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Analysis of the effect of parathyroid hormone (PTH) treatment on osteoblastogensis from leptin receptor–positive mesenchymal stem cells
（副甲状腺ホルモンによる Leptin 受容体陽性間葉系幹細胞の骨芽細胞分化機構の解析）

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松本歯科大学大学院歯学独立研究科博士（歯学）学位申請論文

Analysis of the effect of parathyroid hormone (PTH) treatment on osteoblastogensis from leptin receptor–positive mesenchymal stem cells

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Bone marrow mesenchymal stem and progenitor cells (BM–MSPCs) maintain homeostasis of bone tissue by providing osteoblasts. Although studies have suggested that MSPCs are observed as leptin receptor (LepR)–positive cells in BM, these cells still contain non–MSPC populations. On the other hand, genetic lineage tracing approaches revealed that intermittent parathyroid hormone (iPTH) treatment induced osteoblastic differentiation from BM–MSPCs. However, little is known about the mechanistic details of these process in vivo. Here, we demonstrate that the LepR+MSPC population contains Runx2–GFPlow sub–population, which possesses higher stem cell activity, than the Runx2–GFP– stromal population. In response to iPTH treatment, LepR+MSPCs differentiate into Type I collagen a (Col1)+mature osteoblasts. Along with osteoblastogenesis, the number of Col1+ mature osteoblasts increased around the bone surface, although most were characterized as quiescent cells. However, the

number of LepR+MSPCs also increased in the vicinity of bone tissue, and the cell cycle was accelerated in these cells by iPTH treatment. The expression levels of osteoblastic markers were increased in the LepR+MSPC population in response to iPTH treatment. In contrast, the expression levels of markers for adipocytes decreased in this population. Altogether, our results indicate that Runx2 is weakly expressed in the LepR+MSPC population without osteoblastic commitment, and iPTH treatment expanded the LepR+MSPC population and skewed their lineage differentiation from adipocytes toward osteoblasts through cell cycle withdrawal.