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PhD in Pharmaceutical Sciences 2017-2018

INVITATION to the Public defence of

Giulia ALBERTINI

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

**Glial modulators of extracellular glutamate and their
involvement in pathological behavior**

Friday 2 March 2018

Auditorium **Vanden Driessche**, 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

Glial cells express a variety of glutamate transporters such as system xc⁻, responsible for non-vesicular glutamate release, and excitatory amino acids transporters, that clear glutamate from the synaptic cleft. Imbalances in the delicate continuum between glutamate release and uptake can have tremendous effects upon neurons and underlie disorders of the central nervous system and pathological behavior.

In the present study, we evaluated the effects of genetic deletion of system xc⁻ in inflammatory conditions, known to be involved in disorders such as depression and epilepsy. We first demonstrated that peripheral inflammation enhances hippocampal protein expression of xCT, the specific subunit of system xc⁻, while reducing the expression of GLT-1, an excitatory amino acids transporter. Moreover, mice lacking functional system xc⁻ (xCT^{-/-} mice) are less susceptible to the central and clinical outcomes of peripheral inflammation, such as activation of resident immune cells and sickness and depressive-like behavior. We then subjected xCT^{-/-} mice and their wild-type littermates to a viral-induced model of epilepsy. Although we detected changes in glial glutamate transporters, seizure severity and brain pathology were similar between genotypes. Finally, we characterized a novel model of epilepsy, the 6 Hz corneal kindling model, with a focus on neurobehavioral comorbidities and changes in glutamate transporters, demonstrating the face validity of this model. Taken together, the findings of the current doctoral thesis enlarge our understanding of the contribution of glutamate transporters to inflammation- and epilepsy-induced pathological behavior, with a particular emphasis on system xc⁻.

Curriculum Vitae

Giulia Albertini was born on November 27th 1989 in Savigliano, Italy. In 2008, she started the study of Pharmaceutical Sciences at the University of Pavia. In 2013, she conducted her master thesis at the Center of Neurosciences of the VUB in the frame of an Erasmus exchange program, developing a keen interest for the central nervous system and glial cells. After successfully achieving her master degree in Pharmacy with highest distinction, Giulia started her PhD at the Center of Neurosciences of the VUB in January 2014, under promotorship of Prof. Ilse Smolders and Prof. Ann Massie. Her research focused on glutamate transporters in several inflammatory disorders of the central nervous system, such as epilepsy, multiple sclerosis and depression. In addition, Giulia performed extensive behavioral research. During her PhD, Giulia visited the lab of Prof. Karen Wilcox, chair of the Department of Pharmacology and Toxicology of the University of Utah (USA) and director of the Anticonvulsant Drug Development program, where she had the opportunity to learn and apply novel animal models of epilepsy. Giulia is author of fourteen peer-reviewed publications, among which two as first author. Two additional manuscript are currently in preparation. Her work was presented at various national and international scientific conferences orally and by poster. After her PhD, she will continue her scientific career as a postdoc in the "Serotonin in plasticity and disease" team of Prof. Luc Maroteaux and Prof. Anne Roumier at the Institut du Fer à Moulin (Paris).