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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2022-2023

INVITATION to the Public defence of

Margo WILLEMS

To obtain the academic degree of

'DOCTOR OF MEDICAL SCIENCES'

Unravelling the mechanisms behind testicular fibrosis in Klinefelter men

The defence will take place on

Thursday, **8 December 2022 at 5 p.m.**

In Auditorium Vanden Driessche
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

and can be followed online, accessible through the following link**:**

https://gf.vub.ac.be/redirects/PhD_defense_Margo_Willems.php

Summary of the dissertation

Klinefelter syndrome (KS) occurs in 1-2 in 1000 newborn males. Affected men display a karyotype of at least one supplementary X chromosome (e.g. 47,XXY). Two main testicular features of KS patients include germ cell loss at a very young age and testicular fibrosis from puberty onwards. The mechanisms behind both the germ cell loss and the testicular fibrosis remain unclear. Sperm extraction from KS testes is possible due to focal spermatogenesis, however, the retrieval rate is hampered because of the testicular fibrosis. Unravelling the mechanisms behind the testicular fibrosis could lead to strategies to inhibit/slow down the fibrosis and eventually lead to a higher chance of finding sperm and thus a higher chance of genetically own offspring for these patients. In this thesis, the transcriptome, the extracellular matrix proteins, the immune cells (e.g. macrophages and mast cells) and the vasculature were studied regarding their role in KS-related testicular fibrosis. In addition, an ex vivo model was developed and validated to be used as a model to study KS-related testicular fibrosis. Based on the findings described in this thesis, we can conclude that (1) The upregulation of X-linked genes MXRA5 and DCX and the downregulation of X-linked gene VCX3B may induce KS-testicular fibrosis ; (2) mast cells and macrophages play a role in testicular fibrosis but are not involved in the initiation of the fibrotic process ; (3) decorin may become an early biomarker for testicular fibrosis ; (4) the vasculature of KS patients is comparable to controls except for an increase in the smallest blood vessels in KS boys ; and (5) xenografting could become an ex vivo model to study KS-related testicular fibrosis, but the model needs further optimization.

Curriculum Vitae

Margo Willems was born on September 23rd 1996 in Asse. She followed secondary education (Sciences-Mathematics) at Sint Donatus Merchtem. She continued her education at the Vrije Universiteit Brussel and in June 2019, she obtained her MSc degree in Biomedical Sciences. During her thesis year, she did an internship at the Biology of the Testis (BITE) laboratory of Prof. Dr. Ellen Goossens. During that internship, she studied the role of macrophages and mast cells in the fibrotic process seen in the testes of men suffering from Klinefelter syndrome under supervision of Prof. Dr. Dorien Van Saen. In September 2019 she started her PhD at the BITE laboratory, continuing her research concerning the initiation of testicular fibrosis in Klinefelter men. During her PhD, she has guided several students in their pursuit of a master degree. Her research has been published in high-impact factor peer-reviewed journals and she has had the opportunity to present her scientific work at several international conferences and workshops. She has been awarded a travel award for the andrology congress in 2020 and she also received the ASA international travel award. Furthermore, she has been co-president of PhD United since 2020, which has allowed her to organize several activities for the PhD students at the campus in Jette.