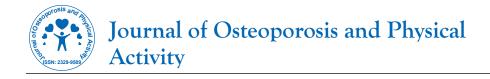# Regulation of MicroRNAs in Bone Remodeling and Potential Applications as Osteoporosis Biomarkers

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DESCRIPTION

MicroRNA (miRNA) is a short non-coding RNA molecule that is present in plants, animals, and some viruses. In addition to its role in RNA silencing, microRNA also plays a role in the post-transcriptional regulation of gene expression. Though miRNAs are not entirely complementary to the mRNA sequence, they interact with targets that have similar sequences and prevent the translation of many genes. According to reports, miRNAs influence the expression of 1%-4% of human genes via controlling 30% of human mRNAs. Because of this, miRNAs are crucial for a variety of biological processes, including tissue development, the development of cancer, the development of diabetes, neurodegenerative illnesses, systemic autoimmune diseases, and cardiovascular diseases. Interestingly, miRNAs have been linked to numerous bone metabolic diseases, including osteoporosis, as well as the process of bone remodelling. The balance between bone formation by osteoblasts and bone resorption by osteoclasts is essential for bone mass maintenance. Numerous miRNAs, including miR-223 and miR-103a, have been found to control bone metabolism by altering the differentiation and activity of osteoblasts and osteoclasts [1-3]. As a result, miRNAs are thought to be one of the key regulators of bone remodelling.

The Wnt pathways are involved in bone remodelling and homeostasis. Wnts are regarded to be anabolic factors that promote osteoblast progenitor proliferation and differentiation. A receptor complex for Wnt ligand was created by certain Frizzled (FZD) proteins and the low-density lipoprotein receptor related protein 5/6 (LRP-5/6). LRP-5 or LRP-6 binds to Wnt ligands, releasing and stabilising β-catenin. β-catenin is translocated to the nucleus and controls its target genes, including Runx2 with the help of Transcription Factor 4 (TCF-4) or Lymphoid Enhancer-Binding Factor 1 (LEF-1). Additionally, Wnt signalling improves the development of bone marrow Mesenchymal Stem Cells (MSCs) into osteoblasts by raising the levels of Runx2 and osterix. On the other hand, by inhibiting the adipogenic proteins CCAAT/enhancer-binding protein (C/EBP)

and Peroxisome Proliferator-Activated Receptor (PPAR-), Wnt signalling could prevent the development of adipose-derived stem cells into adipocytes. Additionally, Wnt signalling affects the secreted Frizzled-related protein 1 (Sfrp1), a binding site for Frizzled proteins, which inhibits osteoclast function. Sfrp1 binds to RANKL in a competitive manner to inhibit bone resorption. OPG levels are inhibited by β-catenin [4]. Therefore, bone loss was caused by osteoblast progenitors having reduced levels of β-catenin. Dual-X ray Absorptiometry (DXA) and the Fracture Risk Assessment Tool (FRAX) are the recognised instruments for evaluating osteoporosis and bone fragility in a clinical context, respectively. DXA, however, has a number of drawbacks. One drawback is that, rather than using 3D scans, DXA bases its assessment of BMD on 2D images. DXA is unable to measure the characteristics of bone tissue, such as bone microstructure, which are important for bone strength. The axial asymmetry of cross sections, the buckling ratio assumptions, and the tissue mineralization assumption are other quality control problems with DXA.

FRAX is not appropriate for patients who are at high risk but do not have an osteoporotic BMD since it measures fractured risk using BMD criteria. Other characteristics, such as muscle strength and the likelihood of falling, can also affect fracture risk. Procollagen type I N-propeptide (P1NP) and beta C-terminal telopeptide (beta-CTX) are two indicators for measuring bone metabolism that is crucial for gauging bone turnover and how well patients respond to treatment [5]. These values, meanwhile, are not very specific and persistent in serum. An absolute rate of bone loss could not be predicted by a single measurement of bone turnover. Additionally, they are not accurate indicators of bone fragility for those postmenopausal osteoporosis patients. Therefore, it is important to investigate the stable biomarkers in serum that may be utilised to identify postmenopausal osteoporosis patients at high risk of fracture.

CONCLUSION

High-density lipoproteins, which shield miRNAs from external

RNase digestion, have been found to promote miRNAs to remain stable in extreme circumstances such as boiling, acid/alkaline environments, and freeze-thaw cycles. Exosomes carry lipo-bound miRNAs from the donor cells to the receiving cells. Serum miRNA expression levels are stable and repeatable across individuals, suggesting that serum miRNAs might be good biomarkers for people who have osteoporosis.

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