Pathogenic leukocytosis and their susceptibility QTLs for vasculitis and crescentic glomerulonephritis in a model of SCG/Kj mice

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Introduction.—The spontaneous crescentic glomerulonephritis-forming/Kinjohe (SCG/Kj) mouse, a model of human crescentic glomerulonephritis (CgGN) and systemic vasculitis, is characterized by the production of MPO-ANCA and marked leukocytosis. This study was done to identify the specific population(s) of leukocytes associated with CgGN, and their susceptibility loci on SCG/Kj genome.

Methods.—Four hundred and twenty female (C57BL/6 (B6) × SCG/Kj) F2 intercross mice were subjected to serial flow cytometry examination of the peripheral blood (PB) and serum titer of autoantibodies including MPO-ANCA. Kidney granulocytes and monocytes were histopathologically examined with anti-Gr-1 and anti-F4/80 antibodies. Linkage analyses were done with 102 polymorphic microsatellite markers.

Results.—Correlation studies revealed that increase of the Gr-1+granulocyte, F4/80+ macrophages/monocytes, CD3+CD4+CD8+ T cells, and dendritic cells (DCs) in peripheral blood were significantly associated with GN, crescent formation, and renal vasculitis. In kidney sections, F4/80low cells were observed in crescent, while F4/80high cells were correlated with peripheral blood F4/80+ cell numbers. Numbers of but not with interstitial F4/80+ cell numbers.

Discussion.—Derived from SCG/Kj and inherited in a recessive manner.

but QTL on chromosome 17 only affected granulocytes. These QTLs localized to chromosome 17. QTLs on chromosome 1 affected DCs, granulocytes and F4/80+ cells, while QTLs on chromosome 1 affected DCs, granulocytes and F4/80+ cells.

References


Anti TNF-α drug inhibits initial process of vasculitis in animal model of Kawasaki disease

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Introduction.—Kawasaki disease (KD) is one of the vasculitis syndrome in childhood. Recently, anti TNF-α drugs are administered for some KD patients who are resistant to IVIG therapy. Previously we revealed histologically that TNF-α drug could inhibit the development of
of experimental arteritis, however inhibitory mechanism against arteritis has been still unclear. The present study aimed to elucidate the effect of TNF-α drug on the process of development of arteritis.

**Methods.**—Candida albicans Water-Soluble Fraction (CAWS) was used as inocula. Mice were injected CAWS for five consecutive days. They were sacrificed on the 6, 12, 24th hour and 2, 5, 8, 11, 14, 28th day after injection of CAWS. Etanercept (ETA) was used as anti-TNF-α drug. ETA (20 mg/kg) was administered subcutaneously twice weekly, total 8 times.

**Results.**—In control (no treatment) group, endoarteritis was observed in mice which were sacrificed on 6th hour, 2nd day. After 2nd day, inflammation of adventitia was observed in addition to endoarteritis. Panarteritis was observed in mice, which were sacrificed on 11, 14, 28th day. On the other hand, no endoarteritis was observed until 11th day after inoculation in ETA Group. And the size of vasculitis observed on 28th day was smaller than that of control.

**Discussion.**—Anti TNF-α drug could inhibit the development of vasculitis by control of endoarteritis. It is known that TNF-α directly and indirectly promotes adhesion between endothelial cells and inflammatory cells, especially neutrophils. These findings support our present results. However, our study were unable to clarify whether the involvement of TNF-α was limited to just the onset and progression of endoarteritis, or extends even to the process of establishment of panvasculitis following endoarteritis.

**Conclusion.**—It is suggested that TNF-α plays an important role in initial process of development of vasculitis. We declare no potential conflicts of interest.

**Further readings**

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**P17**
**The role of quantitative trait loci (QTL) in the pathogenesis of experimental autoimmune vasculitis (EAV)**

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**Introduction.**—The genetic susceptibility to anti-neutrophil cytoplasm antibody (ANCA) associated vasculitis is incompletely understood. We have recently discovered that the Wistar Kyoto (WKY) rat is susceptible to experimental ANCA associated vasculitis (EAV), but Lewis (LEW) rats are resistant. We have generated congenic rat strains to dissect out the role of selective quantitative trait loci (QTL) in EAV.

**Methods.**—Rats were immunised with human myeloperoxidase (MPO) in adjuvant to induce disease. Control rats were immunised with human serum albumin (HSA) in adjuvant. Disease progression was assessed by measuring proteinuria, haematuria, serum ANCA titre and by histology. Double congenic WKY rats with introgression of QTL from LEW chromosomes 13 and 16 were used.

**Results.**—WKY rats developed proteinuria (figure 1), haematuria (+++ or ++ through weeks 3–8) and glomerular abnormalities (7.1% of glomeruli abnormal at week 8 in MPO immunised animals versus 0.3% in HSA immunised animals; P < 0.05). Double congenic WKY rats, introgressed with loci from the Lewis strain, did not develop proteinuria or haematuria and were protected from glomerular injury. Both WKY and double congenic strains developed equivalent ANCA titres.

**Figure 1**

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**P18**
**The protective role of NADPH oxidase in ANCA-induced vasculitis**

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**Introduction.**—ANCA-activated neutrophils and monocytes cause necrotizing crescentic glomerulonephritis (NCGN). In vitro studies suggest