Scientists develop new antibody for bowel disease

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Sadikshya Bhandari, a Ph.D. student in molecular and cell biology, 'passing cells,' or feeding them, to keep them from overgrowing. Credit: Taylor Hudak '18 (CLAS, ED)/UConn Photo

UConn molecular and cell biologist Michael Lynes and an international team of researchers have been awarded a patent for a novel antibody

therapeutic that may prove to be safer in the treatment of Inflammatory Bowel Disease (IBD) than other antibodies currently available.

Existing antibody treatments for IBD are ineffective in some IBD patients and pose a risk to the normal functioning of the immune system.

The new antibody, co-invented by the UConn researchers together with a team from Ghent University in Belgium, is designed to prevent the patient's immune system from attacking its own body and potentially causing irreversible damage.

More than 1.6 million Americans have IBD. Two of the most common forms of IBD are Crohn's disease and ulcerative colitis, chronic but treatable conditions that affect children and adults. One in 10 people with IBD are under 18, according to the Crohn's & Colitis Foundation.

More than a decade ago, Lynes, professor and head of the Department of Molecular and Cell Biology at UConn, and his research team discovered a novel and important role that a protein called metallothionein (MT) plays in influencing the body's immune function. The body produces MT when cells are under stress, and extended periods of stress cause MT to be released from the cells that produced it, Lynes says. MT is an unusual protein that holds onto chemicals in the body – both those that are beneficial, such as zinc and copper, and those that are harmful – such as cadmium and mercury.

While studying MT, Lynes and his research team noticed that MT released from cells could mimic some of the signals that the immune system uses as cues to tell cells to go to one place or another in the body. Under normal circumstances, immune cells use these signals to guide them to local infections or other tissue damage. When cells are stressed over prolonged periods, this can mean that there is persistent inflammation accompanied by damage to nearby healthy tissue.

About 50 million people, or 20 percent of the U.S. population, suffer from some form of autoimmune disease or chronic inflammation, according to the American Autoimmune Related Diseases Association. More than 80 autoimmune diseases have been identified, and autoimmune diseases are becoming increasingly prevalent, for reasons unknown, according to the National Institute of Environmental Health Sciences. While causes of autoimmune diseases also remain largely unknown, scientific consensus is that autoimmune diseases are probably triggered by a combination of genetic and environmental factors.

A team of Belgium doctors and scientists studying IBD had published a paper saying that their sickest patients were those whose bodies produced the most MT. The MT protein, which serves as a normal part of the cell's internal machinery inside the cell, was getting outside the cell and causing damage. That paper by Dr. Martine DeVos, Debby Laukens, and Lindsey Devisscher led to a collaboration with Lynes.

Since the protein serves an essential purpose, researchers can't shut it off all together; so they had to find a way to stop MT from prolonging inflammation and damaging healthy cells. Lynes and his team produced an antibody protein that basically attaches itself to MT when it is outside the cell and inactivates it – preventing the body from attacking its intestinal system. This approach dramatically reduced IBD in mouse models of the human disease.

"It's like we have created a partner for MT that binds it and hugs it and won't let it go," Lynes says.

The UConn team has been testing this treatment on mice, and is working on creating a form of the antibody that their collaborators can test in humans.

Since one form of stress on cells comes from environmental triggers,

Lynes and his team have received funding support from the National Institute of Environmental Health Sciences. He and his team have also received funding from UConn and from the state's quasi-public investment agency, Connecticut Innovations, to commercialize the anti-MT therapeutic. This includes $50,000 from UConn's SPARK Technology Commercialization Fund, and $500,000 from the Connecticut Bioscience Innovation Fund managed by Connecticut Innovations. He has also worked with the External Advisory Board and received funding for the project from Yale University's Program in Innovative Therapeutics for Connecticut's Health (PITCH).

"This is a prime example of cutting-edge research from a UConn lab being translated into a potentially life-changing treatment for patients," says Jeff Seemann, vice president for research at UConn and UConn Health. "The exciting research being conducted by internationally recognized faculty at UConn is not only important for the scientific community, but also for our citizens and our state's economy."

Lynes' research is significant, because while there is a great deal of research being done to try to keep autoimmune diseases at bay, his work seeks to learn more about the causes. Autoimmune diseases are increasing in both industrialized and developing countries, so his work has strong public health and commercial potential.

Meanwhile, Lynes is also working with Ciencia Inc., an East Hartford-based biotech company, to develop a test that could measure 1,000 different kinds of molecules in a drop of blood to find patterns of molecular biomarkers that can serve as red flags for the early onset of autoimmune disease.

"We are excited about the opportunity presented by Dr. Lynes' innovative work," says Arturo Pilar, president of Ciencia. "UConn has been a great partner, and university support for this effort has been

critical to the substantial progress made to develop a commercial product."

Early detection can mean that treatment can begin earlier in the disease, thus improving people's chance for better health.

"It appears this has the potential to identify someone's propensity to develop an autoimmune disease, and to enable treatments that are more effective," Lynes says.

Often, by the time people have symptoms of autoimmune disease that brings them to their doctor, irreparable damage has been done to their bodies. Developing these biomarkers won't cure the disease, he adds, but will allow for medical intervention early, minimizing the damage.

Provided by University of Connecticut