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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2021-2022

INVITATION to the Public defence of

Stefanie BROCK

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

Genotype-Phenotype correlations in Malformations of Cortical Development (MCD) – integrating complementary approaches for a better understanding of MCD

The defence will take place on

Thursday, **13 January 2022 at 4 p.m.**
In Auditorium Vanden Driessche

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

ADMITTANCE: Due to Covid restrictions, please contact the PhD candidate if you want to attend the public defence in person.

The public defence can also be followed online through the following link:

https://gf.vub.ac.be/redirects/PhD_defense_Stefanie_Brock.php

Summary of the dissertation

The development of the human cerebral cortex requires precise regulation of three major processes. These include the proliferation of neuronal progenitor cells, neuronal migration and post-migrational organization of mature neurons into neuronal circuits. Malformations of cortical development (MCD) compromise a broad spectrum of disorders caused by acquired or genetic disturbances.

To date, more than 200 monogenetic causes of MCD have been reported, but correlations between clinical features and the genetic cause remain sparse.

This thesis includes seven studies that gather patients with rare phenotypes and correlate all available clinical and genetic data aiming at (1) expanding the phenotypic spectrum and establishing genotype - phenotype correlations for four genes (*TUBG1*, *TUBB2A*, *GRIN1* and *GRIN2B*) that have been associated with dysgyria, a subtype of MCD; (2) providing a comprehensive overview of the clinical and genetic MCD spectrum that is easily applicable in daily clinical practice with special focus on polymicrogyria, symptoms affecting the peripheral nervous system and the neuropathology of MCDs; and (3) correlating neuropathological and molecular features of MCD to provide further insight into the underlying mechanisms of normal and disturbed cortical development.

In addition, this thesis highlights the importance of tackling rare diseases such as MCD on a multidisciplinary and multinational level to provide a comprehensive understanding of the disease.

Curriculum Vitae

Stefanie Brock obtained her Master of Medicine at the Vrije Universiteit Brussel in 2018. She started her training to become a Pathologist in 2018 at the Department of Pathology at the Universitair Ziekenhuis Brussel. Despite her full-time clinical position, she simultaneously pursued working on her Ph.D. She continued research on genotype-phenotype correlations of Malformations of Cortical Development (MCD), which has already been her focus of interest during her B.sc and M.sc. thesis.

Stefanie is the author of 14 peer-reviewed publications (6 first author, 1 senior author and 7 co-author) and has presented her work at several international conferences. She is member of the COST Action 16118 – NeuroMIG, reuniting scientists worldwide to improve our understanding of MCDs.