Reversing aging

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Technology developed by researchers at The University of Texas at Austin could significantly reduce the time and cost to finding a cure for Alzheimer's disease and help answer one of the greatest biological questions: why do we age?

The research, led by Cockrell School of Engineering Associate Professor Adela Ben-Yakar and College of Natural Sciences Assistant Professor Jon Pierce-Shimomura, aims to prevent degeneration of the nervous system, which occurs through natural aging and diseases like Alzheimer's.

Degeneration has become a pervasive and growing problem in the last century due to new treatments that extend lifespan but cannot prevent neurological decline. This year alone, 5.4 million Americans are living with Alzheimer's, and every 69 seconds another American develops the disease, according to the Alzheimer's Association. The toll of the disease extends beyond those living with it. It impacts their families, caretakers and society, which will pay $183 billion this year to care for people with Alzheimer's.

"We can treat cancer when we diagnose it on time and maybe find solutions for heart problems, but when it comes to the brain we don't have many effective solutions," said Ben-Yakar, from the Department of Mechanical Engineering. "[Neurodegeneration] is a big problem for all of humanity. As an engineer, it excites me to find new ways of doing things, but the end result is what really motivates me and my colleague."

Ben-Yakar and Pierce-Shimomura were selected late last month to receive a competitive $3 million Transformative Research Projects Award from the National Institutes of Health (NIH) for their research.

The grants are part of a $143.8 million funding initiative provided by NIH this year to 79 researchers around the nation, including Biomedical Engineering Professor Aaron Baker, who received the New Innovator award.

"The awards are intended to catalyze giant leaps forward for any area of biomedical research, allowing investigators to go in entirely new directions," said James M. Anderson, director of the NIH Division of Program Coordination, Planning and Strategic Initiatives.

The answers could be in a worm

Many neurological diseases, like Alzheimer's, can be caused by the mysterious faulty function of neuronal proteins, which are still not understood in the scientific community.

Because of this, scientists don't know how neurological diseases develop, what causes their progression or how to stop it. Even the very reason for aging remains elusive.

"We do not know the real reason why we should age. Basically, the body's certain parts are shutting down slowly or abruptly," Ben-Yakar said. "So what things can interfere with this pathway, the natural or biological, to give us insight on how it works? Answering that will give us insight and, secondly, it will help us develop techniques to protect our neurons so that we can live longer and healthier lives."

A challenge to understanding aging and development of degenerative diseases is that new technology is needed to directly characterize how

neuronal proteins are distributed across the entire nervous system over time, and how specific neurons degenerate and are malformed with age. A second huge barrier to preventing or treating diseases like Alzheimer's disease is the amount of time it takes to identify drugs that work effectively. Typically, drugs are tested on mice — a process that is expensive and requires one to two years for mice to age while testing just a few dozen drugs at a time.

With the NIH grant, Ben-Yakar, Pierce-Shimomura and a team of students aim to eliminate both hurdles by developing an automated system that rapidly reduces the time and cost of drug testing. Instead of mice, the researchers will use a short-lived, 1 mm-long worm, known as C. elegans, to test the effectiveness of millions of drugs.

Despite having only 302 neurons compared to the billions of neurons in the human brain, the worms have a genetic makeup similar to humans – making them prime for testing drugs.

Researchers in Pierce-Shimomura's lab engineered a new strain of worm that develops Alzheimer's disease. Just as in humans, a subset of the worm's brain degenerates in "middle age" – which conveniently is only 5-days-old in the tiny worms. The dying neurons can be visualized easily through the transparent body. The researchers have recently discovered that candidate drugs for treating human Alzheimer's disease also prevent the death of neurons in their worm model. This result provides the basis to use their worm model to search for new drugs that may delay or prevent neurodegeneration in humans.

It will be up to Ben-Yakar to develop the novel optical techniques and microfluidic devices capable of determining — within a matter of seconds — which drugs are effective at repairing or regenerating neurons within the worms.

Ben-Yakar, whose engineering feats already include developing a precise laser nanosurgery for nerve regeneration studies in C. elegans and the first laser microscalpels capable of removing cancerous cells without damaging neighboring cells, said the worms will be genetically engineered to have color-coded neurons with florescent probes. Neurons in the worm that emit a strong florescent signal will indicate that the specific neurons in the worm are healthy and that the drug being tested is working.

"Using Adela's microfluidic system, we will automate the monitoring of the nervous system, enabling us to test how millions of candidate medicines might prevent or delay neurodegeneration," said Pierce-Shimomura, an assistant professor in the Section of Neurobiology. "A drug screen of this size has never been attempted."

Research is personal

For Ben-Yakar and Pierce-Shimomura, the research is as much about scientific discovery as it is a personal cause. Ben-Yakar's mother has Alzheimer's disease and one of Pierce-Shimomura's sons has Down syndrome, a condition that predisposes him to Alzheimer's.

"I know the disease and I live with it daily, so for me this research is very important," Ben-Yakar said.

"Most people with Down syndrome develop Alzheimer's between 40 and 60 years. When I look at my 10-year-old son, I feel the clock ticking," added Pierce-Shimomura.

Together, the two researchers are combining their backgrounds and disciplines to tackle a complex challenge with new approaches.

"We're constantly sharpening our research approach by collaborating,

sharing ideas and bringing our different areas of expertise to the table," Ben-Yakar said. "That's our advantage. If we can find new ways to accelerate finding of new treatments and help people, we'll have done our jobs."

Provided by University of Texas at Austin