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Long non-coding RNA analyses for osteoporosis in Caucasian women

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Osteoporosis is a prevalent bone metabolic disease characterized by bone fragility. As a key pathophysiological mechanism, the disease is caused by excessive bone resorption (by osteoclasts) over bone formation (by osteoblasts). Peripheral blood monocytes (PBMs) represent a major systemic cell type for bone metabolism by serving as progenitors of osteoclasts and producing cytokines important for osteoclastogenesis. Protein coding genes for osteoporosis have been widely studied by mRNA analyses of monocytes in high vs. low hip BMD (bone mineral density) subjects. However, long non- coding RNAs (lncRNAs), which account for a large proportion of human transcriptome, are few reported. In our study, microarray analyses of monocytes were performed using Affymetrix 1.0 ST arrays in 73 Caucasian females (age: 47-56) with extremely high (mean ZBMD =1.38, n=42, 16 pre- and 26 postmenopausal subjects) or low hip BMD (mean ZBMD=-1.05, n=31, 15 pre- and 16 postmenopausal subjects). LncRNA profile was analyzed by re-annotating exon array for lncRNAs detection via noncoder software. 575 lncRNAs were differentially expressed between the two groups. In high BMD subject, 309 lncRNAs were upregulated and 266 were downregulated. To investigate the relationship between protein coding genes and lncRNAs, we identified the genes transcribed within 10kb nearby lncRNAs via UCSC Genome Browser. Four genes and lncRNAs pairs were found to be significantly correlated and cooperatively differentially expressed in high vs. low BMD subjects. In these four pairs, the protein coding genes, NR4A1 and ABCG1, have been reported to be important for monocytes differentiation and survival in tissues. Overall, our findings for the first time reported the lncRNAs profiles for osteoporosis and may suggest the regulatory mechanism between lncRNAs and protein coding genes in bone metabolism.

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