Significant role of cytokines and signaling pathway in rheumatoid arthritis, nasal polyposis and human airway smooth muscle cells

Surasakdi Wongratanacheewin

In this issue, there are 2 interesting papers related to the role of cytokines in pathogenesis of autoimmunity in rheumatoid arthritis (RA), and nasal polyposis (NP).The pathogenesis of RAis currently unclear although T, B cells and some macrophages are found to play role in articular inflammation.[1,2] This inflammation was documented to be one of the major factors in pathogenesis of RA. The proinflammatory cytokine such as TNF-α, produced from various cells such as macrophages, mononuclear cells, T-lymphocytes, and synovial membrane fibroblasts, could promotes the generation of osteoclasts that lead to bone destruction.Interleukin 32 (IL-32) is relative by new discovered cytokine and reported to be involved in development of autoimmune diseases.[3] It induces other pro-inflammatory cytokines such as TNF-α, IL-1, IL-6, IL-15, IL-17, and IL-18 and chemokines in human and rat cells. Recent study has demonstrated that IL-32 was involved in RA.[4] In this issue of APJAI, Ming Gui and colleagues[5] reported the significant higher levels of both mRNA and protein of IL-32 and TNF-α in peripheral blood mononuclear cells of 97 patients with RA compared with 36 patients with non-RA connective tissue diseases. The IL-32 expression was positively correlated with TNF-α, ESR, CRP, RF and DAS28 in patients with RA.

Another inflammatory disease reported in this issue is nasal polyposis (NP). The pathophysiology of NP is still unclear although accumulation of eosinophils, T cells, neutrophils, and plasma cells in the mucosa was reported. The Th2 and Th17 responses were found to associate with this disease. IL-6, a pro-inflammatory cytokine, activator of transcription 3 (STAT3) leading to Th17 differentiation may involve in pathogenesis of several diseases such as RA, Crohn's disease and asthma.[6-7] Wang et al.[8] from the first Affiliated Hospital of Chongqing Medical University in China, reported in this issue using immunohistochemistry and western blot analysis showed that significantly higher numbers of pSTAT3+ cells and pSTAT3 proteins level were detected in the NP patients compared to control and non-atopic groups. When IL-6,sIL-6R, and IL-17A levels were determined by ELISA, they were all significantly higher in NP. This result indicates that IL-6 pathway may play role in pathogenesis of NP in Chinese patients.

Another interesting paper in this issue reported by Kumasawaet al.,[9] from Nihon University School of Medicine, Japan. Cysteinyl leukotriene (LT) induces bronchoconstriction and airway inflammation whereas heparin-binding EGF-like growth factor (HB-EGF) is associated with remodeling in airway smooth muscle (ASM) cells in bronchial asthma. A disintegrin and metalloproteinase (ADAM) 12 is an enzyme implicated in the release of HB-EGF. They determined whether LTD4 involved in HB-EGF and ADAM12 expression and the regulatory mechanism in human ASM cells. By using real time PCR and western blot analysis, they demonstrated that p38 MAPK and ERK are capable of regulating LTD4-induced HB-EGF and ADAM12 expression in human ASM cells. Therefore the specific inhibitor of p38 MAPK and ERK may be a new alternative way for controlling airway remodeling and inflammation.

From Department of Microbiology and Melioidosis research center, Faculty of Medicine, Khon Kaen University, KhonKaen, Thailand.
E-mail: sura_wng@kku.ac.th

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