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The role of interleukin-8-immunomodulatory pathway in the differentiation of stem cells from human exfoliated deciduous teeth into odontoblast-like cells

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Abstract

Interleukin-8 (IL-8), a pro-inflammatory cytokine, has been reported to be implicated in odontogenesis and involved in odontoblast-mediated immune responses but the exact mechanism remains unclear. Hence, our group conducted a study to investigate the role and mechanism of IL-8 in the differentiation of stem cells from human exfoliated deciduous teeth (SHED) into odontoblast-like cells. SHED were seeded on human amniotic membrane (HAM) and treated with bone morphogenetic protein 2 (BMP-2), and following treatment, SHED were harvested on day 1, 7, 10, and 14. Odontogenic differentiation potential was assessed by the expression of odontogenic markers using reverse transcriptase PCR, and calcium deposition was analysed by Alizarin Red S staining. Thereafter, the optimal concentrations of reparixin, an IL-8 inhibitor, and recombinant human IL-8 (rhIL-8), an IL-8 inductor, were determined using Real Time PCR. The effects of IL-8 inhibition and induction were then analysed using Real-Time PCR and Western blotting. The levels of IL-8 protein secretion of SHED with and without IL-8 induction and inhibition during odontogenic differentiation were analysed using ELISA, while the effect of IL-8 in calcium deposition of SHED was determined using Alizarin red S staining. The results of our present study showed that odontoblast specific markers *DSPP*, *DMP1*,and *OPN* were highly expressed on day 7 onwards as odontogenic differentiation occurred. For IL-8 downstream pathway analysis, PI3K/AKT/mTOR and JAK2/STAT3 signalling pathways were suggested to be involved in odontogenic differentiation as the expression of all the markers were high, whereas inhibition of IL-8 using reparixin caused significant reduction of their expression. In conclusion, our study suggests that inhibition of IL-8 receptor by reparixin promotes odontogenic differentiation of SHED when cultured on HAM and treated with BMP-2.

Keywords: Interleukin-8 (IL-8); SHED; odontogenic differentiation; reparixin

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