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GLOMERULAR DISEASE

Role of tonsillar B cells in IgAN

> APRIL expression in tonsillar germinal centres was associated with increased proteinuria and with response to tonsillectomy [in patients with IgAN]

In Japan, patients with IgA nephropathy (IgAN) frequently undergo tonsillectomy, which has been associated with a decrease in serum IgA levels and an improvement in clinical outcomes. However, the rationale for this treatment is unclear. Now, researcher Yusuke Suzuki and colleagues report that overexpression of A proliferation-inducing ligand (APRIL) by tonsillar germinal centre B cells might have a key role in the pathogenesis of this disease.

Previous studies have shown that increased serum levels of APRIL are associated with worse prognosis in patients with IgAN, and have also suggested a role of Toll-like receptor 9 (TLR9) in the development of this disease. In their recent study, Suzuki and colleagues found that expression of APRIL was increased, and correlated with increased expression of TLR9, in the tonsillar germinal centres of patients with IgAN compared with those of patients with chronic tonsillitis. In addition, TLR9 stimulation induced APRIL expression on tonsillar germinal centre B cells from patients with tonsillitis.

In tonsillar germinal centres from patients with IgAN, antigen-experienced B cells with a switched IgG or IgA B-cell receptor expressed both the common cleavable form of APRIL and an uncleavable membrane-bound form (APRIL-δ/ζ). Moreover, APRIL expression in tonsillar germinal centres was associated with increased proteinuria and with response to tonsillectomy in these patients — those with the highest levels of tonsillar APRIL expression experienced the greatest decreases in proteinuria and serum levels of galactose-deficient IgA following the surgery.

"Our study shows that overexpression of APRIL on tonsillar germinal centre B cells is a key event in the pathogenesis of IgAN," says Suzuki. "Moreover, we identified two novel mechanisms of APRIL overexpression on these cells: genetic variants (APRIL-δ/ζ) and APRIL induction via the TLR9 signalling pathway. The latter mechanism might answer the long-standing clinical question of why mucosal infection in the upper respiratory tract exacerbates IgAN."

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ORIGINAL ARTICLE Muto, M. *et al.* Toll-like receptor 9 simulation induces aberrant expression of a proliferation-inducing ligand by tonsillar germinal center B cells in IgA nephropathy. *J. Am. Soc. Nephrol.* http://dx.doi.org/10.1681/ASN.2016050496 (2016)