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Rogue receptor opens door for rare kidney disease

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Effects of a particularly devastating human kidney disease may be blunted by making a certain cellular protein receptor much less receptive, according to new research by scientists from North Carolina State University and a number of French universities and hospitals.

The findings take a major step toward suggesting a beneficial treatment for rapidly progressive glomerulonephritis (RPGN), a rare but debilitating kidney disease that causes renal failure and death in humans.

In a paper published online in Nature Medicine, the researchers show that blocking the ability of the epidermal growth factor (EGF) receptor – an important component in wound healing – to bind with certain molecules in the kidneys of mice can eliminate the harmful effects of a mimic version of RPGN.

EGF receptors act like important keyholes on a cell's surface, says Dr. David Threadgill, professor and head of NC State's Department of Genetics and a co-author of the paper. Certain keys, or in this case molecules, can fit with the receptor and "open the door" to a cascade of cellular processes leading to inflammation, which can be good when your body needs to heal a wound or a cut. It's bad, however, when the inflammation runs amok, as when RPGN takes hold.

How important are EGF receptors in RPGN? When EGF receptors were taken out of the equation – through special mice from Threadgill's lab that were genetically engineered without EGF receptors – the disease

was unable to take hold and degenerate kidney tissues.

The study also showed that certain drugs that inhibit EGF receptors – think of them as pieces of gum in the keyholes – not only prevented mouse kidneys from degrading but also reversed the harmful effects four days after mice were exposed to the RPGN mimic.

"EGF receptors are essential components for life, but are implicated in not only RPGN but also a number of cancers like colon cancer and breast cancer," Threadgill says. "They must be tightly regulated. If we can inhibit these receptors for short periods of time, we may be able to stop out-of-control cell proliferation and inflammation and thus prevent or treat certain cancers or diseases."

More information: "The Epidermal Growth Factor Receptor Promotes Glomerular Injury and Renal Failure in Rapidly Progressive Crescentic Glomerulonephritis; the Identification of Possible Therapy" Martin Flamant, et al. *Nature Medicine*, Online Sept. 25, 2011.

Provided by North Carolina State University

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