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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2020-2021

INVITATION to the Public defence of

Christelle ORLANDO

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

Novel insights in inherited antithrombin deficiency: from laboratory diagnosis to clinical presentation.

The defence will take place on Tuesday, 15 June 2021 at 4 p.m.

and will be organised online

via Zoom meeting, accessible through the following link:

https://qf.vub.ac.be/redirects/PhD_defense_Christelle_Orlando.php

and in Auditorium Piet Brouwer

ADMITTANCE to the auditorium will only be granted upon presentation of the personal invitation from the PhD candidate.

Summary of the dissertation

Antithrombin is one of the most important inhibitors of blood coagulation. Inherited antithrombin deficiency is a rare disorder predisposing to the development of venous thromboembolism, even at young age.

Over the years, the UZ Brussel has become the reference center for inherited antithrombin deficiency in Belgium, resulting in a large database including over 450 patients. This gives us the unique opportunity to study a large number of patients and their family members. The work presented in this doctoral thesis addresses several aspects of inherited antithrombin deficiency.

We showed that commercial assays for measuring antithrombin activity in plasma differ greatly in their sensitivity to diagnose Antithrombin Type II Heparin Binding Site Deficiency, a subtype thought to be associated with a milder thrombotic phenotype. Our results suggest that this subtype might be more prevalent and less benign than previously assumed.

In a second part, we studied the molecular background of inherited antithrombin deficiency. Out of the 91 different mutations we identified in *SERPINC1*, the gene encoding for antithrombin, only 47 were reported previously. We characterized functionally one of these unreported mutations and proved that it is a founder mutation from Black-African origin.

In the last section, focusing on inherited antithrombin deficiency in children, we showed that neonates with Type I Antithrombin Deficiency are at high risk of developing cerebral venous sinus thrombosis. Invasive procedures during delivery were shown to be important risk factors.

Taken together, the results presented in this work contributed to our knowledge on laboratory diagnosis, molecular background and clinical presentation of inherited antithrombin deficiency.

Curriculum Vitae

Christelle Orlando was born on June 18th 1983 in Anderlecht, Belgium. After completing her secondary education at the Regina Caeli lyceum in Dilbeek, she started studying Biomedical Sciences at the Vrije Universiteit Brussel. She graduated *magna cum laude* in 2005 and started working as a scientific collaborator in the laboratory of hemostasis of the Universitair Ziekenhuis Brussel immediately thereafter. Christelle performed her PhD research on antithrombin deficiency under the supervision of Prof. Dr. Kristin Jochmans, while being responsible for the hemostasis unit of the clinical laboratory.

Christelle obtained a grant from the Wetenschappelijk Fonds Willy Gepts to fund her research.

Until now, she (co-)authored 14 papers published in international peer-reviewed journals. Her work was presented at several national and international scientific conferences. Christelle has been awarded twice the Paul Capel prize for best oral presentation by the Belgian Society on Thrombosis and Haemostasis (BSTH). Since 2020, Christelle is executive board member of the BSTH where she fulfills the task of secretary. She is also an active member of the Scientific Subcommittee on Plasma Coagulation Inhibitors of the International Society on Thrombosis and Haemostasis.

She lives together with her partner, Roel, and is the proud mother of Tobias, born in 2017.