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VRIJE UNIVERSITEIT BRUSSEL

PhD in Pharmaceutical Sciences
2018-2019

INVITATION to the Public defence of

Joeri Van Liefferinge

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

Vesicular and non-vesicular astrocytic glutamate release in temporal lobe epilepsy.

Tuesday 18 September 2018
Auditorium **Piet Brouwer**, 17:00
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

Epilepsy is one of the most common acquired chronic neurologic disorders, not only characterized by neuronal hyperexcitability and sudden, synchronized electrical discharges that can manifest as seizures, but also by an increased incidence of comorbid conditions such as anxiety, depression, cognitive dysfunction, and sudden unexpected death. About 70 million people worldwide suffer from epilepsy, with temporal lobe epilepsy (TLE) being is the most common and progressive form. Surprisingly, up to one-third of all people with epilepsy are refractory to current medications. As such, the development of new, more effective and specific drugs is still of upmost importance. It is generally accepted that glutamate is a key player in the initiation as well as the maintenance of epileptic seizures. Some anti-seizure drugs (ASDs) exert their effect via antagonism of glutamate receptors, however up to date, no ASDs are available that specifically target glutamate transporters. Glutamate transporters might represent innovative targets as their malfunctioning can lead to altered glutamate levels and worsening of seizures. Yet, the importance of vesicular glutamate transporters (VGLUTs) and the cystine-glutamate antiporter (system x_c^-) in TLE remains poorly investigated. In this thesis we demonstrated for the first time the involvement of astrocytic vesicular (VLGUT3) and non-vesicular (system x_c^-) glutamate release in human TLE samples. Next, we highlighted the importance of the use of proper negative controls when performing histological analyses in xCT research in order to avoid generating conflicting data and drawing wrong conclusions. Finally, the potential of system x_c^- as a novel target for anti-epileptogenic and/or disease-modifying therapies was demonstrated for the first time in three distinct chronic epilepsy mouse models.

Curriculum Vitae

Born on 28th November 1987 in Halle.
Studied Wiskunde-Wetenschappen in OLV College in Halle, followed by three bachelor years in Pharmaceutical Sciences and two master years in Drug Development at the Vrije Universiteit Brussel. Graduated with great distinction in June 2010.
Obtained IWT scholarship in January 2011.
Conducted research for this PhD in Pharmaceutical Sciences from January 2011 - June 2015, under the supervision of Prof. dr. Ann Massie and Prof. dr. Ilse Smolders. This research resulted in 17 peer-reviewed publications, of which three as a first author.
Since July 2015 active as QA Release Engineer in the Quality Aseptic Operations team of Pfizer Puurs.