

治療骨質疏鬆新標靶分子或生物標記

Novel therapeutic targets or biomarkers in the management of osteoporosis

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The human bone metabolism is a complex process involving many cytokines, hormones and growth factors. Novel proteins or factors implicated in bone turnover are ever-increasingly found, analyzed, and designed as potential therapeutic targets for osteoporosis treatment. Several of these proteins are introduced in this brief report.

Fibroblast growth factor (FGF)-23 is a protein responsible for phosphate homeostasis. It is secreted by osteocytes in response to elevated vitamin D and acts on the proximal tubule of the kidney, where it decreases the expression of sodium-phosphate cotransporter 2, resulting in phosphate diuresis and calcium loss. Polymorphism in *FGF23* gene leads to autosomal dominant hypophosphatemic rickets. Excessive FGF-23 production by tumors results in premature phosphaturic osteomalacia. SLE patients treated with cyclosporine A exhibited high level of FGF-23, which is partly responsible for low bone mass in these patients.

Cathepsin K is a lysosomal cysteine protease involved in bone resorption and remodeling, primarily expressed in osteoclasts, which is highly specific for kinins and can degrade elastin, collagen, as well as gelatin, resulting in bone resorption. A similar action is also working in the lung leading to the loss of elasticity and recoil in emphysema. Its inhibitor, odanacatib, shows great potential in restraining osteoporosis. Cathepsin K is degraded by Cathepsin S in a process called "controlled cathepsin cannibalism". Its production is enhanced by proinflammatory cytokines during or after tissue injury.

Dickkopf related protein 1 (DKK-1) is a ligand protein secreted in the circulation, involving in embryonic development and adult bone turnover. It inhibits the WNT signaling pathway that enhances transformation of preosteoblast to mature osteocyte. Elevated DKK-1 is associated with osteolytic bone lesions. A neutralizing body against DKK-1 can reverse androgen induced baldness. Whether it can also stop the bone losing process is a matter of debate.