Adipokines effects on the regenerative capacity of human periodontal cells

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Obesity is increasing throughout the globe and characterized by excess adipose tissue, which represents a complex endocrine organ. Adipose tissue secrets bioactive molecules called adipokines, which act at endocrine, paracrine, and autocrine levels. Obesity has recently been shown to be associated with periodontitis, a disease characterized by the irreversible destruction of the tooth supporting tissues, that is, periodontium, and also with compromised periodontal healing. Although the underlying mechanisms for these associations are not clear yet, increased levels of proinflammatory adipokines, such as leptin, as found in obese individuals, might be a critical pathomechanistic link. Our studies have shown that leptin affected the regenerative capacity of human periodontal ligament (PDL). Leptin caused a significant downregulation of growth (TGF□1, and VEGFA) and transcription (RUNX2) factors as well as matrix molecules (collagen, and periostin) and inhibited SMAD signaling under regenerative conditions. Moreover, the local expression of leptin and its full-length receptor was significantly downregulated by inflammatory, microbial, and biomechanical signals. In the other side, decreased plasma levels of adiponectin (an anti-inflammatory adipokine) is found in obese individuals. Our in vitro studies have also shown that adiponectin stimulated significantly the expression of growth factors and extracellular matrix, proliferation, and wound healing. In addition, adiponectin reduced significantly the constitutive TNF-□ expression, and caused a significant upregulation of its own expression. The beneficial actions of enamel matrix derivative on a number of PDL cell functions critical for periodontal regeneration were partially enhanced by adiponectin. In conclusion, we have demonstrated that increased levels of leptin and reduced levels of adiponectin negatively interferes with the regenerative capacity of PDL cells, suggesting those adipokines as a pathomechanistic link between obesity and compromised periodontal healing.