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FACULTEIT GENEESKUNDE EN FARMACIE

Doctoraat in de Medische Wetenschappen
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UITNODIGING

Voor de openbare verdediging van het
doctoraatsproefschrift van

Sophie HERNOT

donderdag 29 september 2011

U wordt vriendelijk uitgenodigd op de openbare verdediging van het proefschrift van

Sophie HERNOT

'Nanobody-Loaded and –Coated Microbubbles : A Tool for Drug Delivery and Molecular Imaging'

Op **donderdag 29 september 2011** om **17 uur** in auditorium **auditorium 3** van de Faculteit Geneeskunde & Farmacie Laarbeeklaan 103, 1090 Brussel

Situering van het proefschrift

Many publications have demonstrated that ultrasound contrast agents or microbubbles (µBs) became indispensable tools for functional and molecular imaging. Additionally, µBs can act as drug delivery systems, where drug delivery is triggered by ultrasound. The aim of this thesis is to develop µBs for targeted drug delivery and molecular imaging by making use of small antigen binding fragments called nanobodies. In the first part, we will investigate the bio-effects caused by ultrasound-mediated µB destruction. More specifically, we will evaluate in a rat model the impact of these effects on perfusion and function of the heart using a technique called pinhole-gated SPECT. Secondly, as µBs themselves have been proposed as drug delivery vehicle, we will design polymeric µBs that allow loading of nanobodies in order to improve the pharmacokinetics of the nanobody. These µBs will be characterized and evaluated for ultrasound-triggered drug release. Next, we will focus on the molecular targeting of the vascular cell adhesion molecule VCAM-1, a marker of inflamed endothelium. Hereto, nanobodies will be generated against this target. The application of radioloabeled anti-VCAM-1 nanobodies for the noninvasive imaging of atherosclerosis will be studied in vivo and a lead compound will then be selected for further experiments. Finally, by coupling the selected lead nanobody to the surface of µBs, VCAM-1 targeted-µBs will be designed and characterized. This system will in the end be evaluated in vivo for the molecular imaging of VCAM-1 expression with ultrasound.

Curriculum Vitae

Sophie Hernot was born on September 17th, 1983 in Uccle, Belgium. After graduation from Mater Dei Institute in Sint-Pieters-Woluwe in 2001, she studied Bio-engineering at the Vrije Universiteit Brussel and chose the division cell and gene biotechnology, medical biotechnology. She obtained her MSc degree in 2006 after completion of her master thesis on 'In vivo Imaging of Tumors Using Radiolabeled Nanobodies'. This work was performed under the supervision of prof. P. De Baetselier (Laboratory of Cellular and Molecular Immunology, CMIM) and prof. T. Lahoutte (Laboratory of In vivo Cellular and Molecular Imaging, ICMI). Later that year, she also obtained the European Certificate category C on Laboratory Animal Sciences. She continued in the ICMI group to perform her PhD research, where she investigated the application of 'Microbubbles and Nanobodies for Drug Delivery and Molecular Imaging Purposes'. In 2007 and 2011, she worked during 5 months as a research fellow at the University of Virginia, Charlottesville, VA, USA in collaboration with prof. A.L. Klibanov. Her PhD-research resulted in 17 publications, of which 4 as first author in peer-reviewed journals.