Board of examiners

Dr. Frédéric Simonin
Biotechnology and Cellular Signaling – Team GPCR, pain and inflammation
Université de Strasbourg (France)

Prof. Dr. Serge Van Calenbergh
Department of Pharmaceutical Sciences, Laboratory of Medicinal Chemistry
Universiteit Gent

Prof. Dr. Em. Dirk Tourwé
Department of Chemistry, Research Group of Organic Chemistry
Vrije Universiteit Brussel

Prof. Dr. Mathieu Vinken
Department of Pharmaceutical Sciences, Laboratory of In Vitro Toxicology and Dermato-Cosmetology
Vrije Universiteit Brussel

Prof. Dr. Debby Mangelings, Chair
Department of Pharmaceutical Sciences, Laboratory of Analytical Chemistry, Applied Chemometrics and Molecular Modelling
Vrije Universiteit Brussel

Prof. Dr. Ilse Smolders, Promotor
Department of Pharmaceutical Sciences, Laboratory of Pharmaceutical Chemistry, Drug Analysis and Drug Information
Vrije Universiteit Brussel

Prof. Dr. Steven Ballet, Promotor
Department of Chemistry, Research Group of Organic Chemistry
Vrije Universiteit Brussel

Prof. Dr. Ann Van Eeckhaut, Co-promotor
Department of Pharmaceutical Sciences, Laboratory of Pharmaceutical Chemistry, Drug Analysis and Drug Information
Vrije Universiteit Brussel

Prof. Dr. Dimitri De Bundel, Co-promotor
Department of Pharmaceutical Sciences, Laboratory of Pharmaceutical Chemistry, Drug Analysis and Drug Information
Vrije Universiteit Brussel

Prof. Dr. Vicky Caveliers, Co-promotor
In Vivo Cellular and Molecular Imaging Laboratory
Vrije Universiteit Brussel

VRIJE UNIVERSITEIT BRUSSEL

PhD in Pharmaceutical Sciences
2018-2019

INVITATION to the Public defence of

An DE PRINS

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

Development and biological evaluation of neuromedin U analogs as tools for functional elucidation: focus on stress-related disorders.

Wednesday 12 December 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

It is accepted that neuropeptides have an enormous therapeutic potential due to the observation that they are preferably released when the nervous system is challenged or stressed. Since psychiatric and neurological disorders comprise a medical field with unmet therapeutic needs, peptide drug candidates could possibly offer an answer to this unrequited demand.

Neuromedin U (NMU) is a highly conserved neuropeptide across species which is involved in a variety of physiological and pathophysiological processes. In the present study, we evaluated the NMU peptide system as potential target in the treatment of stress-related disorders. Our current hypothesis suggests that central-acting antagonists would reduce or normalize the functioning of the hypothalamus-pituitary-adrenal axis at the level of the paraventricular nucleus.

An elaborate structure-activity relationship study was performed around the NMU-8 sequence aiming for the development of potent, proteolytically stable and NMU receptor-subtype selective agonists and antagonists. A broad range of NMU-8 analogs have been developed, but all displayed agonist properties. One of the most promising NMU agonists has been tested for its anorexigenic properties, a function ascribed to NMU receptor agonists, in a food intake study and was found to reduce food consumption.

Finally, we demonstrated that central NMU-8 administration induces stress-related behavior in mice under normal physiological conditions. Moreover, it was found to worsen the outcome of stressful situations, such as the forced swim test. Additionally, activation of key brain regions, involved in the regulation of the stress-response, was observed.

Curriculum Vitae

An De Prins was born on 12th February 1990 in Vilvoorde, Belgium. In 2008 she started the study of Pharmaceutical Sciences at the Vrije Universiteit Brussel. After graduation in 2013, she obtained a doctoral grant from the Vlaams Agenschap Innoveren en Ondernemen (VLAIO) and started her doctoral research at the Center for Neurosciences (Department of Pharmaceutical Chemistry, Drug Analysis and Drug Information, Prof. Ilse Smolders) in collaboration with the Research Group of Organic Chemistry (Departments of Chemistry and Bio-engineering Sciences, Prof. Steven Ballet), both part of the Vrije Universiteit Brussel. Her research focused on the neuromedin U peptide system and its role in the regulation of the stress response. During her doctoral thesis, An visited the Laboratory for Molecular Pharmacology under supervision of Prof. Birgitte Holst and Prof. Mette M. Rosenkilde at the University of Copenhagen (Department of Biomedical Sciences), where she had the opportunity to learn and perform *in vitro* pharmacological receptor studies. An is author of six peer-reviewed publications, among which two as first author. One additional manuscript is currently in preparation. Her work was presented at various national and international scientific conferences orally and by poster presentations.