# Abstract

Osteoporosis is an age-related disease characterized by impaired bone remodeling and cellular senescence. MicroRNAs represent important regulators of these processes. The aim of this study was to identify senescence-associated miRNAs in the bone tissue of patients with osteoporosis and to evaluate their relationships with clinical parameters.

A total of 46 patients undergoing total hip arthroplasty were included in this single-center cross-sectional study, comprising 21 patients with osteoporotic fracture (OP) and 25 patients with osteoarthritis without fracture as a control group. RNA was isolated from femoral neck bone biopsy specimens, and a predefined panel of 11 miRNAs associated with senescence and osteoporosis was analyzed using qRT-PCR. Expression was evaluated using ΔCt values, relative expression levels (2^−ΔCt), relative changes in expression (fold change; 2^−ΔΔCt), t-tests, correlation analyses, and generalized linear models (GLM).

In the primary analysis, miR-106a-5p was significantly upregulated in the OP group, whereas miR-34a-5p, miR-218-5p, and miR-155-5p were significantly downregulated; miR-92a-3p showed only a trend toward upregulation, and miR-181a-5p showed a trend toward downregulation. After adjustment for clinical parameters in the GLM, miR-106a-5p remained independently positively associated with osteoporosis, whereas miR-34a-5p and miR-218-5p showed independent negative associations; after adjustment, an independent positive association of miR-92a-3p and an independent negative association of miR-181a-5p with osteoporosis were also demonstrated.

Network analysis revealed that deregulated miRNAs target genes involved in the DNA damage response and cell-cycle regulation (ATM, AURKA, CUX1, ALDH9A1, AGO1/AGO4), representing key components of the ATM–p53–p21 and p16–CDK4/6–RB pathways implicated in bone tissue senescence.

A key added value of this study is the analysis of miRNA expression profiles directly from human bone tissue biopsies in one of the largest patient cohorts published to date. The study enables direct linkage of molecular findings with clinical parameters of the disease. It therefore provides a biologically highly relevant insight into the molecular mechanisms of osteoporosis directly in human bone tissue and eliminates limitations associated with extrapolation of data from animal models or peripheral biological materials.