P705

Gene Expression Profiling of Osteoclast Differentiation

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Bone homeostasis is maintained by the balanced action of bone-forming osteoblasts and bone-resorbing osteoclasts. Multinucleated, mature osteoclasts develop from hematopoietic stem cells via monocyte-macrophage lineage, which also give rise tomacrophages and dendritic cells. Despite their distinct physiological roles in bone and the immune system, these cell types share many molecular and biochemical features. To provide insights into how osteoclasts differentiate and function to control bone metabolism, we employed a systematic approach to profile patterns of osteoclast-specific gene expression by combining suppression subtractive hybridization (SSH) and cDNA microarray analysis. Here we examined how gene expression profile of mature osteoclast is different from macrophage or dendritic cell, how gene expression profile changesduring osteoclast differentiation. This approach revealed a set of genes coordinately regulated for osteoclast function, some of which have previously implicated in several bone diseases in humans. Here we also found a novel member of the leukocyte receptor complex (LRCX)-encoded family expressed specifically in OCs (OC-associated receptor (OSCAR)). Its putative ligand (OSCAR-L) is expressed primarily in osteoblasts/stromal cells. Moreover, addition of a soluble form of OSCAR in co-culture with osteoblasts inhibits the formation of OCs from bone marrow precursor cells in the presence of bone-resorbing factors, indicating that OSCAR may be an important bone-specific regulator of OC differentiation.