脊椎關節炎的骨免疫學

Osteoimmunology in Spondyloarthritis (SpA)

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Spondyloarthritis (SpA) is a family of chronic arthritis diseases, and it comprises several subtypes, including ankylosing spondylitis (AS), reactive arthritis (ReA), psoriatic arthritis (PsA), inflammatory bowel disease (IBD)-related arthritis, and undifferentiated spondyloarthritis (USpA). AS, a prototype of SpA, is a chronic auto-inflammatory rheumatic disease with characteristics of sacroiliitis, inflammatory back pain with stiffness, peripheral arthritis, enthesitis and anterior uveitis. Abnormal bone remodeling with new bone formation such as syndesmophyte may result in "bamboo spine" with significant limitation of spinal motion in AS. Eventually, the disease can lead to heavy economical and mental burdens in patients, their families and the whole society. Osteoimmunology, an interdisciplinary research field, is focused on the understanding of crosstalk between the immune and bone systems to affect the bone remodeling process through the immuno-skeletal interface. It contained three major pathways: (1) receptor activator of nuclear factor-κB ligand (RANKL) pathway; (2) WNT pathway and (3) bone morphogenetic protein (BMP) pathways.

RANKL and osteoprotegerin (OPG) belong to the members of TNF-α superfamily. RANKL is a potent stimulator of bone resorption, while RANKL binding to RANK on osteoclast (OC) precursors, maturation and activation of OC is induced. OPG is the soluble decoy receptor of RANKL, which blocks the RANKL/ RANK interaction and inhibits the activation of OC. RANKL is mainly produced by OC and also the activated T cells, and OPG is predominantly secreted by osteoblast (OB). The imbalance of RANK、RANKL and OPG may induce osteoclastogenesis and osteolytic lesion. The Wingless (WNT)/*β*-catenin pathway stimulates bone formation by accelerating OB differentiation, blocking the differentiation of mesenchymal cells toward chondrocytes or adipocytes, inhibiting OB apoptosis and osteoclastogenesis. Dickkopf homolog-1 (Dkk-1), a soluble antagonist of WNT protein, has been considered to be a master regulator of bone remodeling in inflammatory arthritis. Dkk-1 not only suppresses OB differentiation but also decreases the expression of OPG, leading to increased osteoclastogenesis. Besides, inhibition of Dkk-1 stops the

bone destructive process in inflammatory arthritis and changes it to a new bone-forming pattern in the vicinity of heaviest inflammatory area. BMP, belonging to transforming growth factor superfamily, can induce a cascade of endochondral bone formation and participate in embryonic development, cell lineage determination and osteoblastic differentiation. BMPs are involved in the development of new bone formation and recombinant human BMPs were effective in inducing bone healing and enhancing spinal fusion. Therefore, we will introduce these pathways and elucidate the relationship between osteoimmunology and AS.