Comparison between platelet-rich plasma (PRP) and vascular endothelial growth factor-111 (VEGF-111) as a therapeutic tool in tendon healing process

Kaux JF\(^1\), Drion P\(^2\), Libertiaux V\(^3\), Pascon F\(^3\), Colige A\(^4\), Le Goff C\(^5\), Lambert C\(^4\), Nusgens B\(^4\), Gothot A\(^5\), Cescotto S\(^3\), Defraigne J-O\(^6\), Rickert M\(^7\), Crielaard J-M\(^1\)

1. Physical Medicine Service, Department of Motility Sciences, University Hospital of Liège, University of Liège, Belgium.
2. Animal Facility of University Hospital of Liège, ULG-GIGA-R, University of Liège, Belgium.
3. Department Argenco, University of Liège, Belgium.
4. Laboratory of Connective Tissues Biology, GIGA-R, University of Liège, Belgium.
5. Department of Clinical Biology, University Hospital of Liège, University of Liège, Belgium.
6. CREDEC, Laboratory of Experimental Surgery, University of Liège, Belgium.
7. Department of Orthopaedic Surgery, University of Heidelberg, Germany.

**Introduction:**
In spite of the availability of various treatments for tendinopathy, this pathology often becomes chronic. For this reason, it is of interest to develop new treatments. Among them, the injection of platelet-rich plasma (PRP) seems to be a promising one. Indeed, several animal models have demonstrated that injection of blood platelets can initiate and stimulate tendon and ligament repair by releasing growth factors (GF) locally. Among all the GF released by activated platelets, the vascular endothelial growth factor-A (VEGF-A) is known to induce positive effects on vascular function and angiogenesis, and could be implicated in the healing process of tendons. Recently, a novel VEGF-A isoform was identified, the VEGF-111, a biologically active and proteolysis-resistant VEGF-A isoform, also known to present beneficial effects on ischemic diseases. This prompted us to evaluate whether VEGF-111 would have a therapeutic interest within the framework of the tendon pathology.

**Aim of the study:**
We hypothesized that the healing of ruptured Achilles tendons, which is the last stage of the Blazina’s classification, could be improved by injection of VEGF-111 that was compared to the potential effect of PRP injections using a rat model.

**Methods:**
A 5mm defect was surgically induced in rat Achilles tendon after resection of plantaris tendon (Fig. 1-3). Rats were divided into 3 groups: A: control (no injection), B: PRP treatment and C: VEGF-111 treatment. Rats received a local injection of PRP (50μL) or VEGF-111 (100ng) in situ after the surgery and were placed in their cage without immobilization. After 5, 15 and 30 days, the rats were euthanized in each group. The traumatized Achilles tendon of each rat was removed and dissected during the healing process (Fig. 4). Immediately after sampling, tendons were submitted to a biomechanical tensile test up to rupture, using a “Cryo-jaw” (Fig. 5-6).

**Results:**
Our results show that developed force necessary to induce tendon rupture during biomechanical tensile test was more important for tendons which had received an injection of PRP or VEGF-111. Moreover, the tensile force necessary to break tendons is higher with PRP than with VEGF-111. These results were already noticed from day 5 onwards.

**Conclusion:**
This experimentation has shown that both PRP and VEGF-111 injections stimulated tendon healing process as suggested by the increased force needed to break tendons during its healing process. Furthermore, this acceleration of the cicatrization process was more significant with PRP than with VEGF-111. This could be explained by the release from platelets of a “cocktail” of growth factors acting in synergy on the healing process.

**Acknowledgement:**
This experimentation was partly financed by “Standard de Liège 2007” and “Lejeune-Lechien 2008” grants.

jfkaux@chu.ulg.ac.be