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Effect of Notch2 Pathway Mediated by miR-146a-5p On Differentiation of Human Dental Pulp Stem Cells into Cementoblasts

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ABSTRACT This work explored the potential regulatory role of the miR-146a-5p/Notch2 signaling axis in directing the cementoblast-like differentiation of mesenchymal stem cells originating from human dental pulp. Cells received transfection with miR-146a-5p mimics or inhibitors, their respective negative controls, or a Notch2-knockdown plasmid, in addition to a non-transfected baseline group. Suppressing miR-146a-5p activity enhanced ALP levels, facilitated matrix mineral deposition, and elevated the expression of cementogenesis-associated genes (Notch2, CAP, BSP, OCN, OPN). In contrast, miR-146a-5p overexpression or interference with Notch2 resulted in reduced ALP activity and diminished mineralization and marker expression. A dual-luciferase assay confirmed that miR-146a-5p directly binds to the 3' UTR of Notch2. Collectively, reducing miR-146a-5p levels releases Notch2 from repression and accelerates cementoblastic commitment, highlighting the miR-146a-5p/Notch2 pathway as a promising target for periodontal cementum regeneration.