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PhD in Pharmaceutical Sciences
2021-2022

INVITATION to the Public defence of

Yana VAN DEN HERREWEGEN

To obtain the academic degree of

'DOCTOR OF PHARMACEUTICAL SCIENCES'

A promising DREADDED strategy: Exploring the role of astrocyte signalling on synaptic plasticity and refractory epilepsy

The defence will take place on

Tuesday, 13 September 2022 at 5 p.m.

In Auditorium Vanden Driessche

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

and can be followed online, accessible through the following link:

https://gf.vub.ac.be/redirects/PhD_defense_Yana_Van_Den_Herrewegen.php

Summary of the dissertation

Astrocytes are star-shaped glial cells and are the most abundant cell type of the central nervous system (CNS). In addition to ensuring brain homeostasis, they are established as active players in the synapse. An increasing amount of evidence indicates that astrocytic G-protein coupled receptors (GPCRs) are critically involved in regulating rodent behavior as well as in various CNS disorders. However, due to the lack of specific tools, their downstream signalling and the resultant effect in disease remain poorly characterized. Currently, 30% of epilepsy patients are not adequately treated with the clinically available anti-seizure drugs, emphasizing the need for innovative treatments. Mesial temporal lobe epilepsy (MTLE) is a particularly difficult-to-treat type of epilepsy, manifesting through the occurrence of recurrent focal seizures and severe comorbidities, such as cognitive dysfunction and depression.

In this PhD research, we use a recently developed state-of-the-art tool, so-called DREADDs (Designer Receptors Exclusively Activated by a Designer Drug). In combination with an astrocyte-specific gene therapy approach, this technology allows us to selectively modulate GPCR signalling in astrocytes. We use two types of DREADDs: 1/ the hM3Dq DREADD (Gq-coupled GPCR), and 2/ the hM4Di DREADD (Gi-coupled GPCR). First, we explored the effect of DREADD-mediated astrocyte manipulation on intracellular calcium signalling and synaptic transmission in ex vivo hippocampal slices. In the second part, we focused on epilepsy as a brain disorder and evaluated the potential of DREADDed astrocyte modulation as a strategy to tackle pharmacoresistant seizures and psychiatric comorbidities in a mouse model for MTLE.

Curriculum Vitae

Yana Van Den Herrewegen was born on the 14th of April 1993 in Vilvoorde, Belgium. After finishing secondary school in the field of Mathematical Sciences, she went on to pursue an academic education in Pharmaceutical Sciences at the Vrije Universiteit Brussel (VUB). In her first years at university, Yana discovered her passion for epilepsy research, during a 3-year project on the add-on anti-seizure drug, Pregabalin. Later, during her final year, she spent 3 months at the La Sapienza University of Rome, where she performed the experimental work for her master's thesis under the supervision of Prof. Dr. Joeri Aerts (VUB). She obtained her master's degree in Drug Development with summa cum laude and was awarded the Pharmacist Nedeljkovic prize. Following this fruitful academic trajectory, Yana obtained a competitive FWO grant, allowing her to become a PhD candidate at the Research group of Experimental Pharmacology under the supervision of Prof. Dr. Ilse Smolders, Prof. Dr. Dimitri De Bundel and co-supervisor Prof. Dr. Ann Van Eeckhaut. As a PhD candidate, Yana focused on exploring the role of astrocytes on synaptic plasticity and refractory epilepsy and she spent 1 year abroad at the University of Bristol at the renowned lab of Prof. Dr. Zuner Bortolotto. In addition, she taught practical sessions for Pharmaceutical Chemistry I and guided 3 Master thesis students. Yana obtained an additional grant from the Scientific Fund of Willy Gepts (UZ Brussel), allowing her to continue her research at the VUB. She presented her research at several (inter)national conferences and published 5 research papers, of which 2 as a 1st author related to her PhD research. Currently, Yana pursues her passion for epilepsy research at UCB, an international pharmaceutical company with a strong record in drug development for epilepsy.