EXPRESSION PATTERN OF OSTEOPOROTIC GENES BY DNA MICROARRAY

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Introduction
Osteoporosis is a common and progressive skeletal disease primarily caused by genetic factors and hormonal imbalances. Alteration of gene expression caused by hormonal imbalances may be one of critical causes for osteoporosis. In particular, estrogen plays a key role in age-related bone loss (1). Estrogen deficiency accelerates the rate of cancellous bone loss at the early phase of osteoporosis. Although many genes have been implicated to play roles in age-related osteoporosis, systematic studies are necessary to identify osteoporosis related genes.

Methods
To identify differentially expressed genes associated with age-related osteoporosis, we used DNA microarray technology. Bone tissues were obtained from both premenopause and postmenopause patients. Cancellous bone was excised with scissors and cultured for 2 or 3 weeks to expand osteoblast-like cells. The mRNA from osteoblast-like cells was purified, reverse transcribed with Superscript II RNase H-reverse transcriptase and labeled with Cy3-dUTP (premenopause) as control and Cy5-dUTP (postmenopause). Labeled probes were hybridized to the cDNA chip containing 3,063 human mesenchymal cell derived genes (http://hair.knu.ac.kr) (2). The array was washed with high stringency washing buffer. Fluorescent intensities at the spot were measured using Scanarray 4000 and the data were analyzed using Quantiarray software. More than 2 fold in the ratio of fluorescence intensity (Cy-3/Cy-5) was counted for significant signals.

Results
We identified highly up- and down-regulated genes in osteoporosis. Those up-regulated genes included IGFBP2, endoglin, transforming growth factor beta inducible early growth response, nuclear factor related to kappa B binding protein, and ornithine decarboxylase (Fig. 1). The down-regulated genes were progesterone membrane binding protein, signal transducer and activator of transcription 1, and transcriptional adaptor3-like (PCAF histone acetylase complex). We also identified several genes that were not known in function (Fig. 2).

Discussion
These results suggest that the fluctuations of genes identified in this study may critically contribute to develop osteoporosis in vivo. Functional analysis of these genes may provide valuable information to understand the molecular mechanism of osteoporosis.

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References

Fig. 1. Expression pattern of osteoporosis related genes

Fig. 2. Expression of uncharacterized genes in postmenopause patient

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