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Possible implication of Proline-rich tyrosine kinase 2 (Pyk2) in the pathogenesis od Kawasaki disease.

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Introduction: Kawasaki disease (KD) is a pediatric vasculitis. Although its etiology remains elusive, a line of recent experimental studies implies that some kind(s) of infectious stimuli are implicate in the vasculitis through uncontrolled innate immune systems such as pattern recognition receptor (PPR)-mediated inflammatory signaling. Among macromolecules regarding in the PRRs-dependent signaling pathways, it has recently emerged that proline-rich protein tyrosine kinase (PYK2) is involved in the processes through NF-kB activation. Employing an established animal model for KD, thus, we investigated a possible relevance of Pyk2 in the pathogenesis of KD.
Methods: Pyk2-knock out (Pyk2-KO) and wild-type C57BL/6 mice (WT) were administered Candida albicans water-soluble fraction (CAWS) to induce KD-like vasculitis. Extension of the experimental vasculitis was immunohistochemically determined with anti-MPO antibody. CAWS-stimulated NF-kB activation was evaluated by quantifying nuclear translocation of NF-kB p65 subunit. In peritoneal macrophages isolated from PYK2-KO and wild-type mice in vitro.
Results: Pyk2-KO mice didn't show any apparent defective phenotype. While marked inflammation was observed in the aortic root of CAWS-treated WT mice, such vasculitis was barely detected in CAWS-treated Pyk2-KO mice. CAWS-induced NF-kB activation was also less observed in macrophages from Pyk2-KO mice.
Conclusions: These results indicate that Pyk2 play indispensable rules in the pathogenesis of KD. Pyk2 may be a potential therapeutic target for KD.