SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Molecular and Cellular Life Sciences

has the honor to invite you to the public defense of the PhD thesis of

Yang LIU

to obtain the degree of Doctor of Sciences

Title of the PhD thesis:

Identification and characterization of genes involved in the differentiation of mouse embryonic stem cells towards mesodermal and cardiac cell types.

Promotor:

Prof. Luc Leyns

The defense will take place on

February 5 2020 at 17:00h

in Auditorium D2.01 at the Campus Humanities, Sciences and Engineering of the Vrije Universiteit Brussel, Pleinlaan 2 - 1050 Elsene, and will be followed by a reception.

Members of the jury:

Prof. Gustavo Gutierrez (chairman)
Prof. Geert Raes (secretary)
Prof. Karen Sermon
Prof. Isabelle Migeotte (ULB)
Prof. An Zwijsen (KUL)

Curriculum vitae

Doctoral student of Science: 2012-2019 - Vrije Universiteit Brussel.
Master in Veterinary Medicine: 2011-2012 - Jilin University, China.

Publications:

"Loss of Emp2 compromises cardiogenic differentiation in mouse embryonic stem cells."Y. Liu, E. Dakou, Y. Meng, L. Leyns Biochemical and Biophysical Research Communications (2019) 511(1):173-178

"Wnt/β-catenin signaling contributes the mESC differentiation towards cardiac-related formation correlated with Nodal and Bmp4 pathways." submitted

Abstract of the PhD research

To better understand the mouse embryonic development, especially the gastrulation stage, we established an *in vitro* mouse embryonic stem cell (mESC) platform allowing the investigation of the critical processes and involved genes during embryoid body (EB) differentiation. Wnt/β-catenin is a crucial signaling pathway that modulates the differentiation during the gastrulation process. We generated the *Wnt3*, *Wnt8a*, and *Wnt2b* knock-out mESCs and differentiated them into EBs, in order to unveil the effects caused by the loss of these genes and find out the molecular mechanisms underlying the distinct phenotypes obtained.

To achieve that, we utilized TALEN and CRISPR DNA-editing tools. Besides, we developed a culture of three-dimensional EBs aggregating mESCs as an *in vitro* cell differentiation model.

Our results highlighted the importance of *Wnt8a* and *Wnt2b* in the mesodermal and cardiac differentiation, with *Wnt8a* being more essential, which was evidenced by the delayed EB morphogenesis upon the loss of *Wnt8a* or *Wnt2b*. Our results also suggested that the defects in Wnt/β-catenin signaling affected the exit from naïve to primed pluripotency during lineage-commitment differentiation, as well as the EMT progression. Moreover, our data illustrated the influence of Wnt/β-catenin signaling on other fundamental signaling pathways.

Finally, we also explored the biological functions of a series of novel genes including *epithelial membrane protein 2* (*Emp2*). We found that *Emp2* participated in the gastrulation-like and cardiac-relevant differentiation. Furthermore, we discovered a connection between *Emp2* and Wnt/β-catenin pathway by activating the Wnt/β-catenin signaling to rescue the phenotype of *Emp2* knock-out EBs. We also attempted to find out the potential link between *Emp2* and FAK/Src, which was analyzed based on the specific inhibition of FAK/Src EB models.

In this thesis, we characterized a series of genes involved in the gastrulation-like and cardiac differentiation of mESC using the EB formation and differentiation platform.