

## Board of examiners

### **Prof. Ramiro Jover**

Department of Biochemistry and Molecular Biology, Faculty of Medicine  
Universidad de Valencia Valencia, Spain

### **Prof. Isabelle Leclercq**

Laboratory of Gastroenterology, Faculty of Medicine  
Université Catholique de Louvain, Brussels, Belgium

### **Prof. Kristien De Paepe**

Department of *In Vitro* Toxicology and Dermato, Faculty of Medicine and Pharmacy  
Vrije Universiteit Brussel, Brussels, Belgium

### **Prof. Hendrik Reynaert**

Department of Gastroenterology-Hepatology  
Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel

### **Prof. Yvan Vander Heyden, Chair**

Department of Analytical Chemistry, Applied Chemometrics and Molecular Modelling  
Faculty of Medicine and Pharmacy  
Vrije Universiteit Brussel, Brussels, Belgium

### **Promoters:**

#### **Prof. Robim M Rodrigues**

Department of *In Vitro* Toxicology and Dermato-Cosmetology  
Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel

#### **Prof. Tamara Vanhaecke**

Department of *In Vitro* Toxicology and Dermato-Cosmetology  
Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel

#### **Prof. Vera Rogiers**

Department of *In Vitro* Toxicology and Dermato-Cosmetology  
Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel

### **Co-promoter:**

#### **Prof. Joery De Kock**

Department of *In Vitro* Toxicology and Dermato-Cosmetology  
Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel



PhD in Pharmaceutical Sciences  
2019-2020

INVITATION to the Public defense of

## **Joost BOECKMANS**

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

## **Development and characterization of a human stem cell-based *in vitro* model for anti-NASH drug testing**

The defense will take place digitally on

**Wednesday, 8 July 2020 at 5 p.m.**

via Zoom meeting, accessible through the following link:

[https://gf.vub.ac.be/redirects/PhD\\_defense\\_Joost\\_Boeckmans.php](https://gf.vub.ac.be/redirects/PhD_defense_Joost_Boeckmans.php)

---

## Summary of the dissertation

Non-alcoholic steatohepatitis (NASH) is a severe chronic liver disease that affects about 5% of the population. NASH is characterized by hepatic lipid accumulation, inflammation and fibrosis and can progress to cirrhosis and hepatocellular carcinoma. There are currently no drugs available to treat NASH.

Investigation of NASH traditionally relies on animal models, which are often not representative for the human situation. Therefore, the aim of the doctoral thesis was to develop a human-based *in vitro* model that can recapitulate the molecular and cellular mechanisms that drive NASH and can be used during anti-NASH drug development.

To this end, we created a NASH-specific hepatic environment *in vitro* by exposing human stem cell-derived hepatic cells (hSKP-HPC), primary human hepatocytes (PHH) and human hepatic cell lines (HepG2 and HepaRG) to key NASH-inducing factors. The obtained models mirrored NASH characteristics and could be used to evaluate anti-lipogenic and anti-inflammatory properties of PPAR agonists, a class of anti-NASH drugs that are under clinical evaluation. The hSKP-HPC-derived model most closely mimicked the PHH-mediated drug testing responses, highlighting its possible future position in preclinical drug development.

Furthermore, genetic predisposition of patients to develop NASH could be evaluated *in vitro* using hSKP-HPC, paving the way for the investigation of patient-specific genetic etiologies of NASH.

In conclusion, a pragmatic human- and disease-relevant stem cell-derived *in vitro* NASH model has been developed that can be implemented in drug testing and personalized medicine.

***Thanks to Mireille Aereus.***

## Curriculum Vitae

Joost Boeckmans was born on the 19<sup>th</sup> of February 1993 in Geel (Belgium) together with his twin brother Toon. He followed secondary education direction mathematics-sciences at *Sint-Jozef Instituut Bokrijk* in Genk, Belgium. In 2016, he obtained a master's degree in pharmaceutical sciences with greatest distinction from the *Vrije Universiteit Brussel (VUB)* (Brussels, Belgium) which included a 3-month Erasmus exchange at the *Universitat de Barcelona* (Barcelona, Spain) for the preparation of his master's thesis under the promotorship of Prof. Kristien De Paepe.

Hereafter, Joost started a PhD-project at the department of *In Vitro Toxicology and Dermato-Cosmetology (IVTD)* of the VUB under promotorship of Prof. Robim M Rodrigues, Prof. Tamara Vanhaecke and Prof. Vera Rogiers and co-promotorship of Prof. Joery De Kock. He obtained a grant from the Research Foundation Flanders (FWO-SB) and was further supported by the Research Chair Mireille Aereus for alternative animal-free research methods.

Joost presented his results at several international and national conferences through 6 oral and 12 poster presentations. He authored 15 scientific publications in internationally peer-reviewed journals of which 9 as first author. Furthermore he supervised 3 master's theses in pharmacy and 1 in medicine and also guided an internship in biochemistry & biotechnology.

Joost received together with his promoters a 'review writing grant' of the 'Humane Society International' and was a recipient of two poster prizes at scientific conferences.