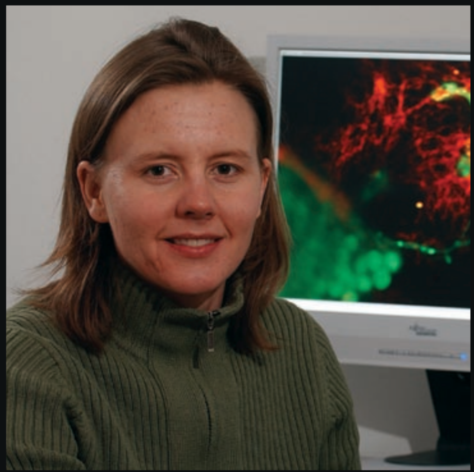
Revolutionary science fights brain diseases

By Nicole Branan



Just 33, Melissa Mahoney is making great strides toward growing healthy brain tissue to fight the effects of Parkinson's and other diseases. Behind her is a microscopic shot of the hydrogels she's developing to grow and multiply cells.

Imagine a world in which doctors keep spare body parts in the back of their operating rooms. While working on a patient, they could determine which body part was malfunctioning, retrieve a manufactured replacement out of the body shop, exchange the old part with the new one and — voilà — problem resolved.

While reality is still limping behind this dream, researchers working in the burgeoning field of tissue engineering are making strides toward filling such body shops with organs and tissues grown outside the body in the lab. As a matter of fact, CU-Boulder researchers are working on building one of the most complex of all body parts: the human brain.

Melissa Mahoney, assistant professor of chemical and biological engineering, and her team are developing techniques for growing patches of healthy brain tissue that could be transplanted into patients suffering from such nervous system diseases as Alzheimer's and Parkinson's.

Mahoney, who at 33 could easily be mistaken for a graduate student, laid the foundation for developing brain transplants as a graduate student at Cornell and postdoctoral researcher at Duke. Unlocking the biochemical signals that orchestrate growth and development in the brain was the first step on the path to brain tissue engineering.

"I had studied how certain molecules move inside the brain when they were released from a synthetic material," she says. "Then, during my postdoctoral research, I looked at what these molecules do to the brain cells." Now Mahoney applies these skills and knowledge to her work at CU.

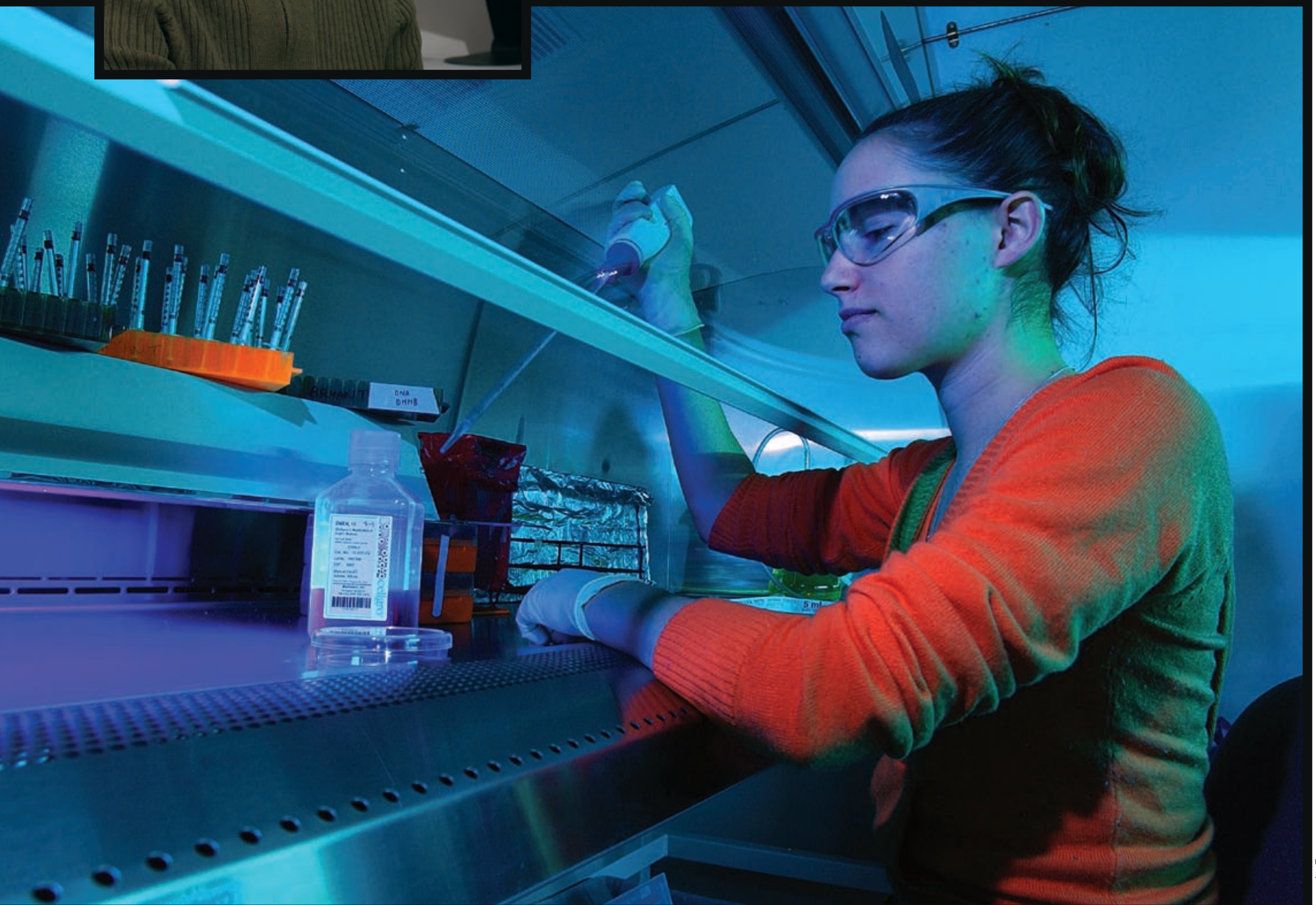
She says the molecular biotechnology initiative on campus brought her to CU two years ago. "I chose to come here because there is a very strong interdisciplinary group of people here interested in approaching difficult problems. It's nice that there is a big commitment at this university to do the kind of research I do. It's also exciting to be part of the new undergraduate bioengineering program we started at CU this year."

A long, promising path

Her time in CU's research labs is paying off, although it may be a dozen years or more before her team is ready to test human applications of its work.

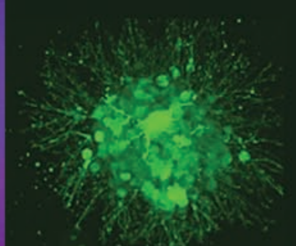
"One factor that has been limiting the widespread application of brain cell transplantation is the lack of suitable donor tissue," Mahoney explains.

Because she and her team grow large replacement parts from only a few healthy cells, their technique could create a nearly unlimited source of donor cells. Their transplants could also have a major advantage over drug treatments that merely treat symptoms, Mahoney



Casey A. Cass photos

Rachael Mooney, a grad student in chemical and biochemical engineering, works with Melissa Mahoney to develop hydrogels that promise to allow the growth of healthy brain cells.



Melissa Mahoney's work on tissue engineering led *Technology Review* magazine to name her one of the top 35 young innovators who have "the potential to profoundly impact the world."

explains. New brain parts could help cure many types of brain diseases because they replenish damaged cells regardless of what destroyed them.

Growing healthy brain cells

Diseases such as Alzheimer's and Parkinson's kill brain cells, gradually wiping out the patient's memory or causing the loss of motor control. Because these disorders primarily affect the elderly, they are on their way to overtaking cancer as one of the leading causes of death in our rapidly aging population. Finding treatments for those diseases is challenging, Mahoney says.

Take Parkinson's. "So far it's not possible to identify patients at high risk for developing Parkinson's before they develop severe clinical symptoms," Mahoney says. By that time patients have already lost about 70 percent of a vital layer of large nerve cells in the midbrain responsible for the functioning of the nervous system, she explains. Researchers who seek to repair the destroyed tissue at that stage are fighting a losing battle because the disease rapidly eats away at the remaining healthy tissue.

That's why Mahoney aims to restore damaged or diseased tissue by growing it from scratch. She and her team are designing special hydrogels, which are three-dimensional jellylike materials that – like the body – are made mostly of water. Then they place a few healthy young cells into the gel and let them grow and multiply. The gels anchor and protect the cells, providing a cocktail of nutrients the cells need to survive as well as surrounding them with biochemical signals that encourage them to grow into healthy brain cells.

"Our hydrogels provide an environment to control the growth of the cells – they act like a surrogate tissue," Mahoney explains. Because the gels are biocompatible they can be injected into the brain. If you zoomed in 10 million times they would look like a huge three-dimensional mesh. The cells can grow along this fence into an organized network that resembles the intricate tissue pattern in the brain.

"After a predetermined time the hydrogels dissolve and disappear to make room for more brain cells," Mahoney explains.

Researchers have been experimenting with brain cell transplants on rats and even a few humans for almost two decades. But these experiments got off to a rocky start.

Mark Saltzman, professor of chemical and biomedical engineering at Yale, explains that without the right cues young brain cells grown outside the body can fall off their career paths. When left to their own devices they can morph into body cells that don't belong in the brain, forming deadly tumors filled with jumbles of skin, hair and muscle cells.

"There is some evidence that cell transplantation in the nervous system can work in certain situations, but so far it just doesn't work well enough," Saltzman comments.

In contrast, the gels Mahoney and team are developing are filled with a mixture of biomolecules that send the right signals at the right time, making the cells feel at home and keeping their development on track.

"Using hydrogels is a great idea because it allows you to replicate some of the environment in the brain," Saltzman says. "Mahoney can control what the cells see and at what time they see it."

Testing on rats soon

Mahoney expects the first prototype gels to be ready sometime next year and plans to test them in rats with Parkinson's' disease together with her collaborators at CU's Health Sciences Center.

However, "using the materials in humans is still a long way off," Mahoney cautions. She says it will be 10 to 15 years before clinical studies might begin.

A big question mark is which types of human cells can be used to grow healthy brain tissue. Stem cells harvested from adult brains may be one possibility. These cells' genetic clocks could be turned back in time so that they are once again in their infant state and can, therefore, develop into different kinds of brain cells. It might also become possible to turn embryonic stem cells into brain cells in the future, Mahoney explains.

"The field of tissue engineering has become very popular within the engineering community," she says.

Saltzman notes that tissue-engineered skin and cartilage already exist, "but those are the easy applications," he says. "Mahoney is working on a much more challenging problem. It's going to take time but I think her work has the potential to become a successful medical treatment."

Nicole Branan is a freelance science writer based in Colorado Springs who often writes about neuroscience topics. Her articles have appeared in Scientific American Mind, Popular Science, Analytical Chemistry *and other magazines.*