SL-04 MafB NEGATIVELY REGULATES RANKL-MEDIATED OSTEOCLAST DIFFERENTIATION

Kabsun Kim, Jung Ha Kim, Junwon Lee, Hye Mi Jin, Ju Young Kwon, Hyun Kook, Kyung Keun Kim, Nacksung Kim

Dept of Pharmacolol, Chonnam National University Medical School, Gwangju 501-746, Korea

Receptor activator of nuclear factor kB ligand (RANKL) induces osteoclast formation from hematopoietic cells via regulation of various transcription factors. Here, we show that MafB negatively regulates RANKL-induced osteoclast differentiation. Expression levels of MafB are significantly reduced by RANKL during osteoclastogenesis. Overexpression of MafB in bone marrow-derived monocyte/macrophage lineage cells (BMMs) inhibits the formation of TRAP-positive multinuclear osteoclasts, but phagocytic activity of BMMs is retained. Futhermore, overexpression of MafB in BMMs attenuates the gene induction of NFATc1 and osteoclast-associated receptor (OSCAR) during RANKL-mediated osteoclastogenesis. In addition, MafB proteins interfere with the DNA binding ability of c-fos, Mitf, and NFATc1, inhibiting their transactivation of NFATc1 and OSCAR. Furthermore, RNAi-mediated reduced expression of MafB enhances osteoclastogenesis and increases expression of NFATc1 and OSCAR. Taken together, our results suggest that MafB can act as an important modulator of RANKL-mediated osteoclastogenesis.

Key Words: Osteoclast, MafB, RANKL, Transcription factor