FACULTY OF VETERINARY MEDICINE
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UNIVERSITEIT GENT

INVITATION PUBLIC DEFENSE

Bridging biology and biomaterials: Development of a representative *in vitro* tendon model to study the regenerative potential of mesenchymal stromal cells

Marguerite Meeremans

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PROMOTORS

Prof. dr. C. De Schauwer
Veterinary Stem Cell Research Unit, Faculty of Veterinary Medicine, UGent

Prof. Dr. S. Van Vlierberghe
Polymer Chemistry and Biomaterials Group, Faculty of Science, UGent

Curriculum Vitae

Marguerite Meeremans was born in Ostend on 24 August 1996 and obtained her secondary school diploma in Latin-Mathematics at the Atheneum Voskenslaan in Ghent in 2014. She subsequently studied Veterinary Medicine at Ghent University, where she participated in the Honours Programme and was awarded a Top Student certificate for academic excellence and voluntary externships, and graduated with great distinction in 2020 with Equine Medicine as her major. Motivated by a strong interest in regenerative medicine, she began an interdisciplinary PhD at Ghent University, supported by a PhD Fellowship for Strategic Basic Research by the Flemish Research Foundation (FWO), combining expertise from the faculties of Veterinary Medicine and Science. Her doctoral research focused on tendon regeneration, combining stem cell biology, biomaterials and biomechanics, in order to develop an *in vitro* tendon model. The project was embedded in a strong international network and included multiple research visits to laboratories in Austria and South Korea.

Marguerite has contributed to 5 peer-reviewed publications as first author and to 9 publications as co-author. She has presented her research at major national and international conferences and participated in 2 webinar series, ensuring broad dissemination of her work. In addition to her research activities, she supervised 10 Master's students and actively contributed to outreach initiatives such as 'Dag van de Wetenschap'. Marguerite completed the Doctoral Training Programme of Ghent University and obtained certification in laboratory animal science, further strengthening her academic and professional profile.

Where?

The defense will take place on Tuesday, 17/03/2026 at 17.00h

Kliniekauditorium A
Faculty of Veterinary Medicine
Ghent University, Campus Merelbeke
Salisburylaan 133, Merelbeke

The defence will be followed by a short reception.

How to attend?

If you would like to attend, please register before 10/03/2026.
Registration by filling in the Google form and kindly confirm whether you will also join the reception.
https://forms.gle/fUc7aQbZUE7dUoz86

Members of the Jury

Prof. dr. Ann Martens
Chair of the Jury
Department of Large Animal Surgery, Anaesthesia and Orthopaedics,
Faculty of Veterinary Medicine, UGent

Prof. dr. Arn Mignon
Department of Materials Engineering,
Faculty of Engineering Technology, KU Leuven

Prof. dr. Roger Smith
Department of Clinical Sciences and Services,
Royal Veterinary College University of London, UK

Prof. dr. Eric Gracey
Department of Internal Medicine and Pediatrics,
Faculty of Medicine and Health Sciences, UGent

Prof. dr. Andreas Teuschl-Woller
Department Life Science Engineering,
University of Applied Sciences Technikum Wien, Austria

Prof. dr. Ward De Spiegelaere
Department of Morphology, Imaging, Orthopedics,
Rehabilitation and Nutrition, Faculty of Veterinary Medicine,
UGent

Summary

Tendinopathy of the human Achilles tendon and the equine superficial digital flexor tendon (SDFT) is a common orthopaedic condition in both species and is associated with reduced performance and impaired quality of life. Despite the high prevalence and clinical relevance of these injuries, the biological mechanisms underlying tendon pathophysiology and repair remain incompletely understood, thereby limiting the effectiveness of current therapeutic strategies. Although mesenchymal stromal cell (MSC)-based therapies show considerable potential for regenerative tendon repair, their translation into clinical practice is hampered by the limited insights into their mechanisms of action. To enhance understanding of tendon biology and support therapeutic innovation, well-defined *in vitro* models are required to study cellular behaviour in a controlled and reproducible environment. The general aim of this doctoral thesis was therefore to develop a physiologically representative *in vitro* tendon model as a basis for studying tendon pathophysiology and MSC behaviour under controlled conditions.

MSCs are widely used in regenerative medicine although they represent a heterogeneous cell population, and differences related to species, donor, and tissue source substantially influence their regenerative capacity. In **Chapter 3**, MSCs derived from multiple equine tissue sources were compared, revealing distinct source-dependent differences in proliferation capacity and paracrine effects on tendon cell migration. In addition, a straightforward and robust digital image-analysis method was developed to quantitatively assess MSC tri-lineage differentiation using color deconvolution in ImageJ. This approach enabled objective comparison of adipogenic, chondrogenic, and osteogenic differentiation across species by normalizing lineage-specific staining to nuclear area (**Chapter 3**).

Macrophages play a central role in tissue homeostasis and inflammation-driven regeneration, yet standardized protocols for equine macrophage differentiation and polarisation were lacking. In **Chapter 4**, a solid method to obtain equine macrophages from equine CD172a^{+} peripheral blood monocytes was developed, followed by in-depth characterization of their pro- and anti-inflammatory polarisation. In the context of tendinopathy, macrophages play a central role in regulating inflammation and repair and directly influence tendon cell behaviour. To assess this interaction, conditioned medium from polarised macrophages was applied to tendon cells and it was shown that the conditioned medium modulated tendon cell proliferation and mRNA expression, demonstrating the biological relevance of the macrophage phenotype (**Chapter 4**).

The development of a physiologically relevant *in vitro* tendon model requires careful selection of biomaterials that reflect the native ECM while offering tunability and reproducibility. In **Chapter 5**, gelatin-methacryloyl (gelMA) and norbornene-functionalised gelatin (gelNB) crosslinked using thiol-ene chemistry were evaluated for tendon cell culture. GelNB, particularly with an intermediate degree of substitution crosslinked using 1,4-dithiothreitol, represented a promising biomaterial for *in vitro* tendon models (**Chapter 5**).

In **Chapter 6**, a 3D tendon model was developed using hydrogel ring constructs composed of fibrin, gelNB, or their hybrid, and cultured with equine tendon cells under cyclic tensile stimulation. Cyclically stimulated fibrin-gelNB hybrids emerged as a physiologically relevant *in vitro* tendon model integrating fibrillar matrix architecture, mechanics, and tendon cell function (**Chapter 6**).

In conclusion, this thesis establishes a physiologically relevant and mechanically active *in vitro* tendon model that integrates defined biomaterials, multicellular interactions, and dynamic mechanical loading. It provides a controlled framework to study tendon biology, inflammation-driven pathology, and cell-cell interactions. Moreover, its scalability and compatibility with controlled mechanical stimulation position the platform as a translational and preclinical testing tool for both conservative and emerging regenerative therapies, enabling predictive *in vitro* screening approaches that may substantially reduce the need for experimental animals.