# 骨鬆症藥物治療之新進展

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Osteoporosis involves in an imbalance between bone formation and resorption, leading to net loss of bone mass, detriment of bone microarchitecture, and development of fractures. Activation of osteoclastogenesis is a key to bone resorption. An increase in receptor activator of nuclear factor kappa-B ligand (RANKL) expression has been shown to influence on the final pathway of the osteoclast cycle.

Denosumab, a human monoclonal antibody that specifically binds RANKL, blocks the binding of RANK to its ligand and significantly reduces bone resorption, increases bone density, and lowers the opportunity of fractures. It is administered as a subcutaneous injection every 6 months for the treatment of osteoporosis and regarded as one of the most potent of the antiresorptive agents on bone.

Recent studies have also demonstrated that wingless-type (Wnt) bone formation signaling pathway plays a major role in bone formation. The binding of Wnt proteins to the lipoprotein receptor-related protein (LRP)5/6-frizzled co-receptor on the cell membrane of osteoblasts leads to intracellular signaling cascades, and in turn regulating gene transcription that promotes osteoblastic bone formation. Wnt signaling pathway is negatively regulated by osteocyte-producing sclerostin and the Dickkopf (DKK1) protein secreted in bone; both act directly by binding to the coreceptors LRP5 and LRP6 and thereby inhibit the anabolic effect of Wnt pathway. The anti-sclerostin antibodies (romosozumab, blosozumab) have shown to increase bone mass by neutralizing the negative effects of sclerostin on the Wnt signaling pathway and subsequently enhancing osteoblastic bone formation. Parathyroid hormone PTH 1–34 (teriparatide), the only osteoanabolic agent for treating osteoporosis, also stimulates bone formation through inhibition of sclerostin, DKK1 and frizzled protein.

Other mechanism involving bone resorption includes cathepsin K. Cathepsin K is a protease expressed in osteoclasts that associated with osteoclast-mediated bone resorption. Cathepsin K degrades type 1 collagen in organic bone. Cathepsin K inhibitors (odanicatib) inhibit matrix dissolution, decrease bone resorption, and thus improve bone marrow density in postmenopausal women.

The potential role in treating osteoporosis by these newly developed biologics is promising and further combining these agents with conventional antiresortives may be needed in optimizing the management of osteoporosis.