Nuclear receptor corepressors

Nuclear receptor corepressors 1 (Ncor1) has been reported to regulate different transcription factors in different biological processes, including metabolism, inflammation, and circadian rhythms. However, the role of Ncor1 in periodontitis has not been elucidated. The aims of the present study were to investigate the role of Ncor1 in experimental periodontitis and to explore the underlying mechanisms through an experimental periodontitis model in myeloid cell-specific Ncor1-deficient mice. Myeloid cell-specific Ncor1 knockout (MNKO) mice were generated, and experimental periodontitis induced by ligation using 5-0 silk sutures was established. Ncor1 flox/flox mice were used as littermate controls (LC). Histological staining and micro-computed tomography scanning were used to evaluate osteoclastogenesis and alveolar bone resorption. Flow cytometry was conducted to observe the effect of Ncor1 on myeloid cells. RNA sequencing was used to explore the differentially targeted genes in osteoclastogenesis in the absence of Ncor1. Coimmunoprecipitation (Co-IP), chromatin immunoprecipitation (ChIP) experiments, and dual luciferase assays were performed to explore the relationship between NCoR1 and the targeted gene. Alveolar bone resorption in the MNKO mice was significantly greater than that in the LC mice after periodontitis induction and osteoclastogenesis in vitro. The percentage of CD11b+ cells, particularly CD11b+ Ly6G+ neutrophils, was substantially higher in gingival tissues in the MNKO mice than in the LC mice. Results of RNA sequencing demonstrated that CCAAT enhancer binding protein α (Cebpα) was one of the most differentially expressed genes between the MNKO and LC groups. Mechanistically, Co-IP assays, ChIP experiments, and dual luciferase assays revealed that NCOR1 interacted with peroxisome proliferator-activated receptor gamma (PPARγ) and cooperated with HDAC3 to control the transcription of Cebpα. In conclusion, Ncor1 deficiency promoted osteoclast and neutrophil formation in mice with experimental periodontitis. It regulated the transcription of Cebpα via PPARγ to promote osteoclast differentiation [1)]

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Ma XX, Meng XQ, Wang YL, Liu Y, Shi XR, Shao S, Duan SZ, Lu HX. Ncor1 Deficiency Promotes Osteoclastogenesis and Exacerbates Periodontitis. J Dent Res. 2022 Aug 18:220345221116927. doi: 10.1177/00220345221116927. Epub ahead of print. PMID: 35983582.