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Opinion

Bone Diseases & Therapy

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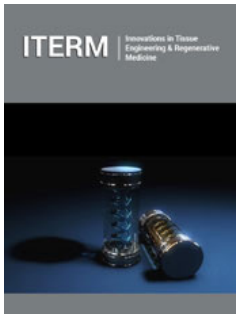

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Opinion

Osteoporosis (OP) is a common degenerative disease in the elderly, which is characterized by the loss of bone mass and the destruction of bone tissue structure. Bone has important functions in the human body, such as supporting the body, regulating metabolism, and hematopoiesis, and plays a vital role in the life activities of the whole organism [1]. Therefore, an imbalance in bone metabolism may lead to OP, which in turn increases the risk of fracture. According to the International Osteoporosis Foundation, more than 8.9 million people worldwide suffer a fracture due to OP each year, which makes research on OP disease essential. Currently, researchers are exploring the pathogenesis of OP and searching for more effective preventive and therapeutic targets. Therapy for OP has a broad prospect, and it is worthwhile to find ways to increase bone formation and maintain bone strength and to explore the functions of therapeutic targets in bone development and their regulatory mechanisms, which are expected to be potential new drug targets for improving OP disease. OP is one of the main factors affecting an older person's quality of life. In clinical terms, anti-osteoporosis medications typically consist of bone resorption inhibitors, including estrogens, calcitonin, and bisphosphonates, which promote bone mass recovery [2]. One of the novel medications for OP is denosumab, a humanized monoclonal antibody that inhibits RANKL and stops osteoclast development. OPG, a naturally occurring RANKL pseudo-receptor, is a gene medication used in the prevention and treatment of OP; it binds to RANKL to suppress osteoclast formation, slowing down bone mass loss and increasing bone mineral density. OPG increases bone mineral density and prevents bone breakdown in mice while they are weightless. OPG has been demonstrated to prevent osteolysis and preserve bone formation in mice while they are not moving. A Cysteine Protease, Tissue Proteinase K (Ctsk) inhibitors, such as Odanacatib (MK0822), and others, have a bone-protective effect. Both osteoblasts and osteoclasts are responsible for maintaining dynamic bone homeostasis and bone remodeling [3].

Osteoblasts and osteoclasts, a basic multicellular unit, rather than being a single activity, bone remodeling is a coordinated process mediated both geographically and temporally by all osteoblasts [4]. Bone marrow cells, immune cells, vascular endothelial cells, and osteoblasts all play a variety of roles in remodeling. New therapeutic approaches that target these osteoblasts and their interactions with one another should help to maintain bone homeostasis and make it easier to find new targets for drugs. A targeted drug is a pharmaceutical that acts at a particular therapeutic site, spreads throughout the body, and may affect other tissues and cells [5]. Furthermore, poor blood flow and the thick structure of bone tissue restrict the osteotropic effects of medications. Thankfully, ligand-based bone-targeted therapy began a new era in 1986 when Pierce first proposed the idea of "bone targeting". To decrease drug loss in the reticuloendothelial system and increase circulation time, a range of drug delivery vehicles, from micro- to nanoscale, as well as surface modification technologies, such as polyethylene

glycol modification (PEGylation, PEG), have been developed. Humans achieve bone-targeting effects by further conjugating these "protected" medications with bone-targeting ligands, which result in active site-mediated bone effects, larger concentrations in bone, longer sustained and localized release periods, and lower minimum effective doses. Nowadays, RANKL inhibitors, bisphosphonates, and anabolic drugs are examples of anti-resorptive drugs that have gained popularity in bone-targeted pharmacological therapy. Medications such as parathyroid hormone receptor type 1 (PTH1R) ligands and Sost inhibitors show remarkable efficacy in treating disorders characterized by abnormal bone remodeling [6]. The improvement in bone metrics indicates the restoration of normal bone remodeling, similar to that of anabolic drugs that slightly stimulate bone resorption or antiresorptive pharmaceuticals that limit bone creation (Sun et al. 2019). However, side effects such as osteonecrosis, rebound fractures, cardiovascular events, and osteosarcoma development make it difficult to treat bone diseases effectively over the long term. Therefore, more accurate treatment may result from improving these targets.

Besides, stem cell therapy is currently receiving a lot of attention. OP has a wide range of potential applications in recent years. Osteocytes, chondrocytes, myogenic cells, astrocytes, stromal cells, adipocytes, tendon and ligament fibroblasts, and chondrocytes are some of the cell types that bone marrow mesenchymal stromal cells can differentiate into [5]. Such as, Xiong et al. [7] discovered that ISLR negatively regulates osteogenic differentiation through the BMP-Smad signaling pathway [7]. Liu et al. [8] found that POLR2A blocks osteoclastic bone resorption and protects against osteoporosis by interacting with CREB1 [8], and Peng et al. [9] found that the lipolytic factor RCN2 was a novel gene for osteoporosis [9]. Hopefully, investigating the roles of therapeutic targets in which they regulate bone formation will reveal new therapeutic targets for the possible treatment of OP disorders.

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