Pulp fibroblasts affect macrophage differentiation and regulate pulp inflammation

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Objective: During pulp inflammation, the recruited macrophages can differentiate into two phenotypes: pro-inflammatory M1 and anti-inflammatory M2. Pulp fibroblasts have been shown to play an important role in the regulation of pulp inflammation. We hypothesized that, upon carious injury, pulp fibroblasts interact with macrophages and affect their differentiation.

Methods: To mimic the cell exposure to carious bacteria, pulp fibroblasts (isolated from human third molars) were stimulated with lipoteichoic acid (LTA) and physically injured. To simulate the cell environment at the periphery of the inflammatory zone, fibroblasts were injured and cultured without LTA. Fibroblast supernatants were then added to undifferentiated macrophages to investigate their differentiation into M1/M2. This was studied by investigating cytokine secretion profiles (TNF-α and IL-10) and cariogenic bacteria phagocytosis capacity. Also, in order to localize the two macrophage phenotypes during the carious process, histological staining and immunofluorescence was performed on human carious tooth sections by using specific markers of M1 (CD86) and M2 (CD206).

Results: LTA-stimulated fibroblasts induced macrophage differentiation into M1 phenotype with a significant increase both in TNF-α secretion and phagocytosis capacity. By contrast, fibroblasts cultured without LTA, lead to M2 differentiation with a significant increase in IL-10 secretion and poor phagocytosis capacity. In carious teeth, M1 macrophages were mainly detected in the pulp zone facing the caries while M2 were mainly detected at the periphery of the inflammatory zone.

Conclusion: During the carious process, the pulp contains a mixed population of M1 and M2. At the carious front, fibroblasts induce macrophages differentiation to pro-inflammatory M1 with high bacteria phagocytosis capacity to control the infection. Pulp fibroblasts at the periphery of the inflammatory zone induce macrophage differentiation to the anti-inflammatory M2 phenotype which controls the inflammation. This fine balance between the two phenotypes is essential and represents a pre-requisite for initiating the regeneration process.