Board of examiners

Prof. L. Piemonti
Diabetes Research Institute
San Raffaele Scientific Institute, Milan

Prof. H-J. Aanstoot
Diabeter, Center for Pediatric and
Adolescent Diabetes Care and Research, Rotterdam

Prof. K. Casteels
Department of Pediatrics
UZ Leuven

Prof. B. Bravenboer
Departement of Endocrinology
UZ Brussel

Prof. E. Anckaert
Laboratory of Clinical Chemistry and Radio-immunology
UZ Brussel

Prof. C. Demanet
HLA and Molecular Hematology Laboratory
UZ Brussel

Prof. P. In't Veld, Chair
Department of Pathology, Molecular and Cellular Medicine
Diabetes Research Center, VUB

Promotoren:
Prof. F. Gorus
Diabetes Research Center, VUB
Laboratory of Clinical Chemistry and Radio-immunology, UZ Brussel
Prof. B. Keymeulen
Diabetes Research Center, VUB
Diabetes Clinic, UZ Brussel

Geneeskunde & Farmacie

GF

PhD in Medical Sciences
2015-2016

INVITATION to the Public defence of

Simke DEMEESTER

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

Biomarkers to predict functional outcome to beta cell therapy trials in type 1 diabetes

Tuesday 21 June 2016
Auditorium **Brouwer**, 17:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:
http://www.vub.ac.be/english/infoabout/campuses

Vrije Universiteit Brussel

Summary of the dissertation

Type 1 diabetes is a chronic T-cell-mediated autoimmune disease leading to a major loss of insulin-secreting beta cells, hyperglycemia and – if not well controlled – life threatening complications. Prevention strategies, aiming to arrest or slow the destruction of the beta cells (before or after clinical onset) or to restore a sufficient functional beta cell mass, have shown promising results, but overall benefits were transient and limited to subgroups. This indicates the need for precision medicine and the identification of biomarkers to discriminate responders from non-responders to a given therapy. In this respect, factors associated with rapid beta cell loss in the presymptomatic or peri-onset period of type 1 diabetes, such as antibodies against prominent islet antigens (insulin, GAD, IA-2, zinc transporter 8) and genetic susceptibility markers of type 1 diabetes (*HLA-DQ2/DQ8*, *-A*24*, *-B*18* and *-B*39*), are obvious candidates. We took advantage of the data and sample base from the previously reported first randomized placebo-controlled anti-CD3 study and from the islet cell transplantation program of the Center for Beta Cell Therapy in Diabetes. Our data suggest that the presence of insulin autoantibodies shortly after diagnosis, in addition to C-peptide release at study entry, predicts good responsiveness to anti-CD3 treatment. In long-standing patients receiving an intraportal islet allograft, presence of *HLA-A*24* and surges in autoantibody levels – most frequently GAD autoantibodies – shortly after implantation associate with poor functional outcome. These results illustrate that immunogenetic biomarkers are capable to identify good responders in beta cell therapy trials, but their nature and meaning may depend on the disease stage and the type of intervention.

Curriculum Vitae

Simke Demeester was born on May 12th 1987 in Asse, Belgium. She studied Pharmaceutical Sciences at the Vrije Universiteit Brussel (VUB; 2005-2010) and graduated as Pharmacist and Master in Drug Development with great distinction. In September 2010, she was appointed as teaching assistant in Chemistry and Biochemistry at the Faculty of Medical Sciences (VUB) and started in parallel a PhD in Medical Sciences at the Diabetes Research Center (VUB) under the guidance of Prof. Frans Gorus. Her PhD topic focused on the identification of good responders in beta cell therapy trials by means of immunogenetic markers. Until now, Simke is (co)author of 7 publications in international peer-reviewed journals and she presented her work at several national and international conferences. Her challenge for the next three years is to complete her training as clinical biologist in UZ Brussel which was initiated in combination with her research work.