Immune dysregulation in immunoglobulin G4–related disease

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Abstract

(IgG4-RD) is an immune-mediated fibrotic disorder characterized by severe resolution of inflammation and dysregulation of wound healing. IgG4-RD has been considered a unique disease since 2003, and significant progress has been achieved in the understanding of its essential features. The central role of B cells in IgG4-RD has been demonstrated by the robust clinical responsiveness of IgG4-RD to B cell depletion and the identification of multiple self-antigens that promote B cell expansion. Studies have increasingly revealed critical roles of these B cells and T cells in the pathogenesis of IgG4-RD, and we and other authors further identified $CD4^+$ cytotoxic T lymphocytes as the main tissue-infiltrating $CD4^+$ T cell subset in IgG4-RD tissues. Additionally, T follicular helper cell subsets that play a role in IgG4 isotype switching have been identified. In this review, we discuss research on IgG4-RD and the roles of B cell and T cell subsets, as well as the functions of $CD4^+$ cytotoxic T cells in IgG4-RD pathogenesis. We highlight our findings from ongoing research using single-cell analysis of infiltrating $CD4^+$ cytotoxic T cells, $CD4^+$ follicular helper T cells, and infiltrating B cells in IgG4-RD and propose a model for the pathogenesis of IgG4-RD.