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Identification of long non-coding RNA involved in osteogenic differentiation from mesenchymal stem cells using RNA-Seq data

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ABSTRACT. The aim of this study was to identify long non-coding RNA (lncRNA) associated with osteogenic differentiation from mesenchymal stem cells (MSCs) using high-throughput RNA sequencing (RNA-Seq) data. RNA-Seq dataset was obtained from the European Bioinformatics Institute (accession No. PRJEB4496), including two replicates each for immortalized mesenchymal stem cells iMSC#3 cultured in growth medium (GM) and differentiation medium (DM) for 28 days. The clean reads were aligned to a hg19 reference genome by Tophat and assembled by Cufflinks to identify the known and novel transcripts. RPKM values were calculated to screen for differentially expressed RNA. Novel lncRNA were screened based on various filter criteria. Subsequently, the underlying function of novel lncRNAs were predicted by functional annotation by ERPIN, a co-expression network was constructed by WGCNA and the KEGG pathway enriched by KOBAS. A total of 3171 RNA differentially expressed between the DM and GM groups (2597 mRNA and 574 lncRNA) were identified. Among the 574 differentially expressed lncRNA, 357 were known and 217 were novel lncRNA. Furthermore, 32 novel lncRNA were found to be miRNA precursors (including miR-689, miR-640, miR-601, and miR-544). A total of

14,275 co-expression relationships and 217 co-expression networks were obtained between novel lncRNA and mRNA. The differentially expressed lncRNA and mRNA were enriched into 6 significant pathways, including those for cancer, ECM-receptor interaction, and focal adhesion. Therefore, novel lncRNAwere identified and their underlying function predicted, which may provide the basis for future analyses of the role of lncRNA in osteoblastic differentiation.

Key words: Long non-coding RNA; Osteogenic differentiation; Mesenchymal stem cells

