Translational Research in inborn errors of immunity: bridging the gap between clinical practice and research

The Centre for Primary Immune Deficiencies Ghent (CPIG) is a multidisciplinary platform including clinicians, clinical biologists, geneticians, paramedics and researchers (Ghent University) treating patients with inborn errors of immunity. CPIG coordinates the clinical care, diagnostic work-up and research on more than 1,500 paediatric and adult patients with inborn errors of immunity (IEI), previously called primary immune deficiency (PID), followed at Ghent University Hospital (UZG).

© PIR - Prof. Dr. Filomeen Haerynck, principal investigator of PID research lab

Inborn errors of immunity (IEI)

IEI are a group of life-threatening genetic disorders of the innate and adaptive immune system. To date, the molecular defect of 480 IEI disorders has been unravelled which has led to significant improvement in the diagnosis and treatment of individual patients. Inborn errors of immunity most often lead to increased susceptibility to severe and/or recurrent infections. In addition, immune defects can also lead to immune dysregulation presenting with autoinflammatory and autoimmune manifestations and lymphoproliferation. IEIs are very complex, heterogenous and rare disorders. As a result, a large number of patients remains undiagnosed lacking appropriate treatment leading to irreversible organ damage and increased morbidity and mortality. This places a heavy burden not only on patients and families, but also on health care systems.

PID Research Lab (PIRL)

The PID research lab (PIRL), founded in 2015, is embedded in the Centre for Primary Immune Deficiencies Ghent (Ghent University and Ghent University Hospital) and builds

bridges between clinicians and researchers. Prof. Dr. Filomeen Haerynck is principal investigator of PID research lab and works together with the Inflammation Research Center at the Flemish Institute for Biotechnology (VIB, Ghent) and international collaborators (National Institutes of Health, Rockefeller University, Cleveland Clinic Research Centre (US), Imagine Paris (Fr), Garvan (AU)). PIRL accommodates a large biobank of more than 20,000 blood samples of patients with IEI and healthy controls. The Haerynck research team has an outstanding track record on IEIs, including Th17 immune disorders, common variable immune deficiency, auto- and hyperinflammatory syndromes and nucleic acid sensing defects. Prof. Haerynck published more than 138 manuscripts in peer-reviewed journals, resulting in a H-index of 39 and more than 9,600 citations.

Research Goals

The PID research lab aims to understand why some children and adults develop severe or life-threatening illnesses with certain microbes, while others exposed to the same microbe do not suffer such outcomes. Additionally, the lab investigates the mechanisms behind uncontrolled immune activation leading to autoinflammatory and autoimmune conditions. Haerynck’s lab employs high-throughput techniques studying patient cells, cellular and animal models to establish a connection between newly discovered genetic defects and the clinical symptoms observed in patients with a suspicion of IEI. Revealing monogenic holes in the host defence is pivotal for early diagnosis, genetic counselling of families and for the development of targeted treatments which will save many lives.

International Recognition

Since 2015, CPIG is recognized as a Jeffrey Modell Foundation Diagnostic and Research Centre. This recognition was instrumental in putting Ghent University and Ghent University Hospital on the international map in the field of translational and clinical research on inborn errors of immunity. In 2021, the CPIG was recognized as member of European Reference Network for Rare Immunodeficiencies, Autoimmune and Autoinflammatory disorders (ERN-RITA), which is pivotal for additional European clinical and translational research. Among the 72 members of ERN-RITA, only two are recognized in Belgium.

Cracking the Code Behind Severe Viral Infections

The Haerynck lab studies the human genetic and immunological determinants of life-threatening viral infections and reveals monogenic holes in the host defence.

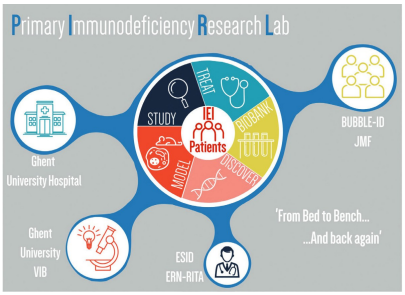
Herpes simplex virus 1 (HSV-1) infections are very common and usually cause only minor symptoms (Herpes Labialis). In rare cases, the HSV-1 infection goes awry and turns into herpes simplex encephalitis, a devastating brain disease that becomes lethal if left untreated. Haerynck's team, in collaboration with VIB Ghent (VIB Grand Challenge Project) and Gack lab (Cleveland Clinic institute), discovered at first a defect in GTF3A gene, a novel key gene that predisposes to HSV-1 encephalitis. They discovered a pseudogene, once considered 'junk' DNA, as an unexpected clue that solved the puzzle. Defects in GTF3A do not induce pseudogenes during HSV infection causing encephalitis.

Innovative Biomarkers for Inflammatory Diseases

The PID research lab coordinates the multi-centre FEBRIS study; a Flemish joint Effort for Biomarker Profiling in Inflammatory Systemic diseases. "We integrate cytokine profiles into the diagnostic workup and management of paediatric and adult patients with inflammatory syndromes such as systemic autoimmune diseases, autoinflammatory disorders, or hyperinflammatory conditions. The validation of our assay in larger cohorts with proven or suspected inflammatory disorders will guide time-, resource- and cost-efficient workup and personalized management."

About Filomeen Haerynck

Filomeen Haerynck, both paediatrician and researcher, started her research career in inborn errors of immunity with a fellowship at the department of Paediatric Immunology-Haematology at Hôpital Necker in Paris. In 2002, she was awarded with the GlaxoSmithKline Award in pneumopediatry and the Pfizer Educational grant. In 2014, she obtained her PhD on innate immunity in chronic infectious and inflammatory diseases. She is founder and coordinator of CPIG, director of Jeffrey Modell Foundation Diagnostic and Research Centre at Ghent University Hospital. Since 2017, she is full-time associate professor at Ghent University and principal investigator of PID research lab. She is the clinical head of the Department of Paediatric Pulmonology and Immunology at Ghent University Hospital and responsible for in- and outpatient paediatric clinics for inborn errors of immunity.



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