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Math model designed to replace invasive kidney biopsy for lupus patients

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Mathematics might be able to reduce the need for invasive biopsies in patients suffering kidney damage related to the autoimmune disease lupus.

In a new study, researchers developed a math model that can predict the progression from nephritis – kidney inflammation – to interstitial fibrosis, scarring in the kidney that current treatments cannot reverse. A kidney biopsy is the only existing way to reach a definitive diagnosis of the damage and its extent.

The model could also be used to monitor the effectiveness of experimental treatments for inflammation and fibrosis.

This fibrosis can follow development of lupus nephritis, which occurs in about 60 percent of lupus patients, according to the National Institutes of Health. Inflammation is linked to the most common type of lupus, called systemic lupus erythematosus. The cause of lupus is unknown and it cannot be cured.

The research is published this week in the online early edition of *Proceedings of the National Academy of Sciences*.

The math model comprises a series of equations that account for the complex inflammatory process leading from nephritis to fibrosis in damaged kidneys. As designed, the model can detect the extent of kidney damage and predict how inflammatory processes will react to

different therapies.

"The most important use of this model will be improving the design of clinical trials for new medications to treat the kidneys before they develop fibrosis," said lead author Avner Friedman, a Distinguished University Professor in The Ohio State University's Department of Mathematics. "Establishing a dose of an experimental therapy is the most difficult part of testing new drugs. The model could give a starting point for an effective dose."

Better management of kidney damage in lupus is an urgent medical need because patients with moderate or severe fibrosis are more likely to develop chronic or end-stage kidney disease, said Brad Rovin, professor and director of the division of nephrology at Ohio State's Wexner Medical Center and a co-author of the paper.

"If a kidney is already damaged, we can't expect to go back in frequently to extract more tissue for multiple biopsies," Rovin said.

Modeling by mathematicians with expertise in biomedical processes has become increasingly important in the health sciences. The modeling reduces the need for guesswork and time-consuming animal testing traditionally required as researchers pursue prevention, diagnosis and treatment of complex diseases. And in this case, math modeling would replace an invasive diagnostic test.

Lupus is an autoimmune disorder, meaning the immune system attacks healthy cells and tissue in the body. Lupus commonly affects the kidneys, where immune cells accumulate in the organ's filtering units. This triggers an out-of-control inflammatory process that eventually leads to scarring and degradation of structures called tubules, which collect filtered fluid and are involved in the production of urine.

Further validation and refinement of the model is required, said Friedman, also founding director of the Mathematical Biosciences Institute (MBI) at Ohio State. But in this study, a comparison with human patient data showed that levels of inflammatory proteins in the urine of patients with mild, moderate or severe fibrosis matched levels predicted by the model.

The model also allows scientists to simulate the scarring injury and detect how the damage would respond to the therapies that target specific pathways to disease – either the inflammatory process or the scarring itself. By identifying vulnerabilities in the process from inflammation to scarring, the model could even point to the cells and proteins that would be the most promising treatment targets, Friedman said.

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