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Title: Peripheral helper-T-cell-derived CXCL13 is a crucial pathogenic factor in idiopathic multicentric Castleman disease

Abstract:

Castleman disease (CD) is a rare lymphoproliferative disorder. Among subtypes of CD, idiopathic multicentric CD-not otherwise specified (iMCD-NOS) has a poor prognosis and its pathogenesis is largely unknown. Here we present a xenotransplantation model of iMCD-NOS pathogenesis. Immunodeficient mice, transplanted with lymph node (LN) cells from iMCD-NOS patients, develop iMCD-like lethal inflammation, while mice transplanted with LN cells from non-iMCD patients without inflammation serve as negative control. Grafts depleted of human CD3+ T cells fail to induce inflammation in vivo. Upon engraftment, peripheral helper T (Tph) cells expand and levels of human CXCL13 substantially increase in the sera of mice. A neutralizing antibody against human CXCL13 blocks development of inflammation and improves survival in the recipient mice. Our study thus indicates that Tph cells, producing CXCL13 play a critical role in the pathogenesis of iMCD-NOS, and establishes iMCD-NOS as an immunoregulatory disorder.