The new therapeutic strategy for autoimmune and chronic inflammatory disease based on the clinical results by IL-6 blocking therapy with a humanized anti IL-6 receptor antibody

○Kazuyuki Yoshizaki[1,2], Keisuke Hagihara[2], Teppei Nishikawa[1], Jian Song[1], Tetsuji Naka[3], Kazuhisa Sugimura[4]
(Health Care Center, Osaka University[1], Graduate School of Medicine, Osaka University[2], National Institute of Biomedical Innovation[3], Faculty of Engineering, Kagoshima University[4])

We have obtained remarkable effects by the IL-6 blocking therapy with a humanized anti-IL6 receptor antibody for Castleman's disease, rheumatoid arthritis (RA), juvenile idiopathic arthritis and Crohn's disease. These clinical results indicated that the hyperfunction of IL-6 might be a central pathogenic cause of chronic inflammatory diseases. Why did a single inhibition of IL-6 show the improvement of clinical symptoms and normalization of laboratory findings such as acute phase proteins, CRP and SAA, on inflammatory status in which a lot of cytokines, including TNF-α, IL-1 and Il-6, were activated.? To answer the question, the signal transduction mechanism of CRP and SAA by cytokine stimulation was analyzed. In result, IL-6 signal pathway especially STAT3 activation was essential, and TNF-α and IL-1 stimulation complimentarily contributed on the induction of CRP and SAA. This in vitro result proved the difference of clinical effects between TNF-α blockade and IL-6 blockade on RA therapy; CRP and SAA were decreased by TNF- α blocking, on the other hand IL-6 blocking showed not only reduction but normalization of CRP and SAA. Using these cytosine blocking therapies and in vitro analysis, the pathogenic causes of cytokines in chronic inflammatory status may be realized.

Furthermore, recently it is known that IL-6 is a regulatory molecule in induction of Th17 cells, an activator of autoimmune disease, and in suppression of Treg cells, a suppressor of autoimmune disease. Therefore, IL-6 blockage may be an adequate therapeutic way for both the onset and the late phases of autoimmune disease.
In this symposium I would like to discuss the clinical and pathogenic significance and the future usage of the IL-6 blocking therapy.