

Board of examiners

Prof. dr. Francisco X. Real

Epithelial Carcinogenesis Group
Spanish National Cancer Research Centre, Madrid, Spain

Prof. dr. Marianne Voz

Laboratory of Zebrafish Development and Disease Models, GIGA
University of Liège, Liège, Belgium

Prof. dr. Leo van Grunsven

Laboratory of Liver Cell Biology
Vrije Universiteit Brussel, Belgium

Prof. dr. Willem Staels

Laboratory of Beta Cell Neogenesis
Vrije Universiteit Brussel, Belgium

Prof. dr. Harry Heimberg, Chair

Laboratory of Beta Cell Neogenesis
Vrije Universiteit Brussel, Belgium

Prof. dr. Ilse Rooman, Promotor

Laboratory of Medical and Molecular Oncology
Vrije Universiteit Brussel, Belgium

Prof. dr. Isabelle Houbracken, Co-promotor

Laboratory of Medical and Molecular Oncology
Vrije Universiteit Brussel, Belgium



PhD in Medical Sciences
2021-2022

INVITATION to the Public defence of

Elyne BACKX

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

The Neoplastic Potential of Pancreatic Cell Populations

The defence will take place on

Tuesday, 26 October 2021 at 5 p.m.

In Auditorium Piet Brouwer

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

ADMITTANCE: Due to Covid restrictions, please contact the PhD candidate if you want to attend the public defence in person.

and will be organised online
via Zoom meeting, accessible through the following link:

https://gf.vub.ac.be/redirects/PhD_defense_Elyne_Backx.php

Summary of the dissertation

Pancreatic ductal adenocarcinoma (PDAC), the most common form of pancreatic cancer, is the third leading cause of cancer-related deaths. Because of late diagnosis and a lack of effective therapies, it is necessary to understand the molecular pathology in the context of predisposing conditions. Pancreatitis is a typical example of a predisposing condition that induces dedifferentiation of pancreatic acinar cells, with activation of embryonic markers reminiscent of duct cells, making them susceptible to tumour development.

This PhD project aimed at understanding this first step in pancreatic tumorigenesis by studying dedifferentiated acinar cells both in human and mouse adult pancreas and during embryonic development of the mouse pancreas. Specifically, the first objective was to uncover the difference in transcriptional expression profile between dedifferentiated (duct cell-like) acinar and native duct cells and to identify a transcription factor, MECOM, uniquely expressed in dedifferentiated acinar cells that had priority for further investigation in the context of tumor development; the second objective was to characterize this specific transcription factor in the context of acinar dedifferentiation and pancreatic tumor formation and the third objective to study the priority transcription factor in pancreatic embryonic development. Loss of MECOM resulted in a distinct phenotype with impaired cell adhesion, more prominent cell death and suppressed acinar cell dedifferentiation by limiting ERK signaling, but its role seemed redundant during embryonic development of the pancreas. Together, this gives us more insight in the early steps that facilitate tumor formation.

Curriculum Vitae

Elyne obtained her Master degree of Biomedical Sciences at the University of Antwerp, after performing a research internship at the Laboratory of Molecular Parasitology at i3s Institute in Porto, Portugal. Her master thesis described the implementation of CRISPR/Cas9-mediated gene editing and luciferase-based *in vivo* imaging of the protozoan parasite *Leishmania infantum*.

In November 2016, she started her PhD in Medical Sciences at the Laboratory of Medical and Molecular Oncology. Under the supervision of Prof. dr. Ilse Rooman and Prof. dr. Isabelle Houbracken, she focused on the characterization of a transcription factor in the context of pancreatic acinar cell (de)differentiation using different *in vitro* and *in vivo* human and mouse experimental models. During her PhD project, she published in international high-impact journals and presented her work at several (inter)national symposia. In January 2020, she performed a research internship at the Centre for Stem Cell and Regenerative Medicine at King's College London for which she was granted an FWO travel grant. During her PhD trajectory, she was also a member of the Ethical Committee for Animal Experimentation and received a Prijs Kankeronderzoek granted by the Oncology Research Centre of the VUB in 2020.