SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Laboratory of Cell Genetics (CEGE)

has the honour to invite you to the public defence of the PhD thesis of

Ying MENG

to obtain the degree of Doctor of Sciences

Title of the PhD thesis:

Functional characterization of novel genes involved in the mesodermal-cardiac differentiation of mouse embryonic stem cells

Promotor:

Prof. Dr. Luc Leyns

The defense will take place on

Wednesday, July 1, 2020 at 9:00
via Teams in this link

Members of the jury

Prof. Dr. Gustavo J. Gutierrez (VUB, chairman)
Prof. Dr. Geert Raes (VUB, secretary)
Prof. Dr. Luc Leyns (VUB, promotor)
Prof. Dr. Karen Sermon (VUB)
Prof. Dr. Isabelle Migeotte (ULB)
Prof. Dr. An Zwijzen (KUL)

Curriculum vitae

Ying Meng graduated as a veterinarian from Jilin University (China) in 2010. She obtained the Master degree of Veterinary Medicine in 2013 from Jilin University. She started her PhD study that focused on cell genetics and embryonic development. So far, her PhD research led to 3 first author publications in international peer-reviewed journals.

Abstract of the PhD research

During early embryogenesis in mice, precise regulation of gene expression and signaling pathways is responsible to ensure the correct occurrence of gastrulation, lineage specification, and the differentiation of tissue progenitors. In order to analyze the mouse embryonic development in vitro, mouse embryonic stem cells (mESCs), possessing the capacity to self-renew and differentiate into all adult cell types, can be aggregated to form three-dimensional embryoid bodies (EBs), which roughly mimic the early stages of embryogenesis.

The objective of my PhD research was to characterize the biological functions of novel genes and their interplay with signaling pathways during mESC differentiation. Initially, we adapted and implemented the CRISPR/Cas9 system in our laboratory to generate loss-of-function mutant mESC models of Nodal and the C-terminal tail (C'-tail) of ß-catenin, which were used as "baseline" control models, in order to display the phenotypes for the loss of Nodal and Wnt/ß-catenin signaling in our in vitro EB platform. Then, the mutations of two novel genes (Pcgf5 and Cgnl1) and the deletion of the C'-tail of ß-catenin were further characterized. We explored their developmental functions through analyzing the phenotypes of these gene mutants during mesodermal-cardiac EB differentiation, including pluripotency exit, germ layer specification, epithelial-mesenchymal transition (EMT), and cardiogenesis.

Polycomb group (PcG) ring finger 5 (PCGF5) is traditionally regarded as a type of epigenetic transcriptional repressor protein that plays a role in gene silencing. In our study, we found that knockout of Pcgf5 influenced germ layer formation, cardiac cell lineages, and EMT processes during EB differentiation. By investigating the effects on different signaling pathways, we highlighted that Pcgf5 was involved in the regulation of the Notch pathway genes.

Cingulin-like 1 (CGNL1) cooperates with other apical junctional proteins to ensure cellular adhesion. However, other functions of Cgnl1 in the regulation of stem cell self-renewal and differentiation remained largely unexplored. In our study, we showed that our Cgnl1 mutation led to the dysregulation of the Wnt/ß-catenin pathway, as well as germ layers differentiation and EMT progression during EB differentiation. Remarkably, activating the Wnt signaling globally rescued the expression phenotypes of Cgnl1 mutant EBs, reflecting that Cgnl1 was involved in a series of early differentiation processes, likely in association with the Wnt/ß-catenin pathway.