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van

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**'Molecular imaging with radiolabeled
anti-HER2 nanobodies for improved
diagnosis and follow-up of breast
cancer - the road to clinical
translation'**

Op **dinsdag 27 september 2011 om 17 uur**
in auditorium **P. Brouwer** van de
Faculteit Geneeskunde & Farmacie
Laarbeeklaan 103, 1090 Brussel

Situering van het proefschrift

Nanobodies, the smallest intact antigen-binding fragments isolated from heavy-chain camelidae antibodies, can target cancer-associated antigens with high specificity. Besides their small size, they are stable, soluble and rapidly eliminated from the bloodstream, all ideal characteristics for molecular imaging probes. We hypothesize that non-invasive molecular imaging of HER2 expression with a radiolabeled anti-HER2 nanobody will offer superior diagnostic performance. The procedure is fast, painless and sampling errors with biopsies are avoided. The imaging procedure can be repeated multiple times so that HER2 overexpression can also be monitored during the disease process. This allows to select patients that are susceptible to a targeted therapy and to monitor the therapy response. In patients that do not have HER2 positive breast cancer, expensive and potentially toxic treatment can be avoided. The aim of this thesis is to evaluate radiolabeled HER2-targeting nanobodies in a preclinical setting, focused on the final endpoint to provide a new radiopharmaceutical that can be translated to a clinical setting for molecular PET imaging of HER2 in breast cancer patients. The thesis is outlined in four parts: Although nanobodies are considered to be low immunogenic, in the first part we investigate if further humanization of nanobodies is feasible. A second part is aimed at a pre-clinical screening of different anti-HER2 nanobodies to select the lead compound for a phase I clinical trial. In a third and fourth part, we propose methods to label the lead nanobody with 68Ga and 18F for PET applications.

Curriculum Vitae

Ilse Vaneycken was born in Mechelen in 1983. She studied Math-Sciences at the Onze-Lieve-Vrouwe college in Vilvoorde where her interest in sciences was intensified. In 2007, she graduated with great distinction in Biomedical Sciences at the Vrije Universiteit Brussel. Motivated by the enthusiasm of the promoters of her master thesis, Dr. Apr. Vicky Caveliers and Prof. Dr. Tony Lahoutte, she started her PhD project in October 2007 at the In vivo Cellular and Molecular Imaging laboratory of the Faculty of Medicine and Pharmacy of the Vrije Universiteit Brussel. This was the beginning of 4 valuable years. Her successful work about anti-HER2 nanobodies got a lot of attention and was published on different websites, among which Science Dailey. In 2010, she received an Emmanuel Van der Schueren grant of the Vlaams Liga Tegen Kanker, a founding for young promising scientists in cancer research, to round off her PhD. Also, her work was often selected for oral presentation on international molecular imaging meetings. Her research has contributed to 4 peer-reviewed publications in well-established international journals of which she is first author of 3 and which form the subject of this thesis.

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FACULTEIT GENEESKUNDE EN FARMACIE

Doctoraat in de Medische Wetenschappen

Academiejaar 2011-2012

UITNODIGING

Voor de openbare verdediging van het
doctoraatsproefschrift van

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dinsdag 27 september 2011