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PhD in Pharmaceutical Sciences
2016-2017

INVITATION to the Public defence of

Thomas DEMUYSER

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

Missing pieces to a gloomy jigsaw

GLUTAMATE TRANSPORTERS IN THE DEPRESSIVE STATE**Friday 14 October 2016**

Auditorium **Brouwer**, 18:00

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:

<http://www.vub.ac.be/english/infoabout/campuses>



Vrije Universiteit Brussel

Summary of the dissertation

Half a century after the formulation of the monoamine hypothesis of depression, current pharmacological research in mood disorders focuses mainly on the involvement of the glutamatergic system. Recently an important role for glial cells in the stressed tripartite synapse was proposed. The cystine/glutamate antiporter or system xc⁻ is responsible for non-vesicular glutamate release from glial cells and glutamate reuptake transporters clear glutamate from the extracellular space into glial cells.

In the present study we phenotyped mice, lacking functional system xc⁻. Our findings indicate that, under physiological conditions, glutamate release via system xc⁻ mediates aspects of higher brain function related to anxiety and depression. Next we evaluated the possible role of system xc⁻ in the depressive state. Therefore we validated a mouse model for depression and anxiety. We subjected the mice, lacking functional system xc⁻, to this validated model and subsequently analyzed their behavior. Our results show that system xc⁻ is not involved in the pathology of depression, since the protective effects of system xc⁻ deficiency in naïve animals, depicted as antidepressant- and anxiolytic-like effects, seem to fade and disappear with higher levels of chronic stress. Furthermore we quantified expression levels of the specific subunit of system xc⁻ (xCT) in animal models of depression as well as in *postmortem* tissue of depressed patients, in different depression-related brain regions. In line with our behavioral observation, we show that xCT protein expression is not affected in the depressive state. On the other hand the expression of glutamate reuptake transporters is downregulated in certain brain areas of animal models and depressed patients, pointing at a disruption of glial glutamate buffering.

Curriculum Vitae

Thomas Demuyser was born on January 26th 1989 in Tienen, Belgium. In 2007, he started the study of Pharmaceutical Sciences at the Vrije Universiteit Brussel (VUB) and he graduated *magna cum laude* as a Pharmacist and Master in Drug Development in 2012. During his master thesis, conducted at the Center for Neurosciences of the VUB, he showed interest in the field of neurological research. After his graduation, he obtained a grant from Flanders Innovation & Entrepreneurship and started his PhD in January 2013 under promotorship of Prof. Ilse Smolders and Prof. Ann Massie. He is author of nine published papers in peer-reviewed journals among which three as first author. His work was presented at national and international scientific conferences orally and by poster. After his PhD, he will pursue the degree of Master in Clinical Biology.