

# Microphthalmia associated transcription factor

The **Microphthalmia**-associated transcription factor (MITF) is a basic helix-loop-helix leucine zipper family factor that is essential for terminal osteoclast differentiation. Previous work demonstrates that phosphorylation of MITF by p38 **MAPK** downstream of Receptor Activator of NFκB Ligand (RANKL) signaling is necessary for MITF activation in osteoclasts. The spontaneous *Mitf* cloudy eyed (ce) allele results in production of a truncated MITF protein that lacks the leucine zipper and C-terminal end. Here we show that the *Mitf*(ce) allele leads to a dense bone phenotype in neonatal mice due to defective osteoclast differentiation. In response to RANKL stimulation, in vitro osteoclast differentiation was impaired in myeloid precursors derived from neonatal or adult *Mitf*(ce/ce) mice. The loss of the leucine zipper domain in *Mitf*(ce/ce) mice does not interfere with the recruitment of MITF/PU.1 complexes to target promoters. Further, we have mapped the p38 MAPK docking site within the region deleted in *Mitf*(ce) . This interaction is necessary for the phosphorylation of MITF by p38 MAPK. Site-directed mutations in the docking site interfered with the interaction between MITF and its co-factors FUS and BRG1. MITF-ce fails to recruit FUS and BRG1 to target genes, resulting in decreased expression of target genes and impaired osteoclast function. These results highlight the crucial role of signaling dependent MITF/p38 MAPK interactions in osteoclast differentiation <sup>1)</sup>.

1)

Carey HA, Bronisz A, Cabrera J, Hildreth BE 3rd, Cuitiño M, Fu Q, Ahmad A, Toribio RE, Ostrowski MC, Sharma SM. Failure to Target RANKL Signaling Through p38-MAPK Results in Defective Osteoclastogenesis in the Microphthalmia Cloudy-Eyed Mutant. *J Cell Physiol.* 2016 Mar;231(3):630-40. doi: 10.1002/jcp.25108. PubMed PMID: 26218069; PubMed Central PMCID: PMC4664053.

From:

<https://neurosurgerywiki.com/wiki/> - **Neurosurgery Wiki**

Permanent link:

[https://neurosurgerywiki.com/wiki/doku.php?id=microphthalmia\\_associated\\_transcription\\_factor](https://neurosurgerywiki.com/wiki/doku.php?id=microphthalmia_associated_transcription_factor)

Last update: **2025/04/29 20:20**

