we could presume that the body would recognize it as similar."

The next wave of experiments designed to measure the enhancement in memory and learning in rats fed aequorin are just as promising; and the data will be revealed later this year.

While Quincy Bioscience was off and running, Underwood quickly recognized the value of relocating the company to a more scientifically charged community. An hour away to the west, the University of Wisconsin-Madison campus was the obvious choice.

Underwood found prime real estate at the University's biotech incubator, University Research Park, and in November, 2004 the group moved in.

According to Underwood, their new location has provided exactly what he was looking for. "We wanted to be in the proximity, in the shadow of UW-Madison," he explains.

“Not only is it a more established research institute with more bench strength, if we wanted to look at different diseases and study this molecule for different mechanisms, we’d be able to utilize the resources that are here.” Underwood is still in the process of meeting with potential collaborators within UW-Madison’s impressive research community, and the opportunities to apply aequorin’s therapeutic potential and role in calcium homeostasis to disorders as wide ranging as stroke, epilepsy and inflammation has interested many scientists.

As exciting as it all sounds, the push to eventually get aequorin into the hands of clinicians treating Alzheimer’s and stroke patients (clinical trials and FDA approval stand in the way) is only part of this story.

What really animates the normally calm Underwood is the imminent launch of the dietary supplement form of aequorin – a protein he and his marketing team named Prevagen. It would represent a first in many arenas – the first calcium binding protein supplement available, the first anti-aging supplement with solid scientific evidence to back it up, and certainly the first dietary supplement derived from a jellyfish.

“We’re excited because we’re using biotech to make a consumer product. Most things that are made with biotechnology are only pharmaceutical products because of the cost of manufacturing, but we have a molecule that expresses at a high enough rate that we can meet real consumer price points,” says Underwood. “We haven’t designed something that only the elite can afford. The way this protein behaves is allowing us to take it to the marketplace.”

Underwood’s pragmatism has not wavered, even in the face of some skepticism. “One of the largest venture capital groups in the world that is involved in pharmaceutical and nutraceuticals said it was absolutely impossible for us to make a biotechnology protein at a price point for the consumer,” he recalls. “And they’re absolutely wrong.”

The Quincy Bioscience motto, in fact, reads: “It Can Be Done.”

The idea to offer aequorin in this form and make it available to anyone and everyone took root years ago when Underwood realized the implications of its potential to slow down brain cell death. The major hurdle prior to that was figuring out a cost efficient way of mass producing it. Ordinarily, as he points out, it takes two tons – or four thousand pounds – of jellyfish to manufacture a mere 125 milligrams of the precious stuff.

Under the guidance of Quincy scientist and recombinant protein expression expert Dr. Dan Moran, their technology and recipe for manufacturing aequorin has now yielded “the world’s largest batch of jellyfish protein.” Underwood expects to break that record many times over before Prevagen is officially launched this September. In the meantime, Quincy plans to work with contract fermentation facilities around the state of Wisconsin in order to crank out Prevagen.

Underwood is way too smart to not use aequorin’s aquatic origin to his advantage in marketing the protein. Prevagen literature from the brochure to the bottle’s label are accented in the company’s signature colors – chartreuse and marine blue – colors that generate a creative vibe and make you think you’re underwater.

The Quincy offices and meeting spaces are bright and hip in design and reflect the energy and drive of the employees who share the modern space. Underwood has assembled a selective and creative team of individuals – eighteen in all. “The most overwhelming strength of this company is that everyone here has resolved to wear several hats,” he says. “Regardless of what their business card may say or their job title may be, everyone is willing to pitch in and do whatever it takes to meet the goals of getting our technology to the marketplace.” He is protective of them, and while their contribution to Quincy may at times take them to places outside of their comfort zone, they prove capable when put to the test.

Underwood’s vision has paid off so far – he has started a company devoted to producing and using the aequorin protein for this novel purpose. He has invited a dynamic, driven

and committed group of collaborators to join him in this endeavor. From top notch scientists to technology managers, business collaborators to marketing experts, the Quincy Bioscience group seems to have an edge as they prepare to launch their products and grab headlines. What makes this company different, and so appealing, is their confidence and their belief in the potential that Quincy Bioscience has in today's market.

“Yes, what we're aiming to do is an all or nothing proposal in some sense but we've already touched something that has a chance to directly affect people,” says Underwood. “Even in big pharma, that's a rare opportunity, so I hope that our team can appreciate that they can be involved in that.”

“Besides, the fact that you put in a good day's work you can go home and have a good night's rest and think, yes, you made a difference. There's probably few true opportunities to really make that type of an impact in any industry.”

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