Involvement of Proline-rich tyrosine kinase 2 (Pyk2) in Kawasaki disease-like murine vasculitis


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Introduction: Although the pathogenesis of Kawasaki disease (KD) is still unclear, some studies suggest the involvement of the innate immune to the vasculitis. Pattern recognition receptor (PRR) plays an important role in the immune system. Mice of vasculitis induced with Candida albicans water-soluble fraction (CAWS) is widely used as an established model of KD, and CAWS is already known as a ligand of dectin-2 which is one of PRR. Furthermore, proline-rich tyrosine kinase (Pyk2) activates NF-kB in macrophage via the PRRs signaling. Hence, we examined whether Pyk2 involves in the onset of KD-like vasculitis by CAWS.

Methods: Pyk2-knock out (Pyk2-KO) and wild-type C57BL/6 mice (WT) were administered CAWS to induce KD-like vasculitis. At 1 and 28 days after CAWS injection, mice were sacrificed. We determined immunohistochemically the onset of experimental vasculitis. NF-kB activation was evaluated by quantifying nuclear translocation of NF-kB p65 subunit in peritoneal macrophages isolated from mice in vitro. Serum cytokines and chemokines across each mice were compared by cytokine array.

Results: Pyk2-KO mice didn’t show any apparent defective phenotype. While marked inflammation was observed in the aortic root including coronary bifurcation of CAWS-treated WT mice on day 28, such vasculitis was barely detected in CAWS-treated Pyk2-KO mice. On day1, it is before the onset of vasculitis, some cytokines/chemokines increased in WT mice and decreased in Pyk2-KO mice. CAWS-induced NF-kB activation was also less observed in macrophages from Pyk2-KO mice.

Conclusions: It is possible that Pyk2 is involved in the pathogenesis of KD through producing cytokines/chemokines related with migration of inflammatory cells. Pyk2 may have therapeutic potential for the treatment of KD.