INVITATION to the Public defence of

**Else M. BALKE**

To obtain the academic degree of ‘**DOCTOR IN MEDICAL SCIENCES**’

**Gene polymorphisms and clinical outcome at various stages of (pre)type 1 diabetes.**

**Thursday 6 September 2018**
Auditorium **Vanden Driessche** 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
Type 1 diabetes (T1D) is a chronic autoimmune disease leading to ablation of pancreatic beta cells and insulin deficiency. In the absence of a genuine cure, the patients depend on lifelong insulin replacement therapy to delay the onset chronic complications. The global incidence is rising annually, calling for prevention strategies aiming to impede the destruction of beta-cells or restore functional beta cell mass. In this context, we focussed on the role of genetic markers to predict clinical outcome at various stages of T1D. Given the strong inter-individual disease heterogeneity, current prediction models for T1D, based on HLA class II haplotypes and autoantibodies, need to be further refined. Several reports have associated the HLA class I alleles A*24, B*18 and/or B*39 with increased disease risk as well. However, their impact on the various asymptomatic stages of T1D, is less well documented. In a large cohort of islet autoantibody positive relatives of T1D patients followed for up to 20 years we showed that unlike HLA class II risk haplotypes, A*24 and B*18 accelerated progression to clinical onset from the stage of multiple autoantibody positivity on.

Next, we investigated whether these HLA class I alleles could also help predict graft outcome after islet cell allotransplantation in long-standing T1D patients. Retrospective analysis of data from a hospital-based patient cohort showed that A*24 carriersonhip hampers achievement of insulin independence. However, less than half of those who failed to achieve this endpoint, carried the allele. We subsequently identified presence of the T allele at rs13266634 of the SLC30A8 gene and high BMI as additional recipient factors associated with poor functional outcome. These findings may assist in the planning and interpretation of new intervention trials.

Else Marieke Balke was born in Deventer, the Netherlands, on August 21st in 1988. She attended secondary school at the ‘Bisschoppelijk College’ in Echt and majored in Nature, Science and Health. In 2007, she started a Bachelor of Pharmaceutical Sciences at the Catholic University of Leuven (KUL) and subsequently obtained her master’s degree in Drug Development and the title of Pharmacist. In 2012, she started working as a Graduate Teaching Assistant in Chemistry and Biochemistry at the Medical School of the Brussels Free University (VUB) and enrolled in the doctoral programme of Life Sciences and Medicine. Since then, she is conducting research at the Diabetes Research Center of the VUB on a project focussed on genetic markers of type 1 diabetes.