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PhD in Pharmaceutical Sciences  
2016-2017

INVITATION to the Public defence of

**Jennifer BOLLEYN**

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

**Is microRNA-based differentiation a new strategy for the development of metabolically stable long-term hepatic cell cultures, applicable in pre-clinical drug development?**

**Tuesday 27 September 2016**

Auditorium **Brouwer**, 17:00

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:

<http://www.vub.ac.be/english/infoabout/campuses>



Vrije Universiteit Brussel

## Summary of the dissertation

The major cause of drug attrition in drug development and post-market withdrawal of an approved drug is drug-induced liver injury. As such, an important goal of the pharmaceutical industry is to uncover this type of toxicity as early as possible in the drug development process.

Cultured hepatocytes have been recognized as the *in vitro* model that most closely represents the *in vivo* liver situation as they are able to retain most differentiated liver-specific functions. Nonetheless, their routine implementation for long-term studies is limited by the progressive deterioration of their liver-specific features. In order to prolong hepatocyte survival and functionality in culture, the host lab introduced a new, molecular anti-dedifferentiation strategy by interfering with epigenetic mechanisms in order to better maintain the *in vivo* hepatocellular phenotype *in vitro*. Over the last years, microRNA-mediated gene silencing mechanisms also gained interest in several research areas as they are able to post-transcriptionally regulate gene expression *via* translational repression or mRNA degradation. Hence, the main goal of this thesis was to investigate the role of these microRNAs in the hepatic (de)differentiation process in order to see whether they could represent a novel target or tool to develop metabolically stable long-term hepatocyte cultures. First, the role of microRNA in hepatic dedifferentiation was studied. Next, the *in vitro* modulation of some specific microRNAs in favour of the *in vivo* differentiated hepatocellular phenotype was envisaged. At last, the rat liver progenitor cell line rLEC was used to investigate the role of microRNAs and their mRNA target interactions during hepatic differentiation.

## Curriculum Vitae

Jennifer Bolleyn was born on December 10, 1986 in Etterbeek, Belgium. She attended secondary school at the Onze-Lieve Vrouwecollege, Vilvoorde where she majored in Science-Mathematics. In 2004, she started the study of Pharmaceutical Sciences at the Vrije Universiteit Brussel (VUB). Her master thesis, entitled 'Karakterisatie van ongedifferentieerde stam/progenitorcellen van verschillende weefsels en species' was carried out at the department of *In Vitro* Toxicology and Dermato-Cosmetology (IVTD). She graduated in 2009 and subsequently started a PhD in Pharmaceutical Sciences on 'Is microRNA-based differentiation a new strategy for the development of metabolically stable long-term hepatic cell cultures, applicable in pre-clinical drug development?' at the same department under the promotorship of Prof. T. Vanhaecke, Prof. J. De Kock and Prof. V. Rogiers. Jennifer's core scientific interests are situated in the field of *in vitro* toxicology, molecular biology, microRNA, hepatocyte cultures and stem cells. She authored 12 scientific publications in international peer-reviewed journals and books, of which 6 as a first author. The results obtained during her doctoral research were presented orally and/or by poster at several national and international scientific congresses. During her PhD, she successfully obtained the certificate of 'expert laboratory animal leader' (FELASA C) and completed the study of Industrial Pharmacy. Jennifer was also co-promoter of 6 master theses and assisted in the practical courses of 'Algemene Toxicologie', 'Farmaceutische toedieningsvormen', 'Farmaceutische Technologie I and II', 'Bio-farmaceutische analyse- geïntegreerd practicum' and the project-related courses 'Moleculen van het leven' and 'Lijnproject' for pharmacy students.