Evaluation of the use of VEGF111 for the treatment of tendon lesions.

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Alterations of tendons are common pathologies resulting from repetitive or abnormal mechanical sollicitations. Very frequently lesions become chronic and may even lead to rupture. As there is no current efficient treatment for curing this type of diseases, new therapeutic approaches are being tested and developed. Injection of platelet-rich plasma (PRP) seems to be a promising treatment by local release of growth factors. Among these factors, VEGF-A is known to induce positive effects on vascular functions and angiogenesis, and could be implicated in the healing process of tendons. Several isoforms of VEGF-A have been described in literature, including VEGF165 and 121. VEGF111 is encoded by exons 1-4 and 8a. The lack of exon 5 enables VEGF111 to resist to proteolytic degradation and the absence of exons 6 and 7 reduces its affinity for several macromolecules present on the cell surface and in the extracellular matrix. In vivo, it has been shown to be highly proangiogenic and diffusible.

A 5mm defect was surgically performed in the Achilles tendon of 60 rats. Two hours after closure of the fascia and the skin, an injection within the wound was performed with PBS alone (n=30) or with PBS containing 100 ng of VEGF111 (n=30). 10 rats of each group were sacrificed at days 5, 15 and 30. The operated tendon was then carefully removed and collected for either immunohistochemical analyses or mechanical testing.

At each time point, the section and the overall appearance of the repairing tendons were similar for PBS and VEGF111-injected tendon. As compared to controls, injection of VEGF111 seemed to promote a faster angiogenesis, although the number of samples was at this stage too low for performing reliable statistical analysis. Mechanical resistance to rupture of the repairing tendons was also measured. No difference between the two groups was observed after 5 or 15 days. By contrast, increased tensile strength was clearly evidenced in the VEGF-treated group after 30 days.

These preliminary data seem to indicate a positive effect of a single VEGF111 injection for restoring the mechanical properties of tendons after their section. Additional experiments are planned for confirmation purposes and for further characterizing the model. It includes a "dose-response" analysis, the use of VEGF165 as an additional control and a study evaluating the effect of several injections.