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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2016-2017

INVITATION to the Public defence of

Sofie DE GROEF

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

Signals that control beta cell formation and survival in injured mouse pancreas

Tuesday 31 January 2017
Auditorium **Piet Brouwer**, 16:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

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

Summary of the dissertation

Current diabetes research focuses on replacing or regenerating the lost insulin producing beta cell mass. These therapies depend on the identification of signals and signaling pathways that regulate beta cell survival, cycling and neogenesis. Partial duct ligation is a surgically induced injury model involving the ligation of the main pancreatic duct, resulting in severe injury and a two-fold increase in beta cell mass, the latter primarily caused by increased beta cell cycling and neogenesis from a NGN3 (re)expressing embryonic-type endocrine progenitor. Discrepancies in the literature stemming from this model, with regard to the increase of beta cell cycling and the extent of $NGN3^{+}$ progenitor cell differentiation towards endocrine cells, emphasize the need for a standardized protocol. In this thesis we provide a detailed protocol and a step-by-step video on how to perform PDL surgery and what outcomes to expect. PDL is used to assess the effect of inflammatory-mediated changes and cytokines and growth factors on endocrine cell survival, proliferation and neoformation. The JAK/STAT pathway, a prominent cytokine and growth factor responsive pathway, is highly activated in multiple pancreatic celltypes in PDL and, using pancreatic cell type-specific *Stat3* knockout mice, we have shown that it plays a role in protection of beta cells from excessive cycling and DNA damage in PDL, sculpting some of the processes that occur in PDL and regulating *Ngn3* expression levels. To further evaluate the role of immune cells in the processes observed following PDL, we have performed PDL surgery on two immunodeficient mouse strains and observed a negative effect on beta cell cycling but not on progenitor cell activation, suggesting a crucial role for immune cells in mediating beta cell proliferation in the PDL model.

Curriculum Vitae

During Masters in Biology (Cell, genetics and Developmental Biology), it was after an interesting course on Adult stem cells, taught by Prof. Harry Heimberg, that I had the opportunity to do my Masterthesis in the lab of Beta cell Neogenesis (BeNe), working on the Partial duct ligation model. During my Masterthesis I became fascinated by the progresses made in the last decades, on signals and signaling pathways that govern beta cell cycling, survival and neogenesis. After a successful application for a FWO mandate I started my PhD at BeNe. These 4 years of research allowed me to go deeper into the PDL model and try to unravel some of its mechanisms. Today undertaking this PhD has made me into a PhD researcher in medical sciences with experience in molecular, cellular and *in vivo* scientific research and expertise in signals and signaling pathways in insulin producing beta cells. I obtained skills including presenting scientific data at national and international congresses and in 11 publications in international peer-reviewed journals. Thanks to prof. Heimberg I also had the opportunity to teach master-courses and supervise masterstudents during their internships and Masterthesis, which contributed to a strong affinity for teaching. For the future I aim to pursue a career in science and research that can be combined with education.