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VRIJE UNIVERSITEIT BRUSSEL

PhD in Pharmaceutical Sciences
2021-2022

INVITATION to the Public defence of

Lise VERBRUGGEN

To obtain the academic degree of

'DOCTOR OF PHARMACEUTICAL SCIENCES'

The cystine/glutamate antiporter system x_c^- and healthy (brain) aging

The defence will take place on

Monday, 28 March 2022 at 5 p.m.

In Auditorium Vanden Driessche
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

The public defence can also be followed online.
Please contact the PhD candidate for more information.

Summary of the dissertation

As the average life expectancy has been steeply rising, obtaining insight into the aging process has become a research priority. The cystine/glutamate antiporter, system x_c^-, has previously been identified as a potential therapeutic target in mouse models for age-related neurological disorders, such as Parkinson's disease. System x_c^- is involved in redox signaling and in regulating the immune response as well as the glutamatergic neurotransmission, all of which are affected during aging. Still, the possible role of system x_c^- in mediating the aging process has so far remained unknown. Therefore, the central aim of this dissertation was to investigate how system x_c^- deficiency affects the physiological aging process in mice, with a focus on the peripheral immune system and the hippocampus, a brain structure that undergoes profound age-related functional changes that contribute to cognitive decline. The results presented in this dissertation show that mice lacking a functional system x_c^- have an extended lifespan, are protected against age-related priming of the innate immune system as well as against age-related changes in the hippocampus and the concomitant decline in hippocampus-dependent memory. Targeting system x_c^- thus seems to have the potential to promote healthy aging and to prevent cognitive decline.

To translate these results towards a clinical setting, there is a need for the development of new molecules that selectively act on system x_c^-. In the second part of this dissertation, we showed that sulfasalazine, the most commonly used inhibitor of system x_c^-, shows adverse off-target effects. This limits its use as an inhibitor of system x_c^- in potential future clinical studies.

Curriculum Vitae

Lise Verbruggen was born on September 2nd 1992 in Mechelen. Lise has a bachelor's degree in Pharmaceutical Sciences and a master's degree in Drug Development from the Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel, Belgium. After obtaining her master's degree, she joined the Neuro-Aging & Viro-Immunotherapy research group (NAVI, Vrije Universiteit Brussel) in 2016, to start her doctoral research which focused on the cystine/glutamate antiporter system x_c^- and healthy (brain) aging. Lise was supervised by Prof. Dr. Ann Massie and Dr. Eduard Bentea. The results reported and discussed in her dissertation were published in two international peer-reviewed journals and presented at several national and international conferences. Since December 2020, Lise is active as a scientific collaborator in the Multidisciplinary Oncological Centre Antwerp (MOCA, Universitair Ziekenhuis Antwerpen), where she focuses on clinical research in the field of cancer.