

PhD position in type 1 diabetes research

Ref. BAP-2019-662

Prof Chantal Mathieu's research team focuses on the pathogenesis of type 1 diabetes (T1D). Research areas of interest are in particular focusing on the special nature of the beta-cell, the possible role in its own destruction and more recently the specific role of inflammation-mediated post-translational modifications in the generation of beta-cell neo-autoantigens. Also her lab is well equipped for performing preclinical studies making use of animal models in T1D and especially demonstrating the value of the vitamin D hormone as a natural immune modulator. Recently her team brought antigen-specific therapies into a new dimension by oral delivery of antigens through genetically modified *Lactococcus lactus* bacteria.

The diabetes research group is part of the Laboratory of Clinical and Experimental Endocrinology, located at Campus Gasthuisberg, KU Leuven. Prof. Mathieu is the coordinator of a large-scale EU consortium INNODIA on translational approaches to disease modifying therapy of type 1 diabetes: an innovative approach towards understanding and arresting type 1 diabetes (www.innodia.eu). The available PhD position will fit in the goals of this EU consortium.

<https://www.kuleuven.be/onderzoek/portaal/#/projecten/user/U0009139?hl=nl&lang=nl>

Project

Applications are invited for a PhD position at the Laboratory of Experimental Medicine and Endocrinology at the KU Leuven, Leuven, Belgium for a project on 'Post-translationally modified beta-cell proteins: a driving force behind type 1 diabetes?'

The laboratory of Clinical and Experimental Endocrinology, headed by Prof. dr. Chantal Mathieu, has a position available for a highly motivated PhD student to study beta-cell autoimmunity with a strong focus on the interaction between immune system and insulin-secreting beta cells.

The position fits within the research interests of the lab, where studies are focusing on the interplay between the beta-cell and the immune system, translational research in T1D patient samples and prevention of autoimmune type 1 diabetes in pre-clinical models and immunological assays. Type 1 diabetes is an autoimmune disease characterized by progressive destruction of the insulin-secreting beta cells. It is a complex disease that results from the loss of tolerance to beta-cell autoantigens. This loss of tolerance can be caused by modifications of beta-cell autoantigens, generating 'neo-autoantigens', and inducing autoreactive T-cell responses. Our lab found that post-translational modifications, i.e. citrullination, of ER chaperones and their subsequent translocation to the plasma membrane of a dying beta cell impacts on type 1 diabetes pathogenesis. Post-translational modifications of beta-cell autoantigens provide a novel hypothesis to understand how autoreactive T cells can escape immune tolerance and cause destruction of beta cells. Additionally, aberrant proteins produced by stressed beta cells can cause their own destruction. This path of research will be taken to the next level in both preclinical in vivo studies and in human patient material. Experiments will involve mass spectrometry, cell culture, multi-color flow cytometry, immunohistochemistry, in vivo animal models, and standard biochemical/molecular approaches.

Relevant references:

Rondas D et al. *Diabetes*, 2015, 64(2):573-86;

Babon A. et al. *Nature Med*, 2016;22(12):1482-1487;

Crèvecoeur I. et al. *Diabetologia*, 2017(60): 475-489;

Buitinga M. et al., *Diabetes*, 2018 Nov;67(11):2337-2348);

Vig S et al., *Cell Death Dis.* 2019 Apr 5;10(4):309)

Profile

- Candidates must have a master in the field of biomedical sciences or equivalent.
- The candidate has excellent communication skills in written and spoken English.
- He/she is highly motivated to work in a multidisciplinary research team, as well as independently, has an open communication style and has a problem-solving attitude.

Offer

- As this PhD project is part of a large-scale international consortium INNODIA (www.innodia.eu), the candidate will be embedded in an international research team, where basic researchers and clinicians work closely together.
- The candidate will have access to state-of-the-art technologies, well-equipped core facilities, and a young and dynamic work environment.
- We offer a fully funded 4-year PhD position.

Interested?

Please email a motivation letter and complete curriculum vitae, and the name and contact information of 2 reference persons, latest by Nov 7th, to:

Dr. Lut Overbergh, email lutgart.overbergh@kuleuven.be.

For more information please contact Mrs. Lut Overbergh, tel.: +32 16 37 74 66, mail: lutgart.overbergh@kuleuven.be.

You can apply for this job no later than November 07, 2019 via the online application tool :

<http://www.kuleuven.be/eapplyingforjobs/light/55437578>

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