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PhD in Medical Sciences
2017-2018

INVITATION to the Public defence of

Leslie STRADIOT

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

Modulation of liver fibrosis by targeting hepatic stellate cells.

Monday 18 December 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

Liver fibrosis is a chronic liver disease, caused by different insults including viral infections, metabolic syndrome, alcohol abuse and drugs. The activation of hepatic stellate cells is a key event to drive this development, which makes them an interesting target for the development of antifibrotic treatments. Still, most therapies are etiology-driven like lifestyle changes or directly acting antiviral agents. Developing an anti-fibrotic therapy specifically would be relevant to treat a bigger group of patients. To achieve this, it is essential to gain a complete view of the inter- and intracellular signaling pathways that are involved in fibrosis. These pathways can consequently help to develop a targeted therapy, ideally specific to hepatic stellate cells. We focused on these different aspects during the experiments that were performed to obtain this PhD. The first part of our study focused on the role of P311 in the development of liver fibrosis, as it was shown for other tissues to stimulate scar formation. We determined that P311 could indeed reduce stellate cell activation in vitro, however its absence in our mouse model did not reduce fibrosis development in vivo. Secondly, we aimed to optimize a protocol to deliver sorafenib, a therapeutic used to treat hepatocellular carcinoma patients, specifically to hepatic stellate cells by encapsulating it in targeted liposomes. This cell specific targeting should reduce side effects and increase efficiency. To conclude we optimized a new isolation protocol, which allows the simultaneous isolation of different cell types from the same mouse. This isolation method should facilitate the use of different cell types in vitro to develop more specialized fibrotic culture models, which could replace the use of animal models in the future.

Curriculum Vitae

Leslie Stradiot initiated her career at the VUB in 2007, when she started studying biomedical sciences. During this period she performed two short internships, one at the Centre of Medical Genetics and one at the Liver Cell Biology Lab. She concluded her education with her master thesis "The role of PW1 in pancreas development and adult islet cells", which she defended in June 2012. For her PhD she returned to the field of hepatology and obtained in December 2012 an IWT SBO grant, which allowed her to perform basic research for four years. During this period, she published two first author papers and contributed to two other manuscripts. She presented her work on national and international congresses. Aside from her scientific work she has been part of different event organizing committees.