SCIENTIFIC REPORT MEDIUM-TERM FELLOWSHIP

AWARDEE

Delfien Bogaert, MD

Function: PhD fellow, pediatrician-in-training

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PROMOTORS OF THE AWARDEE

1. Elfride De Baere, MD, PhD

   Function: Full professor, Head of DNA Laboratory, Senior Clinical Investigator FWO

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2. Filomeen Haerynck, MD, PhD

   Function: Clinician, Clinical Head Dept. of Pediatric Immunology and Pulmonology

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3. Melissa Dullaers, PhD

   Function: Postdoctoral researcher

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DETAILS OF THE RESEARCH STAY

Department of Laboratory Medicine, Clinical Center, National Institutes of Health (NIH), Bethesda, MD, USA

Under supervision of Dr. Sergio Rosenzweig

Period: August 2016 - January 2017

GOALS OF THE RESEARCH STAY AND HOW THEY WERE ACHIEVED

Primary immunodeficiencies (PID) are a heterogeneous group of disorders caused by inborn errors in immunity. In my doctoral research project, we focus on identifying the underlying genetic defect in patients with common variable immunodeficiency (CVID) and CVID-like disorders. By means of whole exome sequencing (WES), we have identified several candidate variants in our patient cohort in the last two years. The host institution is specialized in WES analysis and functional validation of candidate variants in the field of PID.

The goal of my research stay was to gain expertise in WES analysis and (especially) immunofunctional validation of candidate variants, and to transfer this expertise to our own research group in Ghent, Belgium.

In particular, I learned additional techniques regarding WES analysis: new analysis strategies, additional *in silico* prediction tools, and *in silico* protein modeling. Furthermore, I have learned numerous laboratory techniques required for functional validation: making cell lysates of PBMCs, western blot, (co-)immunoprecipitation, RNA extraction from PBMCs, several cell transfection techniques, gene cloning, luciferase reporter assay, etc. The newly learned laboratory techniques were immediately applied to the genetic variants identified in our Belgian patient cohort. First, new variants in the known disease genes *KMT2A*, *RNU4ATAC* and *IKZF1* were functionally confirmed by investigating protein expression, cDNA sequencing, etc. Second, extensive functional screening of variants in two novel candidate disease genes (undisclosed) was performed. Functional validation will be continued in our own research group in Ghent, in collaboration with the host institution.

Finally, I actively participated in the weekly lab meetings and attended research meetings and clinical case presentations.