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学 位 論 文 要 旨

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<p>論 文 題 名 Physiological role of urothelial cancer-associated 1 long noncoding RNA in human skeletogenic cell differentiation (ヒト骨格形成細胞分化における urothelial cancer-associated 1 長鎖ノンコーディング RNA の生理的役割)</p>		
<p>論文内容の要旨 (2000字程度) A vast number of long-noncoding RNAs (lncRNA) are found expressed in human cells, which RNAs have been developed along with human evolution. However, the physiological functions of these lncRNAs remain mostly unknown. In the present study, we for the first time uncovered the fact that one of such lncRNAs plays a significant role in the differentiation of chondrocytes and, possibly, of osteoblasts differentiated from mesenchymal stem cells, which cells eventually construct the human skeleton. The urothelial cancer-associated 1 (UCA1) lncRNA is known to be associated with several human malignancies. Firstly, we confirmed that UCA1 was expressed in normal human chondrocytes, as well as in a human chondrocytic cell line; whereas it was not detected in human bone marrow mesenchymal stem cells (hBMSCs). Of note, although UCA1 expression was undetectable in hBMSCs, it was markedly induced along with the differentiation towards chondrocytes, suggesting its critical role in chondrogenesis. Consistent with this finding, silencing of the UCA1 gene significantly repressed the expression of chondrogenic genes in human chondrocytic cells. UCA1 gene silencing also had a significant impact on the osteoblastic phenotype in a human cell line. Finally, forced expression of UCA1 in a murine chondrocyte precursor, which did not possess a UCA1 gene, overdrove its differentiation into chondrocytes. These results indicate a physiological and important role of this lncRNA in the skeletal development of humans, who require more</p>		

論文内容の要旨（2000字程度）

sustained endochondral ossification and osteogenesis than do smaller vertebrates.