Currently there are no good treatments for scleroderma and no cure,” says Dinesh Khanna, M.D., M.S., the Marvin and Betty Danto Research Professor of Internal Medicine and director of the U-M Scleroderma Program. “But as a clinician, the promise of this research makes me very hopeful. If successful, it could mean a huge improvement in the quality of life and function for patients here at U-M and around the world.”

The potential breakthrough originated in the lab of Rick Neubig, M.D., Ph.D., professor of pharmacology and associate professor of internal medicine in the U-M Medical School.

Neubig heads the U-M Center for the Discovery of New Medicines, whose mission is to support the translation of early research toward patient use — a gray area where funding is scarce — and fully leverage the technical capabilities and intellectual resources at the university in service of discovering the therapies of tomorrow.

“Currently there are no good treatments for scleroderma and no cure,” says Dinesh Khanna, M.D., M.S.
“Most of the ways researchers have tried to treat scleroderma revolve around blocking the initial inflammation,” says Neubig. “But just cutting off the inflammation does not stop the progression of the associated fibrosis. Our compounds target a genetic switch that controls the formation of myofibroblasts — which are a critical cell that produces too much collagen and leads to the thickening of the skin and damage to other organs.”

The agents were discovered during high-throughput screening of compounds related to cancer treatment, and then optimized in the laboratory of Scott Larsen, Ph.D., research professor of medicinal chemistry and head of the U-M Vahlteich Medicinal Chemistry Core.

“The genetic switch that controls the fibrosis process for scleroderma is one that we’ve been studying in my lab for about 10 years,” Neubig adds. “But we only recently discovered new compounds that have shown initial success in blocking that switch. We have begun testing those compounds in fibroblasts from scleroderma patients, and are very enthusiastic about their potential to treat and possibly to reverse scleroderma based on the results we’ve seen so far.”

The next steps, says Neubig, will be to expand testing in patient cells, continue to improve and refine the compounds, and demonstrate beneficial effects in rodent models.

“Showing that they really work in vivo is a critical next step toward one day translating it for use in human patients,” he says.

Other conditions, like idiopathic pulmonary fibrosis and Crohn’s disease, also have the potential to be slowed or stopped by this approach, Neubig adds.

David Fox, M.D., who heads U-M’s Division of Rheumatology, agrees that the initial efforts are promising, but cautions that it could take several years before continued success in the laboratory might translate into clinical trials.

Given the difficult environment for federal research funding, the division is seeking philanthropic support from the scleroderma community to accelerate the completion of the laboratory research and, hopefully, provide benefit to patients sooner.

“We need to expand the cell culture studies, greatly expand the research in animal models, including looking at the ability of these compounds to target fibrosis in the lungs — the most deadly aspect of the disease — and also refine the delivery method to ensure it will be well-tolerated,” Fox says.

“A few years may sound like a long time,” he adds, “but when you’re talking about something that has the potential to dramatically improve the quality of life for hundreds of thousands of patients, it’s important to get the science right.”

The University of Michigan has filed for patent protection for the discovery and is currently looking for a licensing partner to help bring it to market.

Support the research: victors.us/SclerodermaHope