

The Epigenetic Landscape of Chronic Pain and Stress in Prominent Populations:

ME/CFS, Fibromyalgia, and Persistent Pain after Breast Cancer Surgery

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PUBLIC PHD DEFENCE FOR THE DEGREE OF
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& DOCTOR IN BIOMEDICAL SCIENCES (KU Leuven)

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ABSTRACT OF THE RESEARCH

Background:
Chronic pain affects approximately one in five adults, yet it remains unclear why some individuals develop persistent pain after an initiating event while others recover; genetic susceptibility explains only part of this variability. This thesis investigated whether DNA methylation, a dynamic epigenetic mechanism responsive to stress and other environmental exposures, contributes to chronic pain, with emphasis on stress intolerance, in patients with fibromyalgia and in women with persistent pain after breast cancer surgery (PPBCS).

Methods and results:
Part I reviewed the biology of stress intolerance and, in a randomised cross-over study, examined whether methylation of catecholamine-degrading enzymes (*COMT, MAOB*) underlies autonomic dysfunction in fibromyalgia. Patients showed blunted subjective and autonomic stress responses; structural equation modelling revealed disease- and context-dependent associations between methylation, catecholamines, and autonomic function, rather than differences in individual biomarkers. Part II demonstrated higher *OPRM1* promoter methylation in patients with fibromyalgia, including those with comorbid myalgic encephalomyelitis/chronic fatigue syndrome (n = 28), than in healthy controls (n = 26), independent of symptom severity and pain sensitivity. In Part III, 132 women were followed from before breast cancer surgery until six months postoperatively; baseline *MAOB* hypomethylation was associated with PPBCS, but this exploratory finding was not robust to sensitivity analyses, and baseline methylation added no predictive value beyond clinical variables.

Conclusions:
No single epigenetic marker explained or predicted chronic pain. The findings instead indicate subtle, interacting, and context-dependent methylation changes within stress- and pain-related pathways. By employing repeated-measures designs and targeted methylation panels, this work provides a methodological foundation for larger, multi-layered epigenomic studies of chronic pain.

CURRICULUM VITAE



Arne Wyns (born February 23, 1998) obtained his master's degree in Biomedical Research (Great Distinction) at the Vrije Universiteit Brussel (VUB) in 2022. That same year, he began his PhD research at VUB and KU Leuven within the Pain in Motion Research Group, funded by the Berekuyl Academy Chair in rehabilitation oncology (the Netherlands). Arne has (co-)authored 13 peer-reviewed publications and has presented his work at international conferences in the USA and Brussels. He also took part in science communication events such as De Dag van de Wetenschap. Arne secured competitive funding, including a KU Leuven Global Seed Fund (2025) and an FWO travel grant, and completed a three-month research stay in 2025 at the University of Auckland, New Zealand. Alongside his research, he served as teaching assistant at the Berekuyl Academy, supervised 3 master's thesis students (VUB and KU Leuven), 4 laboratory rotation students and 6 Berekuyl students, and was jury member for 6 master's thesis defences. From 2023 to 2025, Arne was president of the doctoral committee "PhD United", representing the doctoral candidates of the Life Sciences & Medicine Doctoral School at VUB, where he co-chaired the annual PhD Day and organised social and science communication events. Within the Pain in Motion management team, he served as PhD representative and social event manager. Arne is dedicated to unravelling the biological mechanisms of chronic pain and stress, combining scientific rigour with the ability to communicate complex research to a broad audience.