New use of VEGF in therapeutics: application in tendon lesions

Kaux JF[1], Le Goff C[2], Drion P[3], Libertiaux V[4], Pascon F[4], Colige A[5], Lambert C[5], Nusgens B[5], Cescotto S[4],Defraigne JO[6], Rickert M[7], Crielaard JM[1]

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

1. Introduction: The VEGF111, which is a biologically active and proteolysis-resistant VEGF-A isoform, was recently identified. It is induced by ultraviolet B and genotoxic drugs. Experimentation shows that, in nude mice, tumors formed by HEK293 cells expressing VEGF111 develop a more widespread peritumoral neovascularisation than those expressing other VEGF isoforms. Good angiogenic activity and resistance to proteolysis makes VEGF111 a potential beneficial therapeutic option for ischemic diseases. As demonstrated in previous studies, mechanical overload, injury and inflammation, hypoxic condition or any combination of the above events can lead to increased expression of VEGF in the tendon. Indeed, some authors are convinced that the neovascularization in tendinopathy is the sign of chronicity while others plead in favour of it being a sign of healing processes. Thus, VEGF111 could participate in the healing of pathological tendons... The aim of our study was to determine whether if VEGF111 could have a therapeutic interest in the framework of tendinous pathology.

2. Methods (*): A 5mm defect was surgically induced in Achilles tendon of 60 rats (Fig. 1-3). Rats were divided into 2 groups of 30: A: control group (without injection) and B: VEGF111 treatment. The rats of group B received an injection of 100 ng of VEGF111 1 hour after surgery inside the site of the tendon lesion. Afterwards, rats of both groups were placed in their cages without immobilization. After 5, 15 and 30 days, 10 rats of each group were euthanized. The traumatized Achilles tendon of each rat was dissected and removed (Fig. 4). Immediately after sampling, tendons were submitted to a biomechanical tensile test up to rupture, using a tensile machine with "Cryo-jaw" (Fig. 5-6). Statistical analyses were made with an ANOVA.

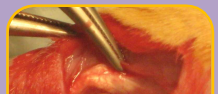
Fig. 1

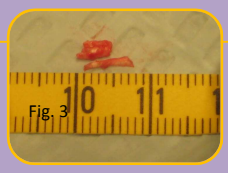
Fig. 3

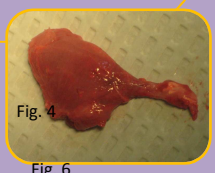
Fig. 4

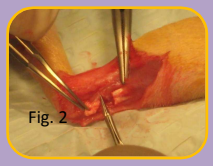
Fig. 2

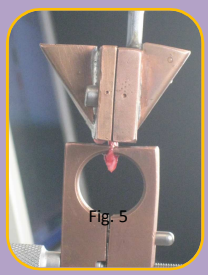
Fig. 5

Fig. 6

3. Results: A significant increase of the force necessary to induce tendon rupture was observed over time for tendons which had been submitted to an injection of VEGF111 ($p=0.016$). The force required to break the tendon was always greater for the VEGF111 group ($p<0.05$) when compared to the control group.

4. Discussion: We demonstrated that the force necessary to induce the rupture of a rat's Achilles tendon during biomechanical tensile testing was greater for tendons which had been submitted to an injection of VEGF111.

5. Conclusion: This experimentation showed that VEGF111 injections could accelerate the tendon healing process and increase the force needed to break tendons in their healing process. VEGF111 could be envisaged as VEGF111 could be a new therapy for tendon lesions. However, other experimentation using a rat model with different concentrations of VEGF111 should be made to ascertain the best concentration for this healing process.

6. Acknowledgement: This experimentation was partially financed by "Standard de Liège" and "Lejeune-Lechien" grants.

(*) All experimental procedures and protocols used in this investigation were reviewed and approved by the Institutional Animal Care and Use Committee of the University of Liège.