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VISTA reduces IL-9-dependent fibrosis in antibody-mediated glomerulonephritis

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Objectives: V-domain Ig suppressor of T cell activation (VISTA), constitutively expressed in kidney-resident macrophages, participates in the repair process from ischemic renal injury. However, its role in antibody-mediated glomerulonephritis remains unresolved.

Methods: C57BL/6 wild-type (WT) and *Vsir* (encoding VISTA)–knockout mice were treated with nephrotoxic serum to induced antibody-mediated glomerulonephritis. Cytokine and fibrosis profiles were compared between WT and *Vsir*^{-/-} mice.

Results: During the glomerular injury, VISTA was primarily expressed in kidney-resident macrophages and less in kidney-infiltrating macrophages. In the early phase (i.e., day 8), *Vsir*^{-/-} mice harbored higher renal T-cell infiltration and interleukin (IL)-9 levels than WT mice, and this immunological milieu in *Vsir*^{-/-} mice resulted in azotemia and proteinuria. Fibrotic materials accumulated in the tubulointerstitium of *Vsir*^{-/-} mice more than WT mice, and this trend remained consistent in the late phase of glomerulonephritis (i.e., day 36).

Conclusions: VISTA in the kidney-resident macrophages reduces immunological milieu of antibody-mediated glomerulonephritis via suppression of T-cell infiltration and IL-9, which ultimately limits tubulointerstitial fibrosis.

Figure 1. Azotemia and proteinuria in GN-induced *Vsir*^{-/-} mice

