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HLA, Moleculaire Hematologie
University Hospital UZ Brussel

Prof. Leo van Grunsven, Promoter

Liver Cell Biology Laboratory
Vrije Universiteit Brussel



PhD in Medical Sciences
2017-2018

INVITATION to the Public defence of

Stefaan VERHULST

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

Liver progenitor cell biology in chronic liver disease.

Thursday 1 March 2018

Auditorium **Vanden Driessche**, 16:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:

<http://www.vub.ac.be/english/infoabout/campuses>

Summary of the dissertation

The liver is responsible for many vital functions and is known for its high regenerative capacity. Unfortunately, this hepatocytic regeneration does not last forever. Severe acute or chronic liver injury leads to hepatocyte senescence which results in the activation of another epithelial cell type, called a liver progenitor cell (LPC). These adult stem cells are capable to proliferate unlimited source of new liver cells. However, mechanisms involved in their differentiation and participation in liver regeneration are still poorly understood. In the first part of this thesis, we revealed the importance of macrophages during the development of the DR and extracellular matrix (ECM) deposition in cholestatic and steatotic mouse models. Our first study showed that partial depletion of macrophages using clodronate liposomes during cholestasis resulted in a minor ductular reaction and less ECM deposition. In a second study, we discovered that infliximab treatment, in comparison with dexamethasone, is a safer approach since it does not increase liver injury, but still allows inflammation to take place while efficiently inhibiting DR and ECM deposition. The second part of this thesis was more focused on the identity of LPCs. By combining transcriptomic data of different human LPC populations from alcoholic steatohepatitis patients, we were able to identify key regulatory cytokines and growth factors involved in LPC activation. In a subsequent study, we merged our human LPC transcriptome data with online available mouse LPC transcriptome data. This approach has led us to the creation of a unique LPC gene signature that could be used to identify primary LPCs, LPC cell lines and LPCs derived from induced pluripotent- or embryonic stem cells and could serve as a tool to evaluate LPC expansion in liver diseases.

Curriculum Vitae

Stefaan Verhulst (born 17th June 1987, in Jette) holds an MSc degree in Biomedical Sciences. His research focuses on liver progenitor cells, their niche as well as their contribution to liver regeneration. He obtained an IWT SBO grant in December 2012, and worked within a Interuniversity Attraction Pole research network (<http://www.iap-hepro.be/>) that aimed for the molecular characterization of liver progenitor cells in liver diseases. He published 3 first author papers and contributed to 10 other manuscripts. He presented his work at national and international conferences with posters and oral presentations. His rising interests in statistics, bioinformatics and stem cell biology stimulates him to pursue his academic career.

Aside from his scientific work, he is active in different governance committees within the Vrije Universiteit Brussel and was elected to be the PhD student representative for the faculty of Medicine and Pharmacy in the University and Academic board from 2015-2019. He is the founder of "PhD United", a group of Phd students/Post docs that organises both social and academic activities since 2014, to stimulate interaction between researchers at the Jette campus (www.vub.ac.be/en/phd/united).

In his spare time, he studies the game of chess and spends time with Liesbeth and their new-born daughter Juliette.