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VUB VRIJE UNIVERSITEIT BRUSSEL

Universiteit Antwerpen

Joint PhD VUB & UA
2019-2020

INVITATION to the Public defence of

Joséphine BEHAEGEL

To obtain the academic degree of **'DOCTOR OF MEDICAL SCIENCES'**

The Bigger Picture of Ex-vivo Cultivated Limbal Stem Cell Transplantation.

Friday, 4 October 2019 at 5 p.m.
Auditorium **Kinsbergen**

UZA, Wilrijkstraat 10, 2650 Edegem

How to reach UZA:
https://www.uza.be/auditorium-kinsbergen

Summary of the dissertation

Limbal stem cell deficiency (LSCD) results from a loss of corneal epithelial stem cells and a breakdown of the limbal barrier, due to acquired or congenital diseases. This condition causes varying ocular surface morbidity, dependent on the degree of limbal stem cell damage. Severe LSCD is characterised by vascularisation and conjunctivalisation of the cornea, leading to pain, photophobia and blindness, and is considered to be one of the most challenging ocular surface conditions to manage. Limbal stem cell grafts aim to restore the limbal barrier and reconstruct the ocular surface, improving rates of subsequent corneal graft survival. While the earliest techniques of stem cell transplantation required large sections of limbal donor tissue, the introduction of ex vivo cultivated limbal epithelial stem cell transplantations (CLET) offered an alternative to overcome the limited access to limbal tissue available for transplantation and the potential risks for the donor eye. The core of this dissertation was the conduction of a multicentre, single-arm phase II clinical trial, to assess the safety and efficacy of transplanting standardized, non-xenogeneic limbal epithelial cell grafts for patients with LSCD. Since the start of the trial in April 2014, a total of 32 transplants have been performed on 26 severe limbal stem cell deficient eyes. Furthermore, in this thesis, we additionally considered aspects 'beyond the limbal stem cell technique'. Doing so, we have made efforts to optimize the CLET procedure: from image-based clinical examination, grading of LSCD and the ethics of consenting, to targeted biopsy harvesting, performing a safer surgery, critically examining adverse events and implementing resolutions, reporting the results over the long-term and, finally, developing better tools for follow-up and grading results.

Curriculum Vitae

Joséphine Behaegel was born in Jette, on the 14th of January 1989. She finished secondary school in 2007 in Bruges (Hemelsdaele), and thereafter started her studies in medicine at the University of Ghent where she graduated in 2014, summa cum laude. She then specialised in ophthalmology at the Vrije Universiteit Brussel (VUB), and simultaneously joined the cornea research group of the Antwerp University Hospital (UZA), as part of a joint PhD project (VUB-UA).

This research group, led by Prof. Dr. Nadia Zakaria and Prof. Dr. Marie-José Tassignon, and later by Prof. Dr. Carina Koppen and Prof. Dr. Sorcha Ní Dhubhghaill, focuses on the different layers of the cornea. The core of the PhD project of Joséphine was the conduction of a phase II multicentre, single-arm phase II clinical trial, to assess the safety and efficacy of transplanting standardized, non-xenogeneic limbal epithelial cell grafts for patients suffering from severe limbal stem cell deficiency. This trial makes part of the ARRESST BLINDNESS, a consortium performing a 4-year research project, funded by the HORIZON 2020 program of the European Commission, in which different groups are developing and validating advanced regenerative and restorative therapies to treat corneal blindness.

The work of the clinical trial at the UZA has led to 2 book chapters, and 4 first-author papers, and was presented on several national and international conferences.