

Quincy Bioscience LLC

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Written By: Deborah Erickson
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Summary: Insights into calcium's role in neurodegeneration is encouraging research into the role it plays in Alzheimer's and other diseases, and in the aging process in general. Much of the work has revolved around the concept of blocking calcium channels, but Quincy Bioscience thinks it has a better approach. Its compound has been utilized in laboratories for 40–some years, but not as a potential drug. It's aequorin, a luminescent protein originally isolated from jellyfish.

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Quincy Bioscience LLC

Treating diseases of aging, with a jellyfish protein

University Research Park

455 Science Drive, Suite 120

Madison, WI 53711

Phone: (608) 233–2475

Fax: (262) 364–3178

Web Site: <http://www.quincybioscience.com>

Contact: Mark Y. Underwood, President

Industry Segment: Pharmaceuticals; Biotechnology

Business: Therapeutics for aging–related diseases

Founded: June 2004

Founders: Mark Y. Underwood; Michael J. Beaman

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Investors: Private

Employees: 12

While most people know that calcium is important for bone growth, few realize just how vital it is to brain functioning. Calcium enables basic communication between neurons, and thus is integral to learning and memory. The calcium molecules migrate into cells through so–called ion channels that act like pores in the skin. But too much of this good thing can be damaging: advances in molecular biology have shown that excessive calcium in a cell kicks off a cascade of events that ultimately kill neurons. This kind of molecular overloading appears to happen increasingly with age, as cells lose the ability to control the amount of calcium that flows into them. Part of the problem is that more pores open up; another seems to be a lack of calcium–binding proteins within the cells.

The insights into calcium's role in neurodegeneration are encouraging a growing number of researchers to investigate its connection in diseases like Alzheimer's and Huntington's, and in the aging process in general. The commercial impetus is obvious: if intracellular calcium levels prove to be as critical as some scientists now theorize, then a product capable of ensuring that cells maintain healthy amounts could be a blockbuster.

Much of the initial work on the calcium hypothesis has revolved around the concept of blocking calcium channels. It's an understandable first step, given that this very mechanism underlies successful cardiovascular medications such as diltiazem (*Cardizem*), amlodipine (*Norvasc*) and nifedipine (*Procardia*), already considered safe in the body. So far, however, the existing medicines have not been shown to have much impact on the problems of neurodegeneration.

The founder of **Quincy Bioscience LLC**, Mark Underwood, believes he has found a better approach to addressing calcium dysregulation in neuronal cells. "The concept of blocking a calcium channel is okay, but it's not the same as restoring the cell to its original condition. If we're losing something as we age, let's replace it," he declares. The compound Underwood is championing is one that has been utilized in laboratories for 40—some years—but not as a potential drug. It's aequorin, a luminescent protein originally isolated from jellyfish. The luminescent activity is not engaged in the therapeutic form of aequorin, so patients will not need to worry about obtaining a healthy glow in the dark.

Aequorin has long been used as a marker in biological experiments, involving many, many kinds of cell and tissues. Scientists looking to measure the amount of calcium transference into a cell, for instance, do so with a luminometer: the intensity of the glow indicates the amount of transfer. "It's very precise and reliable," Underwood observes, noting that many publications cite the protein's use as a reagent or tool for investigation. But aequorin has never been tested as a therapeutic, and there has never been enough of it in the food supply to have been used that way. So Underwood's idea qualified for patent protection. Quincy Bioscience now has a good portfolio around this, he says: the initial patents, like the company, have just turned two years old.

Underwood thinks aequorin will make a good drug because of its structural similarity to human endogenous calcium-binding proteins—and because with all the testing the jellyfish protein has been put to for decades, it has not shown any toxicity issues. Aequorin has never been tested for its impact on entire organisms, Underwood points out, but he's confident that warning signs would have flashed by now if the substance were going to cause a problem. "Because it's been around so long and so much research has been conducted, we believe much of the risk has been taken out of the molecule. We know how it's shaped in 3D; we know how it's made," Underwood explains. These days, jellyfish farming is unnecessary; Underwood says the precise recombinant manufacturing methods are a trade secret, but that it gives good yield.

To test his theory that aequorin can help control calcium levels and thereby cause a good therapeutic outcome, Underwood enlisted Jim Moyer, PhD, an associate professor at the **University of Wisconsin at Milwaukee**. Underwood graduated from the university in 1996, so there's a sweet synchrony there, he says. Moyer was already investigating how calcium effects cell death, and its role in learning and memory when Underwood asked if he'd be interested in testing aequorin. Moyer thought the theory made sense, and agreed to test it. Underwood says, "The right man for the job turned out to be close to home."

So far, the data look good. Underwood says that in mouse models of ischemia (stroke), animals given aequorin experienced 28–45% more protection than those given placebo. The older study animals that received aequorin experienced larger degrees of cell survival than younger ones, he notes. How is the protein producing this effect? "We know we're sequestering calcium ions inside the cell," Underwood says, declining to elaborate, "but all we really need to do is show the neuroprotective effect." Moyer is also testing to see whether or not the protein has an influence on learning and memory; the data on that should be in within months.

Underwood says Quincy Bioscience is first developing aequorin as a treatment for acute ischemia, but is planning to get it into the clinic for testing in neurodegenerative diseases such as Alzheimer's, Parkinson's, Huntington's and ALS. The firm will start down that path soon by testing in mice bred to develop Huntington's disease.

"If we can keep brain cells alive longer, people with neurodegenerative diseases will have enhanced quality of life," Underwood declares. It's a goal personally important to him, and part of the reason he came to consider aequorin in the first place. The molecule came to his attention through an article linking the stings of jellyfish to the symptoms of multiple sclerosis, a disease of the central nervous system that afflicts his mother. The article got Underwood thinking about how jellyfish protect their nervous system, and led him to investigate the calcium connection.

"Look at any neurodegenerative disease—Alzheimer's, Parkinson's, stroke. They all have to do with calcium toxicity," he points out, adding that calcium does a lot of things in the body. It's related to the immune response, the thickness of the blood, control of muscular reactions. "As you get older, things get a little out of control. Our molecule seems to bring things back into control," Underwood asserts.

To Underwood, the pharmaceutical allure of aequorin is apparent. To the big pharmaceutical companies he'd like to partner with, it's just another early-stage compound. "They've got resources, and they want Phase III compounds. But ours is where it is," Underwood says, adding, "We see the value of aequorin, and we're willing to keep working with it until the value is recognized by others." To facilitate eventual partnering, Quincy is spinning its technology off into separate entities focused on different disease categories. The company is privately funded.—**Deborah Erickson**