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RNA-Sequencing-Based Screening of Long Non-Coding RNAs Targeted by Steroid and Xenobiotic Receptor

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Steroid and xenobiotic receptor, SXR, is a nuclear receptor that plays an important role in the detoxification of bile acids and chemical compounds [1]. We have previously showed that vitamin K_2-liganded SXR is a transcriptional regulator of bone marker genes [2,3]. Recent advance in genomic technology enables to identify numerous long non-coding RNAs (lncRNAs), which have no obvious coding capacities with their length >200 bp and widely transcribed in spatiotemporal specific manners [4]. While biological functions of some lncRNAs have been characterized, few lncRNAs have been identified in the context of nuclear receptor-regulated gene network.

Here we screened functional lncRNAs upregulated by SXR agonists in human osteoblastic MG63 cells overexpressing SXR, based on RNA-sequencing analysis. Among RefSeq transcripts with >1.5-fold up-regulation or < 0.67-fold down-regulation by either rifampicin or vitamin K_2 *versus* vehicle, ~10% were identified as NR non-coding transcripts and half of the NR transcripts were up-regulated by either SXR ligand (except transcripts down-regulated by the other ligand). Based on the recent genomic data, one third of the up-regulated NR transcripts were lncRNAs except non-coding variants of coding-genes. Interestingly, known lncRNA *HOTAIR* [5] was involved in the group of putative SXR target lncRNAs. We consider that this integrative screen of lncRNAs will reveal the RNA-mediated transcriptional regulation of SXR, and will provide useful information for the potential use of lncRNAs as new osteoblastic biomarkers and therapeutic targets for bone diseases such as osteoporosis.

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