

# Mechanical stress induces production of angiogenic regulators in cultured human gingival and periodontal ligament fibroblasts

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**Background:** As periodontal tissues are constantly exposed to mechanical stress during mastication, the relationship between mechanical stimulation and biochemical phenomena has been extensively investigated.

**Objective:** The aim of the present study was to assess the change in the production of angiogenic regulators produced by human gingival fibroblasts (HGF) and periodontal ligament fibroblasts (HPLF), cultured on a flexible substrate, before and after application of cyclic tensile stretching.

**Materials and methods:** Both cell types were stretched in a Flexwell Strain Unit to 7, 14 and 28% elongation, at a frequency of 12 cycles/min. Medium cultured with HGF or HPLF was examined by enzyme-linked immunosorbent assay (ELISA) for vascular endothelial growth factor (VEGF), Western blotting of pigment epithelium-derived factor (PEDF) and *in vivo* angiogenesis assay. The residual cells were analyzed by reverse transcription-polymerase chain reaction (RT-PCR) for both VEGF and PEDF mRNA expression.

**Results:** Stretching increased the VEGF mRNA level and VEGF secretion in both HGF and HPLF. The concentration of VEGF in the conditioned medium of the stretched HPLF was almost the same as that of stretched HGF. In the *in vivo* angiogenesis assay, the conditioned medium of HPLF after stretching showed a dramatic increase in tube formation. In contrast, stretched HGF did not show enhanced tube formation, despite the increase in VEGF secretion by stretched HGF. The mRNA levels of PEDF, an inhibitor of angiogenesis, were higher in HGF than HPLF. The protein level of PEDF in HGF was also higher than that in HPLF.

**Conclusion:** These findings suggest that under mechanical stress HPLF promotes angiogenesis via expression of VEGF, whereas under the same conditions angiogenesis is not promoted in HGF, due to the expression of PEDF.

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**Key words:** vascular endothelial growth factor; pigment epithelium-derived factor; human gingival fibroblasts; human periodontal ligament fibroblasts

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