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New indicator found for rapidly progressing form of deadly lung disease

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A diagnosis of idiopathic pulmonary fibrosis is not much better than a death sentence, given a survival rate averaging 4 to 6 years as the disease robs its victim of the ability to breathe.

But researchers at the University of Michigan have discovered a receptor in the immune system that may serve as a marker for a rapidly progressing form of the disease, which causes the body to produce excess fibrous tissue in the lungs.

More than just signaling which patients have the more aggressive form of IPF – a disease that claims about as many lives each year as breast cancer – the researchers hope that targeting the TLR9 receptor may lead to new treatments that could slow or stop the illness' progression. The findings were published in the Nov. 10 issue of *Science Translational Medicine*.

"This finding has the potential to allow physicians caring for IPF patients to better determine the natural history of disease in individual patients, which could markedly facilitate decision making for the patient and their doctors," says pulmonologist Fernando J. Martinez, M.D., M.S., a professor of internal medicine at the University of Michigan Medical School and one of the study's two senior authors. "Moreover, it opens the potential for unique therapeutic approaches."

There is no known cause, cure, or FDA-approved treatment for IPF, and it remains virtually unknown to the general public, even though it is

several times more common than cystic fibrosis and Lou Gehrig's Disease (or ALS), according to the Coalition for Pulmonary Fibrosis. Moreover, IPF only receives a fraction of the funding of those higher profile conditions.

The U-M led research, which drew on expertise from the Departments of Pathology, Internal Medicine and Radiology, found that TLR9, which stands for Toll-like receptor number 9, causes an increase in the growth of fibrotic tissue in the lungs when it recognizes a particular type of DNA frequently found in bacteria and viruses. Higher amounts of TLR9 were found in patients with rapidly progressing IPF than those with slowly progressing IPF.

The researchers also peered into the workings of IPF by transplanting the disease from humans into mice. Those experiments showed a greater fibrotic response to the TLR9-activating DNA using lung cells from patients with rapidly progressing IPF than with cells from people with slowly progressing IPF.

For more than two decades, the National Institutes of Health has funded the U-M group's investigation into the biological basis of IPF as well as novel ways to diagnose and treat patients who suffer from the devastating disorder. U-M's scientists and doctors study human cells to better understand how they are involved in the progressive scarring of the lungs. In addition, clinical testing is used to help better predict the stage of disease and the rate of progression in advising patients for therapy.

"The approach taken by our group really highlights the advantages of translational research in a complex human disease and shows the bench-to-bedside model is really a two-way street," notes Cory M. Hogaboam, Ph.D., a professor of pathology at U-M and the study's other senior investigator.

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