

Soluble CD163: A Novel Biomarker with Diagnostic and Therapeutic Implications in Autoimmune Diseases

To the Editor:

Macrophage activation and function are significantly linked with the pathogenesis of a variety of autoimmune diseases, such as rheumatic diseases including rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). However, the precise mechanisms involved in this correlation are still elusive. Noticeably, we recently read with great interest the article by Peng, *et al*¹ showing serum soluble CD163 (sCD163) levels, mainly secreted by monocyte/macrophage lineage, were significantly increased in the patients with polymyositis (PM) and dermatomyositis (DM) compared with healthy controls. Particularly, they highlighted the involvement of CD163+ macrophage infiltration in the muscle in the development of PM/DM. It is commonly suggested that PM/DM is correlated with the autoimmune disorders, and moreover elevated sCD163 expression and CD163+ macrophage (M2 macrophage) activation are also closely associated with some other autoimmune diseases.

CD163 is a member of the scavenger receptors in the membrane, which are exclusively expressed and can be shed from monocytes and macrophages to induce sCD163 in response to various pathological conditions. Functionally, patients with early RA had significantly higher plasma levels of sCD163 than after 9 months of treatment; these levels are associated with disease activity and predict radiographic progression². Conversely, plasma sCD163 levels decreased significantly after 3 months of treatment from the OPERA (optimized treatment algorithm in early rheumatoid arthritis) trial³, which correlated with the investigated disease activity markers. More importantly, the soluble form of CD163, sCD163, could be observed not only in plasma, but also in other body fluids such as cerebrospinal fluid (CSF) and synovial fluid (SF). In keeping with the local production of sCD163 in SF, increased proportion of CD163+ macrophages and decreased CD69+ lymphocyte numbers were observed in spondyloarthritis (SpA) synovium, which reflected the dual involvement of CD163+ macrophages in both SpA synovitis with global inflammation and impairment of T cell activation⁴.

CD163+ macrophages are involved in the inflammation of the skin in patients with SLE, in whom the number of CD163+ macrophages and the concentration of serum sCD163 are significantly increased in comparison with healthy control subjects⁵. The levels of plasma sCD163 are upregulated in the patients with multiple sclerosis (MS) compared with healthy controls⁶, a factor associated with decreased plasma proinflammatory cytokine levels such as interleukin (IL)-12 and IL-6. More recently, Stilund, *et al* showed that a high sCD163 CSF/serum ratio in patients with MS may reflect macrophage activation in MS lesions⁷. Further, sCD163 is identified as a marker of disease activity in adult-onset Still's disease, which is found to be correlated with ferritin expression in both the lymph node and tonsil⁸.

Taken together, these results elucidated that sCD163 levels are useful predictors in the development of diverse autoimmune diseases. Thus, the pharmacological and genetic intervention of sCD163 might provide a novel strategy in the diagnosis and treatment of autoimmune diseases.

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