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VRIJE UNIVERSITEIT BRUSSEL

KU LEUVEN

Joint PhD VUB & KU Leuven
2022-2023

INVITATION to the Public defence of

Ayla PAUWELS

To obtain the academic degree of

'DOCTOR OF MEDICAL SCIENCES'-VUB
'DOCTOR OF BIOMEDICAL SCIENCES'-KU LEUVEN

Biomarkers of MS disease course in the blood and in the gut

The defence will take place on

Monday, 21 November 2022 at 5 p.m.

In Auditorium Piet Brouwer
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brusse

Summary of the dissertation

Multiple sclerosis (MS) is a chronic, inflammatory and degenerative disease of the central nervous system, with a high incidence in young adults. It is characterized by substantial clinical heterogeneity, and prognostication remains notoriously difficult.

This research project investigated the prognostic potential of blood glial fibrillary acidic protein (GFAP), which has previously been proposed as a candidate biomarker for neurodegeneration. While neurofilament light chain (NfL), a more established biomarker in MS, related to disability worsening in a survival analysis, GFAP did not. This could be due to the small group of progressive patients in our study.

Second, this thesis aimed to contribute to a better understanding of whether and how the gut microbiota and MS disease course are linked. In a large cross-sectional case-control study, implementing methods that take into account the number of bacterial cells in a sample, fecal moisture content was identified as the most important covariate of gut microbiome variation, followed by MS phenotype. Short-chain fatty acid producers were decreased and the inflammation-associated *Bacteroides* 2 (Bact2) enterotype was increased in MS patients relative to controls, which remained significant after controlling for fecal moisture content. The Bact2 enterotype also proved to be associated with disability worsening in MS patients, indicating potential as a prognostic biomarker and as a treatment target, if these results are replicated. In a time-course analysis in recently diagnosed MS, starting a disease-modifying treatment did not alter gut microbiome variability. Finally, investigating gut microbiome metrics during and after a clinical relapse revealed inflammation-associated changes after a relapse, suggesting a link between gut and brain inflammation.

Curriculum Vitae

Ayla Pauwels was born in Jette, Brussels, Belgium, on the 8th of March 1994. In 2011, she obtained her medical degree with greatest distinction at the Vrije Universiteit Brussel (VUB), Belgium. Subsequently, she started her neurology residency at the VUB, in combination with a joint doctoral research project at the VUB and Katholieke Universiteit Leuven (KUL), Belgium.

For four years, she investigated associations between the gut microbiota and multiple sclerosis (MS) disease course, as well as the prognostic potential of blood glial fibrillary acidic protein and neurofilament light chain in MS, resulting in the present PhD thesis.