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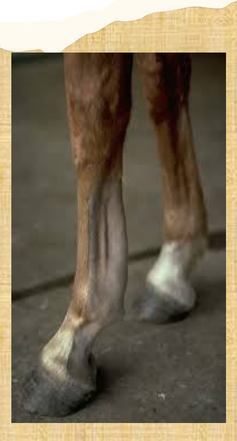
Tendinopathy: the Possible Role of Oxidative Stress, Inflammatory Conditions and Local Anesthetics.

Alessia Tognoloni *and Elisabetta Chiaradia

Dipartimento di Medicina Veterinaria, Università degli Studi di Perugia, Via San Costanzo, 4, 06126, Perugia, IT

*e-mail: alessia.tognoloni@gmail.com

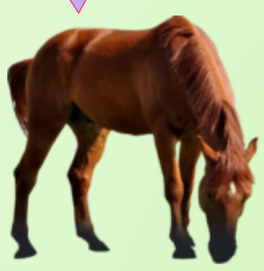


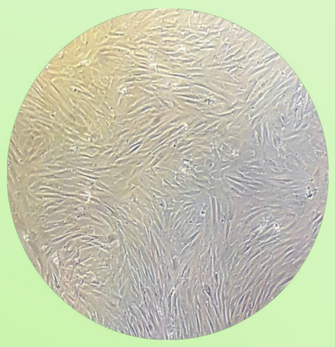
Tendinopathy is a multifactorial spectrum of tendon disorders resulting from degeneration of the extracellular matrix of tendons [1]. Etiopathogenesis remains still poorly defined despite they represent one of the most common pathologies of the musculoskeletal system both in humans and in the athletic horse [2]. Mechanical and oxidative stress due to tendon overuse have been described as the major risk factor for tendinopathy. The healing is critical process that is often also impaired by some drugs, such as local anesthetics which are used to cope the tendon pain [3,4,5].

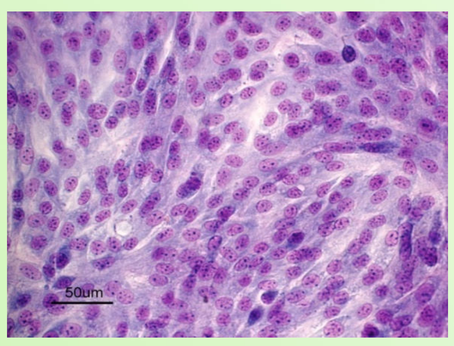
AIM

The aim of this study is to define some metabolic and molecular properties of the equine tenocytes in order to better understand the molecular aspects related to their poor responsiveness to the stressors, that have been described as main causes of tendon injuries.

EXPERIMENTAL DESIGN







Inflammation

- Cytokines (e.g. IL-1β)
- Bioactive Lipids (e.g. PGE2)

Oxidative Stress

- Reactive Oxygen Species (ROS) (e.g. H_2O_2)
- Nitric Oxide (NO)

Local Anesthetics

- Lidocaine
- Bupivacaine
- Mepivacaine

Anti-Inflammatory Conditions

- IL1 Receptor Antagonist (IL-1RA)
- Cox2 Inhibitors

Anti-Oxidant Conditions

- Platelet Rich Plasma (PRP)
- Vitamins (Vit E, Vit C, Vit A), thiols

Cytoprotective Conditions

- Platelet Rich Plasma (PRP)

Cell viability

Apoptosis and Necrosis

Non-collagenous ECM proteins

Collagen I and III

Matrix metalloproteases (MMPs)

Metalloproteinase Inhibitors (TIMPs)

PROTEIN, LIPID and DNA Oxidative Damage

Nrf2 pathways and antioxidant enzymes

Proteomic analysis

NF-kB pathways and Citokynes

EXPECTED RESULTS

The expected results of this PhD project can contribute to extend the knowledge on the molecular mechanisms underlying the onset of tendon injuries and to better understanding the role of oxidative stress, inflammation and local anesthetics in tendon homeostasis and in tendon lesion healing.

REFERENCES

[1] Fu S.C., et al. J. Orthop. Res. 36, 3268–3274. 2018; [2] Dakin S.G., et al.. Vet. Immunol. Immunopathol. 158, 121–127. 2014. [3] Millar N.L., et al.. Nat. Rev. Rheumatol. 13, 110–122. 2017; [4] Yang S.L., et al. L. Med. Sci. Monit. 20, 2478–2483. 2014; [5] Yang et.al, Med. Sci. Monit, 20: 2478-2483, 2014.