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VRIJE UNIVERSITEIT BRUSSEL

PhD in Pharmaceutical Sciences
2018-2019

INVITATION to the Public defence of

Laura WALRAVE

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

Connexin43 hemichannels as druggable targets for future anti-seizure medication.

Thursday 24 January 2019
Auditorium **Piet Brouwer**, 17:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

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Summary of the dissertation

In epilepsy research, emphasis is put on exploring new anticonvulsant compounds with modes of action distinct from the clinically available anti-seizure drugs, to be able to treat therapy-resistant patients. In line with this notion, the main objective of this thesis work was to study glial connexin43 hemichannels (Cx43 HCs) as possible anti-seizure drug targets in several rodent models of seizures and epilepsy. As experimental tool we used the recently developed Cx43 mimetic peptide "TAT-Gap19" that blocks Cx43 HC function without reducing Cx43 gap junction-mediated intercellular communication. We demonstrated that TAT-Gap19 attenuates chemically- and electrically-induced seizures in rodents. Collectively, the results underscore the potential of Cx43 HCs as a novel and druggable target in epilepsy treatment. We also found that Cx43 HC inhibition impairs hippocampal short-term spatial memory, which should be considered for future research, since possible adverse effects on cognitive function might limit the clinical use. Nevertheless, the development of new therapeutic tools to selectively inhibit Cx43 HCs will make them promising targets for several diseases.

Curriculum Vitae

Laura Walrave was born on February 9th 1989 and started as Pharmaceutical Sciences student at the VUB in 2007. She graduated as master in Drug Development in 2012 and continued her career as doctoral researcher and training assistant in Pharmaceutical Sciences under the supervision of Prof. Ilse Smolders (Laboratory of Pharmaceutical Chemistry, Drug Analysis and Drug Information, VUB), in collaboration with Prof. Mathieu Vinken (Laboratory of *In Vitro* Toxicology and Dermato-Cosmetology, VUB) and Prof. Luc Leybaert (Department of Basic Medical Sciences, Universiteit Gent). Her research focussed on astrocytic connexin43 hemichannels as promising anti-seizure drug targets. During her doctoral thesis, Laura had the opportunity to perform experiments at the Center for Interdisciplinary Research in Biology at Collège de France, Paris, under the supervision of Prof. Christian Giaume. Laura is author of 11 peer-reviewed publications, among which 3 as first author. One review is currently in preparation. Her work was presented at various national and international scientific conferences. Since November 2018, Laura is working as medical science liaison at Mylan.