MEDICAL IMAGING RESEARCH GROUP

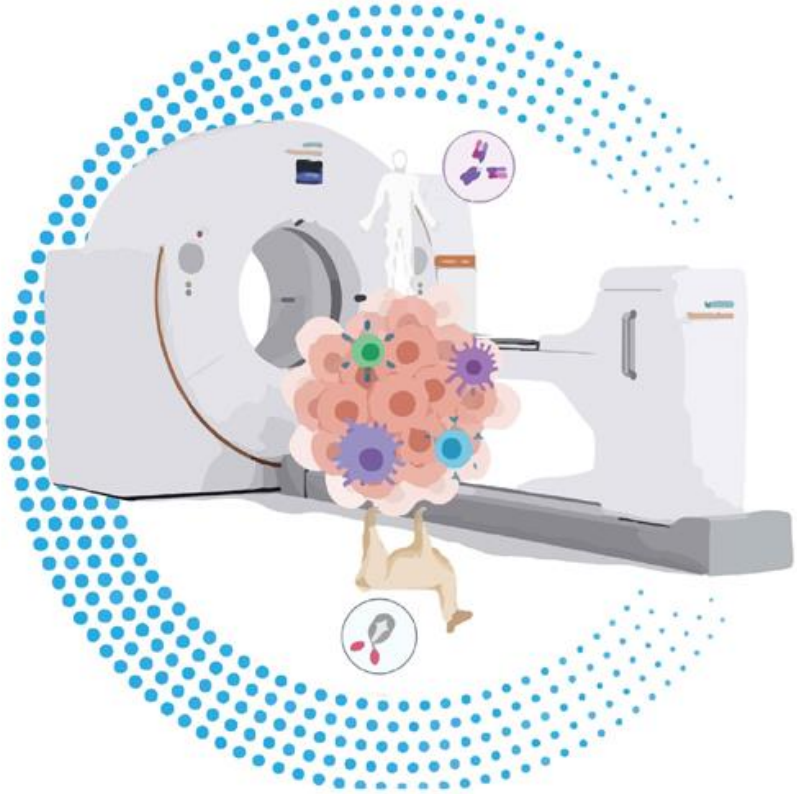
ICMI Brussels
In vivo Cellular & Molecular Imaging

Workshop

Immuno-Imaging and Molecular Therapy

April 19th- April 23rd 2021

8th Edition



innovative medicines initiative

efpia

ImmuneImageO

Online Workshop Immuno-Imaging and Molecular Therapy

Workshop description:

Due to their low immunogenicity, high affinity/specificity and flexibility towards biotechnological engineering, antibodies are interesting vehicles for molecular diagnosis, imaging and therapy.

The online workshop 'Immuno-imaging and molecular therapy' aims to bring together national and international experts in the fields of antibody-engineering, clinical and preclinical nuclear imaging, tracer design, image acquisition and reconstruction, (radio)chemistry, targeted radionuclide therapy, optical and microscopic imaging, immunogenicity and intellectual property. Altogether, a full overview of the research topic 'immunotheranostics' will be provided. In particular, a special focus will be put on nanobodies as an example of engineered antibody vehicles for non-invasive imaging and targeted therapy. This year's workshop will take place in the week of April 19 to April 23. Lectures will be webcasted online, and timing of these lectures can be found below. The time slots are for Central European Time. The language of communications (lectures, discussions) will be English.

This year, the lectures will be complemented by presentations of researchers participating in the workshop. Everybody that performs independent research (Laboratory Technician, Research Associate, PhD student and Postdoctoral Fellow) is highly encouraged to submit an abstract in order to present their work. Ten time slots of 20 min per speaker will be foreseen during the workshop (10 min presentation and 10 min discussion). The workshop aims to create an atmosphere of good interaction, discussion and networking and aims to give young researchers a chance to enhance their presentation skills by presenting in front of a small audience. When you are registered for the workshop itself, you will receive an abstract template and a link to submit the abstract (not for MSc students). The deadline for abstract submission will be **March 22nd, 2021 before 5 PM.** Abstracts will be reviewed by a scientific panel of experts in the field of imaging and therapy. Results of the abstract review will be sent to the author within one week of submission.

For whom?

This online webcasted workshop is targeted towards anybody interested in the broad topic of 'immune-theranostics'. Basic knowledge of radiation, biotechnology, biochemistry, medicine and engineering is required. Master students in Biology, Biomedical Sciences, Biotechnology, (Bio)Chemistry, Medicine or Pharmacy, PhD students, technologists and postdoctoral fellows working or interested in this field of research are encouraged to participate. Participants can

be from any nationality and can follow the webcast from anywhere in the world. Participation to the workshop is free of charge.

How to participate?

Registration for the workshop will be via the link (https://docs.google.com/forms/d/e/1FAIpQLSfsObNJ8D5ndCcpBDxlt28T6PvBxNP0LNJYyeGrQFNESTuAGA/viewform?vc=0&c=0&w=1&flr=0). When you have registered, an acceptance mail will be sent to you, together with an abstract template, a link to submit the abstract and a link to an External Share subfolder of SharePoint. The latter will be used to share essential information like lecture slides and videos of the recorded lectures.

The different lectures of the workshop will be live webcasted using the tool Cisco WebEx meetings. You can use this tool either via your browser or you can download it. But first you will have to make an account on Webex via this link (https://www.webex.com). Click on sign up (free), enter your institutional email address and a new password. You will now already be able to follow the lectures or you can choose to also download the tool via (https://www.webex.com/downloads.html). First scroll down to download the previous app **Webex meetings**, then choose on which operation system you would like to download Cisco Webex Meetings (macOS or Windows).

MacOs: Click on download for macOS, the Webex app will appear in your downloads. Click on webexapp.dmg, a pop up will appear where you have to click on Cisco Webex Meetings.pkg. Next, a window will open named 'Install Cisco Webex Meetings', click on continue 3 times and finally install Webex. When the installation has succeeded, click on close. Go to your Launchpad and the app will appear. Click on the app and sign in with your Webex account to follow the lectures.

Windows: Click on download for Windows, the Webex app will appear in your downloads. Click on Webex.msi, open the file and it will say 'Welcome to the Cisco Webex Meetings Setup Wizard, click on next. A window will pop up where you have to agree to license terms and click install. You can now sign in with your Webex account to follow the lectures.

Once you registered for the workshop and made a Webex account, you will receive invites for each webcast lecture. Simply accept the invitation (RSVP), this lecture will then become visible in your agenda and on the day of the lecture click 'Join a Webex meeting' at the specific timeslot and you will be able to follow the presentation.

For the speakers that give a lecture, Safari does not support sharing your sceen during a Cisco Webex meeting, so you either have to download the tool or you will have to swith to the browsers google Chrome or Firefox.

Hence, the only things you need to participate the lectures are 1) a computer with installed Cisco WebEx meetings software (a mobile phone will also work but will be less practical if you would like to participate in the chat sessions); 2) a microphone (build-in or external); 3) a

headphone or earplugs; 4) a stable internet connection (preferentially using an ethernet cable, a stable WiFi connection will also work) and 5) a webcam (build-in or external).

Webcast schedule:

Monday April 19th to Friday April 23rd, 2021. A time slot is foreseen for each lecture, see program below. The PowerPoint slides of each lecture will be digitally made available to the participants at least a day before the live lecture.

Immune-Image:

This workshop is part of the Immune-Image project that has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 831514. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA. For more information on this project, see www.immune-image.eu and www.imi.europe.eu.

Disclaimer: all communications at the workshop only represent the presenters' view and the Joint Undertaking is not responsible for any use that may be made of the information it contains.

Registration and fee:

The registration deadline for this year's workshop is **April 12th 2021 and the deadline for abstract submission is March 22nd 2021**. We ask all participants, when registered, to maximally attend each lecture. In case this is not possible, please contact the organisers. The workshop is entirely free to attend. Simply register and attend the lectures.

Contact:
Yoline Lauwers
Email: yoline.lauwers@vub.be
Phone: +32 (0)2 477 4991

Organisation Committee:
Director: Prof Nick Devoogdt
Administration: Yoline Lauwers

Program:

Monday April 19th

09u00-10u00	Prof Nick Devoogdt (VUB) *Welcome, testing webcast service and introduction round of all participants*
10u00-11u15	Prof Nick Devoogdt (VUB) *Do's and don'ts in immunotracer design*
11u15-11u45	**Bio-break**
11u45-13u00	Prof Christian Van Hove (UGent) *Overview of imaging modalities, part I*
13u00-14u30	**Lunch**
14u30-15u45	Prof Christian Van Hove (UGent) *Overview of imaging modalities, part II*
15u45-16u00	**Bio-break**
16u00-16u20	Presentation from selected abstract
16u20-16u40	Presentation from selected abstract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Tuesday April 20th

09u00-10u15	Prof Marleen Keyaerts (VUB/UZ Brussel) *Introduction to clinical nuclear medicine*
10u15-10u35	Presentation from selected abstract
10u35-11u00	**Bio-break**
11u00-12u15	Dr Timo De Groof (VUB) *Nanobody discovery and biotechnological applications*
12u15-13u40	**Lunch**
13u40-14u00	Presentation from selected abstract
14u00-15u15	Dr Jessica Bridoux (VUB) *Radiochemistry of nanobodies*

Wednesday April 21st

09u00-10u15	Dr Ahmet Krasniqi (VUB) *Imaging with nanobodies in preclinical models*
10u15-10u35	Presentation from selected abstract
10u35-11u00	**Bio-break**
11u00-12u15	Prof Sophie Hernot (VUB) *Fluorescence applications of nanobodies*
12u15-13u40	**Lunch**
13u40-14u00	Presentation from selected abstract
14u00-15u15	Prof Geert Raes *(VUB/VIB)* *Intellectual property of biologics*

Thursday April 22nd

9u00-10u15	Dr *Chloé Ackaert (ImmunXperts inc, Belgium)* *Immunogenicity of proteins and nanobodies*
10u15-10u35	Presentation from selected abstract
10u35-11u00	**Bio-break**
11u00-12u15	Prof Matthias D'Huyvetter (VUB) *Targeted radionuclide therapy, focus on nanobodies*
12u15-13u40	**Lunch**
13u40-14u00	Presentation from selected abstract
14u00-15u15	Prof Marleen Keyaerts (VUB/UZ Brussel) *Clinical translation of nanobody-tracers*

Friday April 23rd

10u00-11u15	Dr. Marjolijn Lub-de Hooge (UMCG) *Molecular imaging to enlighten cancer immunotherapies and underlying involved processes*
11u15-11u35	Presentation from selected abstract
11u35-13u00	**Lunch**
13u00-13u20	Presentation from selected abstract
13u20-14u35	Kristof Muylle (UZBrussel / Bordet) *Potential impact of Immuno-PET on patient management*
14u35-15u00	**Bio-break**
15u00-16u00	*Online discussion survey*

Information about the lecturers:

Nick Devoogdt
Professor Vrije Universiteit Brussel (VUB)
Research cluster Imaging and Physical Sciences (BEFY)
In vivo Cellular and Molecular Imaging laboratory

Email: nick.devoogdt@vub.be
Phone: +32 2 477 4991

Nick Devoogdt was trained as a Master in Molecular Biology at the Free University of Brussels (Vrije Universiteit Brussel, VUB), where he obtained his degree with high distinction in 1997. He obtained an FWO scholarship and in 2004 obtained a PhD in Applied Biological Sciences under the promotorship of Prof De Baetselier, working on cancer genetics, cellular biology and immunity. Again, he acquired a FWO grant to continue his postdoctoral research for the periode 2004-2007. In 2004-2005 he was a visiting scientist at the National Cancer Institute in Bethesda USA, studying ovarian cancer genetics and biomarkers, after which he returned to VUB in Belgium for additional training as a postdoctoral scientist: in 2005-2006 in the field of cellular immunology and cancer genetics, in 2007 in antibody-engineering and from 2008 onwards in molecular imaging. In 2013 he became assistant professor in the small animal imaging lab ICMI and in 2016 tenure-track full professor. In 2014 he co-founded the spinoff company Camel-IDS (now called Precirix where he is still active as coordinator of the discovery pipeline). In 2020 he co-founded the spinoff company AbScint as well. He is currently workpackage leader in the Immune-Image IMI consortium.

His research aims to develop novel applications in molecular and nuclear imaging and targeted therapies. His current focus is on the nanobody-technology as targeting vehicles. More in particular, his research is focused on the generation of new probes for their application (nuclear or other types of imaging a therapy) in small animal models of disease, and in a second phase on testing in patients. Hence, his preclinical and translational research is supportive and closely connected with clinically oriented research teams within the faculty of medicine and the university hospital.

Christian Vanhove
Associate professor Ghent University
Medical Imaging and Signal Processing
Head of preclinical core imaging facility UGent (INFINITY)

Email: Christian.Vanhove@UGent.be
Phone: +32 9 332 4115

Christian Vanhove graduated as a Biomedical and Clinical Engineer from Brussels University in 1990. From 1991 until 1996, he worked as a Medical Physicist at the Nuclear Medicine department of the Sint-Elisabeth hospital in Zottegem, where he was doing research and developments for the industry in a clinical environment. Research and developments were focused on all aspects of medical image processing, including image reconstruction, image registration and image quantification. In 1996, he moved to the Nuclear Medicine department of the Brussels University Hospital. As a Medical Physicist Expert, he continued his research in the field of medical image processing and obtained his PhD in Medical Science in 2004. During his PhD, a new algorithm for the automatic segmentation and quantification of gated blood pool SPECT images, in both humans and small animals, was developed and validated. In 2005, he was one of the initiators of the small animal imaging lab of Brussels University and worked as a postdoctoral researcher at this preclinical imaging facility. During this period his research was focused on quantitative pinhole SPECT. Since February 2011, he joined the Medical Imaging and Signal Processing (MEDISIP) research group of the Faculty of Engineering of Ghent University, where he is responsible for the INnovative Flemish IN-vivo Imaging TechnologY (INFINITY) lab. This lab focuses on multimodal in-vivo imaging strategies and serves as a core facility for preclinical imaging within Ghent University. The major research domains of INFINITY are the evaluation of pathophysiology in neurological diseases, cancer and inflammation. Christian Vanhove is associate professor and lecturer in molecular imaging.

Marleen Keyaerts
Associate professor Vrije Universiteit Brussel –
In vivo cellular and molecular imaging laboratory
Head of clinics UZ Brussel – Department of nuclear medicine

Email: Marleen.Keyaerts@vub.be
Phone: +32 2 477 50 20

Marleen studied medicine at the Vrije Universiteit Brussel and performed her master thesis at the nuclear medicine department of the UZ Brussel on the biodistribution of a new radiopharmaceutical in healthy subjects. She immediately started her PhD at the ICMI lab after graduation, which was completed in 2011. In her PhD project, Marleen investigated bioluminescence imaging for the assessment of tumor burden. When she moved back to the clinic to complete her clinical training in nuclear medicine, a first nanobody lead compound was ready for first in human testing. Marleen was strongly involved in this phase I clinical trial using anti-HER2 Nanobody PET/CT imaging in breast carcinoma patients and she is currently primary investigator in multiple phase II trials involving nanobody-based imaging.

Timo De Groof
Postdoctoral Scientist at Vrije Universiteit Brussel
Research cluster Imaging and Physical Sciences (BEFY)
In vivo Cellular and Molecular Imaging laboratory

Email: Timo.De.Groof@vub.be
Phone: +32 (0)2 629 1980

Timo De Groof studied Biochemistry and Biotechnology at the University of Ghent where he graduated in 2015. During his master studies, he specialized both in Biomedical Biotechnology and Structural Biology/Biochemistry. During his last year of studies, De Groof performed research in the biopharmaceutical company Argenx where he gained experience on the identification and characterization of llama-derived antibodies in inflammatory diseases and oncology.
From 2015 to 2019, De Groof performed his PhD in the Medicinal Chemistry group at VU University Amsterdam under the supervision of prof. dr. Martine Smit where he focused on development and characterization of nanobodies targeting viral G protein-coupled receptors while also focusing on different applications of these nanobodies as therapeutics and research tools.
From September 2019, De Groof started working as a postdoctoral researcher in the In Vivo Cellular and Molecular Imaging (ICMI) group under the supervision of prof. dr. Nick Devoogdt. As part of the Innovative Medicine Initiative project “Immune Image”, he is currently focusing on the development of nanobody-based immunotracers for non-invasive imaging of immune cells during immunotherapy. Moreover, De Groof supervises, in collaboration with prof. Devoogdt, the immunization and nanobody generation process for the different projects within the ICMI group.

Jessica Bridoux
Postdoctoral Scientist at Vrije Universiteit Brussel
In vivo cellular and molecular imaging laboratory

Email: Jessica.bridoux@vub.be
Phone: +32 2 477 49 91

Jessica studied Engineering Chemistry at the National Engineering School of Caen (Ecole Nationale Supérieure des Ingénieurs de Caen, ENSICAEN, Caen, France) and obtained her diploma in 2016, as well as a Master in Organic Chemistry at the university of Caen, France. She worked for 6 months at PCAS (Limay, France), where she developed and optimized the synthesis process of an active pharmaceutical ingredient and learned about GMP manufacturing. In October 2016, Jessica started her PhD project funded by the Horizon 2020 Marie Curie Actions (PET3D) at ICMI, under the supervision of Prof. Dr. Catarina Xavier and Prof. Dr. Vicky Caveliers. She worked on the development of a radiolabeled Nanobody against the human PD-L1 receptor for PET immune-imaging. In the frame of this project, she spent 2 months at the Karolinska Institute, Stockholm, Sweden, where she focused on click-chemistry mediated radiofluorinations. After her PhD, she will stay at ICMI to focus on the clinical translation of radiofluorinated Nanobodies.

Chloé Ackaert
Senior Scientist at ImmunXperts

Email: Chloe.ackaert@immunxperts.com

Chloé studied Pharmacy at the Katholieke Universiteit Leuven and performed her master thesis at the Hôpital Bichat in Paris, the CHU in Charleroi and the UZ Antwerpen on Enzyme Replacement Therapy in Fabry disease patients. She did an internship in the laboratory of Therapeutic and Diagnostic Antibodies (KUL) on the Immunogenicity of anti-TNFα mAbs in IBD patients, followed by a PhD on the immunogenicity of modified allergens at the University of Salzburg in Austria. After her PhD, she was involved in the start-up of the CRO ImmunXperts, offering integrated immunogenicity services. Since 2015, Chloé worked in the Camel Antibody group within the Cellular and Molecular Immunology lab (VUB) where she focussed on studying the immunogenicity of Nanobodies. She performed the anti-drug antibody measurements in the phase I clinical trial using anti-HER2 Nanobody for PET/CT imaging in breast carcinoma patients and assessed the immunogenicity risk of several Nanobodies by *in vitro* methods. As of October 2018, she joined the team of ImmunXperts again, as a senior scientist for projects dealing with assessment of (un)wanted immunogenicity of biopharmaceuticals in development.

Sophie Hernot
Assistant Professor Vrije Universiteit Brussel – In vivo Cellular and Molecular Imaging Laboratory

Email: Sophie.hernot@vub.be
Phone: +32 2 477 49 91

Sophie Hernot obtained her Master of Science in Bio-engineering from the Vrije Universiteit of Brussels. She completed her PhD thesis in Medical Sciences in 2011 on the use of microbubbles (ultrasound contrast agents) as well as Nanobodies for molecular imaging and drug delivery applications. As post-doctoral researcher in the Laboratory of In vivo Cellular and Molecular Imaging (ICMI, VUB), her focus was initially on cardiovascular molecular imaging. Radiolabeled Nanobodies targeting markers of inflamed atherosclerotic plaques were optimized and their potential for the non-invasive imaging of atherosclerosis was demonstrated. As Tenure Track Professor since 2020, her research interests gradually shifted towards fluorescence molecular imaging in surgical and interventional applications. In this context, near-infrared fluorescently labeled Nanobodies are designed and preclinically validated as tools for image-guided surgery, with the aim of translating them to the clinic.

Matthias D'Huyvetter
Assistant professor Vrije Universiteit Brussel
FWO postdoctoral researcher
In vivo Cellular and Molecular Imaging laboratory

Email: Matthias.Dhuyvetter@vub.be
Phone: +32 2 477 49 91

Matthias D'Huyvetter (1986) is an assistant professor (0.1ZAP) at the Vrije Universiteit Brussel (VUB) and a postdoctoral fellow of the Research Foundation Flanders-FWO. He graduated in 2009 as Master in Biomedical Sciences at the University of Antwerp. In 2014, he received his PhD in Medical Sciences at the VUB for his work on radiolabeled single-domain antibody fragments as theranostic drugs for cancer treatment. During his PhD, he spent one year at Duke University, North-Carolina USA, under the guidance of Michael Zalutsky. Also in 2014, he co-founded the VUB spin-off company Camel-IDS. In 2019, he obtained the degree of executive Master in Business Administration at Antwerp Management School.

His academic research involves the design and characterization of novel theranostic agents in the field of targeted radionuclide therapy, with a dominant focus single-domain antibody fragments as targeting vehicles and alpha- and beta-particle emitters as toxic payload.

Geert Raes
Assistant professor & valorization manager
Vrije Universiteit Brussel
Cellular and Molecular Immunology unit
Staff Scientist at VIB Inflammation Research Centre

Email: Geert.Raes@vib-vub.be
Phone: +32 2 629 19 68

After obtaining a degree in bio-engineering and a PhD in tumor immunology, Geert has been staff scientist at VIB, where he has been involved in projects aimed at translating basic immunology research into industrial applications. Since 2013, he also has a partial appointment as valorisation manager at Vrije Universiteit Brussel, focusing on economic valorisation of nanobody applications in molecular imaging and therapy. Geert is co-inventor on 6 patent families. He is co-founder and IP & Legal Advisor of the VUB spin-off company Precirix and co-founder of Abscint.

Kristoff Muylle
Nuclear Medicine physician UZ Brussel
Head of Nuclear Medicine AZ Delta Roeselare

Email: Kristoff.Muylle@uzbrussel.be
kristoff.muylle@vub.be

Phone: +32 2 629 19 68

After completion of his medical studies in 1999 and his training in Nuclear Medicine in 2004 at the Free University of Brussels (VUB), Kristoff Muylle started his professional career at the Jules Bordet Cancer Institute in Brussels, where his work mainly focused on clinical and research activities related to nuclear medicine procedures in (hemato-)oncology with a specific interest in radioimmunotherapy and immuno-PET. In 2015, he joined the clinical staff of the nuclear medicine department at the University Hospital of Brussels (UZ Brussel) and combines this activity with a position as nuclear medicine physician at AZ Delta in Roeselare since July 2018, currently serving as head of the department.

Kristoff Muylle was President of the Belgian Society of Nuclear Medicine from 4/2014 until 4/2016. He joined the Board of the European Association of Nuclear Medicine (EANM) as President-Elect in 2015 and served as EANM President in 2017 and 2018.

Ahmet Krasniqi
Postdoctoral Scientist at Vrije Universiteit Brussel
In vivo cellular and molecular imaging laboratory

Email: Ahmet.Krasniqi@vub.be
Phone: +32 2 477 49 91

Ahmet obtained his master's degree in biomedical sciences from the Vrije Universiteit Brussel in 2014. Afterward, he started his PhD at the In vivo Cellular and Molecular Imaging (ICMI) laboratory and obtained a four-year doctoral grant from the Agency for Innovation by Science and Technology (IWT) Flanders. During his PhD, he developed radiolabelled anti-CD20 single-domain antibody fragments for radionuclide-based imaging and targeted radionuclide therapy of non-Hodgkin lymphoma. As a post-doctoral researcher, he focuses on evaluating the effect of targeted radionuclide therapy on the tumour-microenvironment and on the immune system.

Marjolijn-Lub-de Hooge
Hospital Pharmacist and professor
University Medical Center Groningen
Department of Clinical Pharmacy and Pharmacology
Department of Nuclear Medicine and Molecular Imaging

Email: m.n.de.hooge@umcg.nl
Phone: (050) 361 40 71

Marjolijn Lub-de Hooge works as Hospital Pharmacist at the department of Clinical Pharmacy and Pharmacology at the University Medical Center Groningen. Since 1999 she is responsible radiopharmacist and qualified person in the department of Nuclear Medicine and Molecular Imaging. In 2006 she obtained her PhD on pharmaceutical aspects and molecular imaging of new receptor targeted drugs. Recently she was appointed as Professor in Hospital Pharmacy, in particular personalized medicine in oncology.

Her research mainly focuses on molecular imaging to support drug development and to optimize treatment of cancer patients with novel (targeted and immuno) therapies. She is an expert in the development, evaluation and translation of new radiopharmaceuticals and optical tracers to the clinical setting. And she is also involved in the subsequent clinical application of these new tracers for drug development, and treatment optimization: visualization of presence of drug target (patient selection), drug biodistribution (pharmacokinetics, optimal dosing, target saturation) and tumor status during treatment (early predictive biomarker, pharmacodynamics).

Information online webcast lectures:

Do's and don'ts in immunotracer design (Nick Devoogdt)

In this presentation, the concept 'molecular imaging' will be introduced and a general overview of different types of tracers will be given. A major focus will be on antibody-tracers: how does the immune system develops an efficient antibody response? what are the molecular and structural features of antibodies? What are the different techniques to generate antibodies and how can they be engineered into different types of antibody-fragments? The pharmacokinetic behavior of antibodies and engineered fragments will be explained, and their relation to molecular and nuclear imaging. The antibody pre-targeting approach will be briefly touched upon. Finally, various concepts related to tracer design will be explained, including 'affinity', 'avidity', 'enhanced permeability and retention', 'the site-barrier-effect in tissue penetration', 'specific activity' and 'antigenic sink'.
This first lecture will also try to provide links and an introduction to other lectures given during the workshop.

Overview of imaging modalities (Christian Vanhove)

In 1895 the German physicist Wilhelm Conrad Roentgen discovered the X-rays, an achievement that earned him the first Nobel Prize in Physics in 1901. These X-rays produced the first medical images in the beginning of the previous century. Nowadays, a wide range of imaging techniques are available that can be roughly sub-divided into two main categories: structural and functional imaging devices. The most commonly used structural imaging technologies are computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound imaging (US). These techniques were developed to non-invasively visualize nonspecific macroscopic anatomical and physiological changes in tissues. Functional imaging modalities, such as single photon emission tomography (SPECT), positron emission tomography (PET) and optical imaging (OI) focus on the visualization of molecular/cellular targets in living subjects. These targets in functional imaging can include transporters, cell surface receptors and intracellular enzymes.
An overview will be presented of the physical basics behind the image formation process of these imaging modalities. The requirements to move from clinical to preclinical imaging will also be discussed for each modality. The presentation will start with CT that can be seen as a direct evolution of X-ray imaging. Secondly, the nuclear imaging techniques SPECT and PET will be presented, including the important evolution of combining these nuclear imaging techniques with CT and MRI. The more complex image formation process of MRI will be shortly introduced. Finally, OI will be presented, including bioluminescence and fluorescence in-vivo imaging, which are of more importance in the preclinical arena.

Radiochemistry of Nanobodies (Jessica Bridoux)

At ICMI, radiolabeled Nanobodies are a produced to be used as therapeutic or diagnostic agents. In this lecture we will discuss the techniques to radiolabel Nanobodies. We will first describe the different radionuclides, their related radiochemistry and how the different chemistries can be applied to Nanobodies. In particular, we will discuss two possible approaches: 1/ a random approach where the radionuclide is coupled onto the Nanobody's structure, or 2/ a site-specific approach where the radionuclide is coupled to the Nanobody in a controlled manner. Finally, we will focus on how to analyze the radiolabeled Nanobodies and see how the techniques can be applied clinical settings. The goal of the lecture is to understand the radiosynthesis process of Nanobodies and the specifications of the obtained radiopharmaceutical for pre-clinical or clinical applications.

Nanobody discovery and biotechnological applications (Timo De Groof)

Llama and camels have unique antibodies comprising a homodimer of heavy chain polypeptide, whereby the antigen is recognized by virtue of one single domain. A straightforward technology was developed to immunize a camelid, to clone the repertoire of antigen-binding fragments, from which the antigen-specific fragments are identified after phage display selections. The resulting recombinant, antigen-binding single-domain antibody fragments are also referred to as Nanobodies (Nbs) because of their size of 4 nm by 2.5 nm in diameter.

Nanobodies are well produced in microbial systems, very robust and highly soluble, bind their cognate antigen with high affinity and specificity. Very often the Nanobody recognizes an epitope that is difficult to target with human or mouse antibodies. The 'humanization' of a camel derived single domain antibody is straightforward. Probably, the largest advantage of Nanobodies comes from their strict monomeric behavior and the ease to tailor them into larger pluripotent constructs.

Such beneficial properties of Nanobodies over other antigen-binding fragments from conventional antibodies inspired many researchers to employ Nanobodies as a versatile tool in various innovative applications in biotechnology and medicine.

Imaging with nanobodies in preclinical models (Ahmet Krasniqi)

In this lecture, the focus will be on nanobodies and their evaluation by nuclear imaging in animal models of various diseases. The lecture will start with a rather detailed overview of protocols to generate good nanobody vehicles and will then look at subsequent attention points on which parameters and criteria should be considered to select a lead compound. We will look at structural features of nanobodies and how this is reflected in their amino acid sequence. A major part of this lecture will consist of an overview of recent published and unpublished applications of nanobodies in small animal nuclear imaging in pathologies ranging from oncology to autoimmune disease, macrophage-tracking, and some examples of nanobody engineering to ameliorate tracer performance.

Introduction to the clinical nuclear medicine (Marleen Keyaerts)

This presentation will give an overview of the routinely performed nuclear medicine examinations in patients, with a focus on the uptake mechanism of different tracers as well as a personal view on the future of clinical nuclear medicine. The session is intended for students and researchers in the preclinical field that would like to get a better understanding of daily practice in a nuclear medicine department in the hospital. Typical images of routinely performed scans will be discussed and interpreted.

Fluorescence applications of nanobodies (Sophie Hernot)

A general overview will be given regarding the application of fluorescence imaging for image-guided surgery. Both the technical aspects of optical imaging devices as well as the design of fluorescent tracers will be discussed. Current and emerging clinical applications will be illustrated, as well as the role the nanobodies in this field.

Clinical translation of nanobody-tracers (Marleen Keyaerts)

The clinical translation of new imaging agents will be discussed using the 68-Ga-labeled MMR and HER2 nanobodies as examples. Participants will get insight into regulatory requirements for clinical trials, including GMP compliance, clinical trial application with the competent authorities and ICH-GCP requirements. A study protocol for a phase I study will be presented and explained, as well as the obtained results.

Targeted radionuclide therapy, focus on nanobodies (Matthias D'Huyvetter)

This presentation will introduce the basics of Targeted Radionuclide Therapy of cancer and highlight different exciting applications that are now available in the clinic. In addition, an important part of the talk will focus on the use of Single-Domain Antibody fragments (sdAbs) as potential vehicles for Targeted Radionuclide Therapy using both beta$^-$- and alpha-particle emitting isotopes as toxic payload.

Intellectual property of biologics (Geert Raes)

Some basic principles of intellectual property rights as they relate to the use of biologics will be discussed, thereby using nanobodies as an example. After a brief overview of the main features and types of intellectual property rights, the focus will be on patents: advantages of patents, requirements for patentability, limitations to patentable subject matter and formulation of patent claims. Finally, the distinction between patentability and freedom-to-operate will be explained.

Immunogenicity of recombinant proteins (Chloé Ackaert)

The immunogenicity of recombinant biopharmaceuticals will be discussed with the focus on clinical impact of immunogenicity and methods available to assess the immunogenicity risk. Participants will get insight into in silico, in vitro and in vivo methods for immunogenicity risk assessment, as well as anti-drug antibody monitoring in clinical trial phases. Case studies will be discussed as illustration and the immunogenicity of the Ga-NOTA-anti-HER2 Nanobody will be presented.

Molecular imaging to enlighten cancer immunotherapies and underlying involved processes (Marjolijn Lub-de Hooge)

The presentation will discuss examples of preclinical and clinical ImmunoPET in the field of cancer immunotherapy.
Cancer immunotherapy has led to impressive antitumor effects. However, not all patients respond to immunotherapy, serious toxicity can occur and combination therapy may be warranted. Thus strategies to improve patient selection and accelerate development of new immune-oncology drugs are urgently required. ImmunoPET can provide non-invasive whole body information on biodistribution of radiolabeled immunomodulatory drugs, heterogeneity and dynamics of target expression, and effects of immunotherapy on immune cells and other cells in the tumor microenvironment.
In this presentation 89Zr-atezolizumab (anti-PDL1) and 89Zr-pembrolizumab (anti-PD1) are discussed as response predictor for treatment with monoclonal antibodies targeting the PD1/PDL1 axis. The value of molecular imaging in cancer drug development to provide insight in pharmacokinetic behavior and tumor targeting is illustrated with examples of radiolabeled probody therapeutic 89Zr-CX-072 and radiolabeled bispecific T-cell engagers. Finally possibilities to obtain more insight in the pharmacodynamic response using T-cell imaging is briefly discussed.

Potential impact of Immuno-PET on patient management (Kristoff Muylle)

Immuno-PET, positron emission tomography with radiolabelled monoclonal antibodies (mAbs), mAb-fragments or nanobodies, combines the high sensitivity and resolution of a PET camera with the specificity of a mAb for specific antigens expressed on the surface of tumour cells. Apart from its diagnostic capabilities and use in treatment planning, immuno-PET has potential for quantification of molecular interactions, which is particularly attractive when immuno-PET is used for simulation of subsequent antibody-based therapy, such as treatments with immunotoxins or radioimmunotherapy. The scope of this presentation is to highlight the potential of radiolabelled mAbs and/or nanobodies for molecular imaging as well as for radionuclide therapy, illustrated by preliminary results in preclinical and clinical trials.