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Prof. Dr. María Dolores Mayán Santos
CellCOM Research Group
Institute for Biomedical Research of A Coruña

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Laboratoire Signalisation et Transports Ioniques Membranaires
CNRS – ERL 7368
Université de Poitiers

Prof. Dr. Pieter Annaert
Department of Pharmaceutical and Pharmacological Sciences
Katholieke Universiteit Leuven

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Research Group Experimental Pharmacology
Vrije Universiteit Brussel

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Department of Pharmacology
Vrije Universiteit Brussel

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Department of Analytical Chemistry and Pharmaceutical Technology
Vrije Universiteit Brussel

Prof. Dr. Mathieu Vinken (promotor)
Department of *In Vitro* Toxicology and Dermato-Cosmetology
Vrije Universiteit Brussel

Prof. Dr. Bruno Cogliati (promotor)
Department of Pathology of the School of Veterinary Medicine and Animal Science
University of São Paulo

VRIJE UNIVERSITEIT BRUSSEL

Universidade de São Paulo

PhD in Pharmaceutical Sciences
2017-2018

INVITATION to the public defence of

Michaël MAES

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

The role of connexins, pannexins and their channels in acute liver failure

Thursday 12 October 2017
Auditorium **Piet Brouwer**, 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

In the past few years, connexin hemichannels and pannexin channels have emerged as so-called pathological pores, since they drive a number of deleterious events, including cell death and inflammation. The objective of this doctoral thesis project was to investigate the role of both channel types, in particular hemichannels consisting of connexin32 (Cx32) and connexin43 (Cx43) as well as pannexin channels built up by pannexin1 (Panx1), in liver disease. Specific focus was hereby put on hepatotoxicity induced by paracetamol, also called acetaminophen (APAP), which is characterized by a substantial degree of cell death and inflammation, and that presently is a major cause of acute liver failure worldwide. Throughout this project, considerable attention has been paid to the testing of the utility of currently available experimental tools to investigate Cx32 and Cx43 hemichannels as well as Panx1 channels. In this respect, the first study showed that whole-body Cx32 knock-out mice qualify less as models to study Cx32 signaling in APAP-induced hepatotoxicity. In the second study, it was found that hepatic Cx43 production increases in mice overdosed with APAP and that Cx43 signaling protects against this type of chemical insult. In the third study, the claimed specificity and efficacy of peptide-based inhibitors of Cx32 and Cx43 hemichannels was confirmed *in vitro* and their subsequent administration to APAP-intoxicated mice resulted in reduced adverse outcome. The latter was equally observed in the fourth study following treatment of APAP-overdosed mice with a peptide-based inhibitor of Panx1 channels. Overall, this doctoral thesis project showed the promising potential of connexin hemichannels and pannexin channels as clinical drug targets, *in casu* in the specific context of APAP-induced acute liver failure.

Curriculum Vitae

Michaël Maes was born on the 27th of September 1989 in Ukkel, Belgium. He completed secondary school, orientation Latin-mathematics, in 2007 after which he started his academic career at the Vrije Universiteit Brussel (VUB). In 2012, he obtained the degree as pharmacist and master in drug development with high distinction. He joined the research group of *In Vitro* Toxicology and Dermato-Cosmetology at the Faculty of Medicine and Pharmacy of the VUB, first as a scientific collaborator and later as a PhD student to investigate the role of connexin and pannexin channels in acute liver failure. This project, part of a double PhD diploma program established between the VUB and the University of São Paulo (USP), and supervised by Prof. Mathieu Vinken (VUB) and Prof. Bruno Cogliati (USP), was funded by the Agency for Innovation by Science and Technology in Flanders (IWT). The results obtained during his doctoral research project have been presented at ten national and international scientific conferences, among which one presentation was awarded with the prize for best oral presentation. Michaël has been involved in two other research projects focused on the role of connexin and pannexin channels in liver fibrosis and non-alcoholic steatohepatitis. His work has resulted in 25 scientific publications in international peer-reviewed journals and five book chapters, of which 13 as first author. During his PhD project, he obtained the certificate of 'Expert laboratory animal leader (FELASA C)' and successfully completed the 'Safety course of cosmetics in Europe'. Michaël has supervised four master theses of both VUB and international students. Furthermore, he assisted to several practical courses of the bachelor and master in pharmaceutical sciences program at the VUB.