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Capping With Calcium Silicates Induces Macrophage Differentiation to M2 Phenotype

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Objectives Depending on their stimulation, pulp fibroblasts have been shown to induce macrophage differentiation into M1/M2 Phenotypes. This work was designed to investigate the effect of subjecting pulp fibroblasts to a tricalcium silicate-based material on macrophage differentiation.

Methods A Calcium silicate-based material (Biodentine™) was placed in MEM medium (0.05cm2 /mL) for 24h to obtain the materials' extracts. Human pulp cells were isolated from third molars and stem cells (DPSC) were separated from fibroblasts using STRO-1 magnetic sorting. Fibroblasts were physically injured and incubated with Lipoteichoic Acid (LTA) to mimic a carious lesion. The material extract was added to these cells to simulate pulp capping. Undifferentiated macrophages (M0) were then incubated with fibroblast supernatants. M0 macrophages chemically induced into M1 or M2 phenotypes were used as controls. Secretion of pro-inflammatory TNF-α and anti-inflammatory Il-10 were analyzed by ELISA; phagocytic capacity of S. Mutans was assessed using Gentamycin protection assay. DPSCs proliferation and recruitment towards macrophage supernatants were investigated with MTT and Boyden chambers respectively.

Results Incubation of fibroblasts with calcium silicate-based material significantly decreased macrophage TNF-α secretion while it increased that of IL-10 as compared to M1 or to macrophages incubated with supernatants of LTA-treated fibroblasts. Use of the Biodentine's extracts significantly decreased macrophage phagocytic activity and DPSCs recruitment which remained comparable to that of M2. DPSCs proliferation significantly increased with M2 and with macrophages incubated with Biodentine-treated fibroblast extracts as compared to those obtained with LTA-treated fibroblasts.

Conclusions These results show that pulp fibroblasts incubation with Biodentine™ induces macrophage differentiation into the anti-inflammatory M2 phenotype. This indicates that the calcium silicate-based material plays an important role in pulp regeneration by modulating the macrophage activity.