Editorial

Novel Osteoporosis Therapeutic Targets Derived from Medical Biotechnology

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Osteoporosis is known as the most prevalent metabolic bone disease. Population aging and increasing life span are making osteoporosis one of the most challenging age-related diseases [1]. Based on reports in 2009, over 500 million people are struggling with this disease. Also, 1 in 5 men and 1 in 3 women over 50 years suffer from osteoporotic fractures during their lifetime. 1.5 million osteoporotic fractures are occurred annually in the United States and it cost the healthcare system in this country about $57 billion in 2018. The disease is caused by an imbalance in bone homeostasis, which is induced by bone formation not compensating for bone resorption. This process lowers the Bone Mineral Density (BMD) and makes bone susceptible to fracture [2,3].

The significant burden of osteoporosis can be decreased since the disease is treatable. Based on the mechanisms resulting in osteoporosis, two main conventional drug categories are used for the treatment of the disease including anti-resorptive agents and anabolic agents [2]. Conventional treatments consist of Selective Estrogen-Receptor Modulators (SERMs), bisphosphonates, parathyroid hormone analogs, and calcitonin. The need for more advanced therapies with fewer adverse effects arises from complications such as increasing risk of cardiovascular diseases, gastrointestinal problems, altering blood calcium levels, potential risks for women in estrogen-related therapies, *etc*. [4,5].

As mentioned previously, the imbalance of bone metabolism causes osteoporosis. In this dynamic complex process of metabolism which is known as bone remodeling, connection or disruption of each specific intra-cellular or inter-cellular link can cause or treat the disease [6]. Hence, this fact represents the remarkable role of medical biotechnology in osteoporosis treatment. Medical biotechnology as an upcoming main pillar of health-related science, has grown so fast in the field of treating disease as well as prevention and diagnosis using a variety of novel approaches [7]. In recent years, biotechnology has introduced some novel therapeutic targets to the medical world to provide more efficient and safe therapies followed by diminishing osteoporosis as a burdensome disease. Monoclonal RANK Ligand (RANKL) antibodies and monoclonal sclerostin antibodies including denosumab, romosozumab, and blosozumab as recently rendered treatments to medicine, have achieved better therapeutic outcomes than conventional treatments [2].

One of the main novel therapeutic targets is microRNA (miRNA)-based treatment. Modified nucleoside oligomers are the most common miRNA inhibitors used for new approaches. Since the clinical transformation of miRNA inhibitors is less difficult than lentivirus transfection, using them to affect the progress of osteoporosis is more feasible. Cathepsin K inhibitors which are involved in bone resorption in addition to remodeling, have been studied in many trials and are being investigated to find a promising one [8].

Another innovation is stem cell therapy which is performed with cell sources from Embryonic Stem Cells (ESCs), induced Pluripotent Stem Cells (iPSCs), and Adult Stem Cells (ASCs). Stem cell therapy provides tissue regeneration which in osteoporosis translates to bone formation. Inducing the growth and differentiation of osteoblasts alongside decreasing activity of osteoclasts via cellular crosstalk are the main roles of stem cell therapy [4]. The Wnt signaling pathway components are recently presented as one of the therapeutic targets. So many clinical trials are being conducted for each component to benefit from the bone mass-maintaining ability of these molecules [9]. The sphingosine-1-phosphate (S1P) signaling pathway and leucine zipper motif (APPL1) extracellular signal-regulated kinase 1/2 (ERK1/2) signaling pathway and the Bone Morphogenetic Protein (BMP) signaling pathway are other targets to point out that play roles in osteogenesis, conducting osteogenic differentiation of stem cells, and promoting angiogenesis [5]. A novel RANKL i-body nominated as ADR3 was introduced with features such as a high affinity for binding to human RANKL (hRANKL) and an ability to tolerate many different physical environments [3]. Also, integrins as cell-adhesion transmembrane molecules have improved postmenopausal women's BMD and made bone loss reversed [6]. Furthermore, in

recent years light has been shed on the bone-related roles of melatonin. Some of its important effects are bone biological rhythm regulatory effects, bone microenvironment modulation, and osteoporosis treatment [10].

Population aging is greatly increasing osteoporosis prevalence and burden thus promoting osteoporosis to become an immense concern for the healthcare system. Hence, researching more effective therapies with fewer side effects has become urgent. Although studies introduced innovative targets as effective therapies, more investigations such as high-quality clinical trials are necessary to provide more evidence proving their efficiency. Despite all the mentioned conventional treatments, innovative targets, and upcoming therapeutic strategies, studying and developing molecular targets with more accurate and detailed mechanisms is indispensable. Undoubtedly, cooperation between basic sciences, especially neuroscience and biotechnology, and internal medicine can create a brighter future for the treatment of endocrine diseases [11-14].

Keywords: Antibodies, Bone density, Cathepsin K, MicroRNAs, Monoclonal, Osteogenesis, RANK ligand, Stem cells, Wnt signaling pathway

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