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PhD in Pharmaceutical Sciences
2020-2021

INVITATION to the Public defense of

An BUCKINX

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

**From cellular excitotoxicity to the epileptic brain:
A new understanding of ghrelin receptor modulation
for combatting hyperexcitability**

The defense will take place on **Wednesday, 19 May 2021 at 5 p.m.**

and will be organised online accessible through the following link:

Microsoft Teams meeting

[Click here to join the meeting](#)

Summary of the dissertation

Despite the availability of a variety of antiseizure drugs for epilepsy patients, 30 % of patients are pharmacoresistant and suffer from ongoing seizures. Ghrelin and its receptor have emerged as potential novel targets for eliciting antiseizure effects. Therefore, the aim of this PhD research was to gain an increased understanding of ghrelin receptor modulation in excitability.

In a first part of the PhD research, we showed that ghrelin receptor-induced anticonvulsant effects are not mediated via activation of the downstream G α q or G α 12 signal transduction pathways, promoting the beta-arrestin signaling pathway for conveying agonism-ghrelin receptor mediated anticonvulsant effects. In a second part, we showed that long-term administration of the ghrelin receptor agonist macimorelin was anticonvulsive in the refractory intrahippocampal kainic acid model for temporal lobe epilepsy, but could not prevent the establishment of chronic epilepsy. Finally, we found that macimorelin increased cell viability in neurons, and to a higher degree in astrocytes in an excitotoxic environment. As we were not able to identify the exact molecular correlate underpinning this protective effect, further studies are required to delineate the exact mechanism-of-action of macimorelin in excitotoxic settings.

Overall, this research has increased our understanding of ghrelin receptor modulation in epilepsy and has demonstrated the potential of macimorelin as a novel treatment option for refractory epilepsy patients.

Curriculum Vitae

An Buckinx was born on January 5th 1993 in Brussels and enrolled in the Bachelor of Biomedical Sciences in 2011 at the Vrije Universiteit Brussel (VUB). She developed a keen interest in neurosciences, and in 2014 she started a Master degree in Biomedical Neuroscience at the University of Antwerp, where she graduated with great distinction. She performed the research for her Master thesis at the European Brain Research Institute in Rome. In 2016, An returned to the VUB to start a PhD in Pharmaceutical Sciences at the Department of Pharmaceutical Chemistry, Drug Analysis and Drug Information under the supervision of Prof. Dr. Ilse Smolders. Her research focused on the role of the ghrelin receptor in epilepsy.

During her research An supervised several Master and Bachelor thesis students and was involved in educational tasks. Additionally, she participated regularly in events focused on science communication. She finished second at the Flemish Battle of the Scientists, wrote an article on epilepsy for the Flemish magazine Knack, and gave multiple talks at scientific events tailored to a broad audience.

An is author of four peer-reviewed publications, of which three as first author. Additionally, one research article and review are currently in preparation. She presented her work at various national and international scientific conferences. Currently, An is working as a postdoctoral researcher at the laboratory of microglia biology at the University of Lausanne, Switzerland.