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VRIJE UNIVERSITEIT BRUSSEL

Universidade de São Paulo

PhD in Pharmaceutical Sciences
2017-2018

INVITATION to the public defence of

Joost WILLEBRORDS

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

The role of connexins, pannexins and their channels in non-alcoholic steatohepatitis

Monday 29 January 2018
Auditorium **Piet Brouwer**, 17:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:
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Summary of the dissertation

While connexin-based gap junctions have been historically considered as goal keepers of tissue physiology, connexin hemichannels and pannexin channels have lately gained considerable attention as drivers of pathological processes, including cell death and inflammation. The objective of this doctoral thesis project was to investigate the role of the latter 2 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. Focus was hereby put on non-alcoholic steatohepatitis (NASH), which is a highly prevalent type of chronic liver disease worldwide and that is characterized by hepatocellular lipid accumulation, oxidative stress and inflammation. In a first study, it was found that diet-induced NASH in whole body Cx32-/- mice results in more pronounced liver damage, inflammation and oxidative stress, thus suggesting a protective effect of overall Cx32 signaling. A second study showed that specific pharmacological inhibition of Cx32 and Cx43 hemichannels alleviates the clinical manifestation of NASH in mice as evidenced by reduced liver inflammation and oxidative stress. The third study demonstrated reduced liver damage, inflammation and oxidative stress in whole body Panx1-/- mice upon diet-based induction of NASH. Collectively, the outcome of these studies confirms the claimed pathological role of connexin hemichannel and pannexin channel signaling, and opens new perspectives for the clinical treatment of NASH.

Curriculum Vitae

Joost Willebrords was born on 8 April 1990 in Leuven, Belgium. After graduation from secondary school (Science-Mathematics) in 2008, he started his higher education at the Katholieke Universiteit Leuven (KUL). In 2014 he obtained his degree as pharmacist and master in drug development with distinction. Subsequently, he joined the research group of In Vitro Toxicology and Dermato-Cosmetology at the Faculty of Medicine and Pharmacy of the VUB to investigate the role of connexin and pannexin channels in non-alcoholic steatohepatitis. Under promotorship of Prof. Mathieu Vinken (VUB) and Prof. Bruno Cogliati (USP), this double PhD VUB-USP diploma project was funded by the European Research Council (ERC) and the São Paulo Research Foundation (FAPESP). The results obtained during his doctoral research are outlined in the submitted PhD dissertation and were presented at several national and international conferences. Joost has been involved in 2 other projects focused on the study of connexin and pannexin channels in liver fibrosis and acute liver failure. This has resulted in 19 scientific publications in international peer-reviewed journals and 5 book chapters. Joost also supervised both bachelor and master theses of the VUB as well as international students. Furthermore, he assisted in practical courses of bachelor and master students in pharmaceutical sciences at the VUB.