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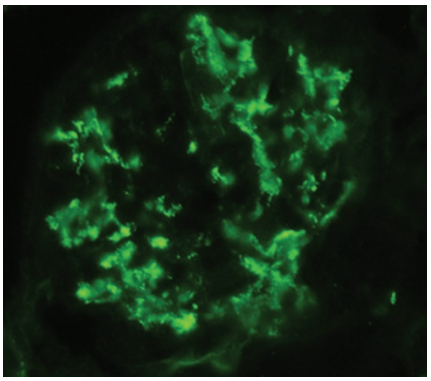
GLOMERULONEPHRITIS

Noninvasive method to monitor disease activity in lupus nephritis

A new study has shown that an MRI-based approach to detect C3 deposits in the kidneys can be used to noninvasively monitor disease activity in a mouse model of lupus nephritis.

Complement cascade proteins and their proteolytically generated fragments are known to be involved in renal injury. Biopsy samples are routinely stained for C3 deposits but obtaining them can cause complications and they only represent a small proportion of the kidney, whereas MRI permits the noninvasive evaluation of both kidneys in their entirety. "We used quantitative immunofluorescence to verify that C3 deposition is a useful biomarker of disease activity in the MRL/lpr mouse model of lupus nephritis," says researcher Joshua Thurman. Progression of renal dysfunction is age-dependent in MRL/lpr mice, and C3b/iC3b deposition was found to increase with age. By contrast, the abundance of the C3d fragment initially increased, but then declined in the terminal stages of the disease.



C3 deposition in the glomerulus of an MRL/lpr mouse. Image courtesy of S. A. Sargsyan, University of Colorado Denver School of Medicine, Aurora, CO, USA.

Disease progression was characterized by increasing C3 fragment deposition in the glomeruli of MRL/lpr mice, but not in the tubulointerstitium where deposition remained largely unchanged over time.

A contrast agent based on nanoparticles conjugated to a chimeric molecule that targets deposited C3 fragments was injected into MRL/lpr and control mice at 12, 16, 20 and 24 weeks of age. MRI was carried out before and 48 h after each injection. The magnitude of the decrease in T2 relaxation times after injection (the 'negative enhancement') increased as the MRL/lpr mice aged, indicating that more of the nanoparticles bound within the diseased kidneys. Therefore, MRI contrast agents targeted to C3 fragments might be useful for monitoring disease activity in glomerulonephritis.

"Although many safety and manufacturing issues need to be addressed before we can test this method in human patients, we are optimistic that this method can improve the care of patients with chronic inflammatory disease of the kidneys," says Thurman.

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Original article Sargsyan, S. A. *et al.* Detection of glomerular complement C3 fragments by magnetic resonance imaging in murine lupus nephritis. *Kidney Int.* doi:10.1038/ki.2011.332