IMAGING FOR LIFE
FROM MOLECULES TO DIAGNOSTICS AND THERAPY

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IMAGING FOR LIFE
FROM MOLECULES TO DIAGNOSTICS AND THERAPY

November 8th and 9th, 2016

WELCOME

Dear Speakers and Participants,

It is our pleasure to welcome you at the meeting "Imaging for Life : from Molecules to Diagnostics and Therapy". The event is feasible thanks to the great support of B·DEBATE, an initiative of Biocat and Obra Social "la Caixa", and the will of two research academic institutions, the Universitat Autonoma de Barcelona (through its Institute for Biotechnology and Biomedicine, and the Department of Biochemistry & Molecular Biology), together with the Jozef Stefan Institute from Ljubljana (through the Department of Biochemistry and Molecular and Structural Biology). A series of entities and companies to which we are indebted. also participate in the event at the scientific, technological and sponsoring level (SCB, XRB, Bruker, PerkinElmer, Novartis, SGSH-Bonsai Advanced).

The deep involvement of Bioimaging and related approaches within the biological, biotechnological and biomedical sciences has been an old and long sought goal. It follows the general principle that "… a picture is worth a thousand words…". However, a dramatic progress was seen in the last decade(s) together with the flourishing of the detailed biological knowledge about living organisms, and with the unveiling and development of strategies and technologies that enable improved visualisation and data accumulation and analysis at the molecular, cellular, tissue and whole organism levels. Nowadays, there is a major demand for clearer visualization and quantitation of specific molecules, cells and tissues, in in-vivo and ex-vivo states, to better understand their functions and interrelations in normal, perturbed and pathological states. This occurs from single-molecules or cells to whole organism levels, and is propelled not only because of the need for more precise and allocated biological knowledge, but also by the growing implications of such demands in pre-clinical and clinical studies including in medical diagnosis, prognosis, targeted drug delivery and surgery approaches, as well as by the wide use in basic science. Because of the general use of these approaches in medicine, even the general society knows something about the use of microscopy, CT, PET and MRI technologies because of, whilst these and other specialized approaches keep growing, improving and developing at very fast rates.

Given that advanced science and technology, including Bioimaging, is more and more dependent of synergies, at both national and international dimensions, fostering contacts and collaborations between very active and leading groups has been and is one of our main goals. Catalonia has a very active scientific community at the biological, biotechnological and biomedical level, and to keep ahead requires its involvement in the establishment and consolidation of international hubs and platforms in such fields. We hope that this meeting contributes to them.

In the well proven forum of BioCat/La Caixa, and with the participation of leading investigators in the field of Bioimaging, we shall discuss the more advanced as well as the emerging hypothesis, proposals and technologies in the field. The evaluation of their capabilities and potentials, and the establishment of relationships and synergies between them, should facilitate its tuning and applicability to the clarification of fundamental biological problems as well as to the detection, analysis, prognosis-diagnosis and therapy of medical distresses and problems. Moreover, it should also provide thoughts for future areas of research and development.

We invite all the participants of the meeting, speakers, chairmen as well as other attendees, to actively participate in the discussions and debates along its development.

Yours sincerely,

Francesc Xavier Aviles–Prof & Boris Turk-Prof. (Scientific Leaders), Scientific Committee and B·Debate

PROGRAM

Tuesday, November 8th, 2016

9:30 **Welcome**
Jordi Portabella, Director, Area of Research and Knowledge, la Caixa Foundation
Marta Soler, Head of Research and Scientific Debate, Biocat
Francesc Xavier Avilés, Professor, UAB
Boris Turk, Professor, Jozef Stephan Institute

9:45 **SESSION 1: STATE OF THE ART IN IN-VIVO IMAGING, APPROACHES AND CHALLENGES**
Chairs: **María García- Parajo,** ICFO, Barcelona, Spain
Matthew Bogyo, University of Stanford, Stanford, USA

Functional and structural connectivity of the normal and diseased mouse brain
Markus Rudin, ETH, University of Zurich, Zurich, Switzerland

Imaging Biologics & Biologics for Imaging
Rainer Kneuer, Novartis Institutes for Biomedical Research, Basel, Switzerland

11:00 **Coffee Break**

11:30 **Well-defined Polypeptide-based architectures: applications in drug delivery and molecular imaging**
María J. Vicent, CIPF, Valence, Spain

MALDI mass spectrometry imaging – latest advances and current potential
Arndt Asperger, Bruker Daltonik, Bremen, Germany

12:30 **Lunch**

14:00 **SESSION 2: SUBCELLULAR, CELLULAR AND SMALL ANIMAL IMAGING**
Chairs: **Anna M. Planas**, IIBB.IDIBAPS, Barcelona, Spain
Vincent Dive, CEA-Saclay, Saclay, France

Nanoscale imaging and spectroscopy of living cell membranes using single molecule optical nanotools
María García- Parajo, ICFO, Barcelona, Spain

Assessing tumoral microenvironment: hypoxia with F18-MISO PET-CT in Cancer Research
Francisca Mulero, CNIO, Madrid, Spain

Molecular Imaging in Drug Development
Oliver Plettenburg, Institute of Medicinal Chemistry at Helmholtz Zentrum, Munich, Germany

15:30 **Coffee break**

16:00 **Imaging Model Diseases in Transparent Organs**
Julien Colombelli, IRB Barcelona, Barcelona, Spain

New bioluminiscent models to target cancer stem cells with nanomedicine
Simó Schwartz, Vall d'Hebron Institut de Recerca (VHIR), Barcelona, Spain

17:00 **Open debate on Sessions 1 and 2**

Wednesday, November 9th, 2016

9:30 **SESSION 3: COMBINING DIFFERENT IMAGING APPROACHES**

Chair: **Oliver Plettenburg,** Institute of Medicinal Chemistry at Helmholtz Zentrum, Munich, Germany
Manel Sabés, ALBA Synchrotron (UAB), Barcelona, Spain

Sensitivity, resolution and long-term biodistribution studies by H and C digital autoradiography : moving from 2D to 3D imaging
Vincent Dive, CEA-Saclay, Saclay, France

PET in drug discovery and development: an overview
J. Raul Herance, Vall Hebron Institut de Recerca (VHIR), Barcelona, Spain

10:30 **Coffee break**

11:00 **Multimodality Imaging - The Ideal Solution to Advance Molecular Imaging?**
Tim Wokrina, Bruker-Mannheim, Ettlingen , Germany

Unraveling therapy response in preclinical glioblastoma using MRSI-based molecular imaging and source analysis
Ana Paula Candiota. CIBER / UAB, Barcelona, Spain

OPTiSPIM: Getting the best of both worlds
James Sharpe, CRG, Barcelona, Spain

12:30 **Lunch**

14:00 **SESSION 4: TOWARDS TRANSLATIONAL IMAGING AND THERANOSTICS**

Chair: **Markus Rudin,** ETH, University of Zurich, Zurich, Switzerland
Carles Arús, UAB, Barcelona, Spain

Small molecule protease probes for imaging cancer and infectious diseases
Matthew Bogyo, University of Stanford, Stanford, USA

Optical Tomography and Its Role in Multimodality Imaging
Kevin P. Francis, Perkin Elmer, Alameda, USA

Precision Markers for Color-Coded Surgery - Imaging tumors and nerves
Quyen T. Nguyen, University of San Diego, San Diego, USA

15:30 **Coffee break**

16:00 **Imaging targeted drug delivery in colorectal cancer models**
Ramon Mangues, Institut d'Investigacions Biomèdiques de Sant Pau, Barcelona, Spain

Cysteine cathepsins as targets for noninvasive whole body imaging and targeted drug delivery
Boris Turk, Jozef Stephan Institute, Ljubljana, Slovenia

17:00 **Open debate and general discussion**

18:15 **Concluding remarks and closing of the meeting**

SCIENTIFIC COMMITTEE

Francesc Xavier Avilés, Professor and Group Leader, **Institute for Biotechnology and Biomedicine , Universitat Autònoma de Barcelona (UAB),** Barcelona, Spain.

F. Xavier Aviles is full professor and outgoing director at the Department of Biochemistry & Mol Biol of UAB and group leader at the Institute for Biotechnology and Biomedicine of this institution. Besides UAB, where he got his PhD, he has been trained in the field of structural biology and biotechnology of proteins at the CSIC (Inst. Rocasolano, Madrid), University of Porstmouth (Biophysics Lab.), ETH-Zurich (Inst. Mol Biol & Biophys, K. Wüthrich group and Dpt. -Nobel Laureate-), Max-Planck Inst. Biochemie Munich (R. Huber group and Dept. -Nobel Laureate-), University of Cambridge (T. Blundell group and Dept. Biochemistry -Sir-), University of Uppsala (& BMC center) and University of Lund (Clinical Medicine Dpt. & Grand Hosp.), with long or medium stays. There, also completed his training in bioinformatics, proteomics and molecular imaging, and became further specialized on proteolytic enzymes and inhibitors. He supervised 42 PhD thesis, co-authored more than 237 peer-reviewed publications (249 at WOS) (H-index 45, ISI), leaded a significant number of research projects (>55) and networks at the national and international levels, organized international meetings and workshops (i.e. for the Protein Society), and was invited to numerous meetings (>95) as speaker or committee member. Also, has been member of the executive committees and/or coordinator of sections of scientific societies (such as SEBBM, SBE, SCB), and member of the editorial boards of international scientific journals, particularly on protein sciences and molecular-structural biology, protein production & modifications, and proteomics (i.e. J Biol Chem and Microbiol. Cell Factory).

Boris Turk, Professor of Biochemistry at **Jozef Stefan Institute & University of Ljubljana,** Ljubljana,Slovenia

Dr. Boris Turk received a PhD degree in Chemistry from the University of Ljubljana,Slovenia, in 1993. Following a postdoctoral work with Ingemar Bjork at The Biomedical Center in Uppsala, Sweden, he received a PhD in Medical and Physiological Chemistry in 1996. He returned to Slovenia and since 1998 he is head of the Department of Biochemistry and Molecular and Structural Biology at the J. Stefan Institute and since 2011 professor of biochemistry at the University of Ljubljana. His lab focuses on the understanding of the role of proteases, in particular lysosomal cysteine cathepsins, in inflammation-associated diseases, including cancer and arthritis. This includes understanding of the molecular mechanisms of involvement of cathepsins in the extracellular milieu with a goal to evaluate their potential in diagnosis and therapy. He was coordinator of the EC-strep FP7 project LIVIMODE (2009-2014) aimed at developing novel imaging agents for noninvasive in vivo imaging of proteases in cancer and arthritis. He is an EMBO member since 2007, a member of Academia Europea (London) since 2013, past president and secretary of International Proteolysis Society and secretary general of European Cell Death Organization (ECDO).

Matthew Bogyo, Professor, **Stanford University**, Stanford, USA.

Dr. Bogyo is a Professor of Pathology and Microbiology and Immunology at Stanford University. He received his doctorate in Chemistry from Massachusetts Institute of Technology in 1997. Dr. Bogyo established an independent scientific career as a Faculty Fellow at the University of California, San Francisco in 1998, where he supervised a small laboratory of post-doctoral fellows and students. In 2001, Dr. Bogyo was hired to establish and direct a Chemical Proteomics Department at Celera Genomics focused on applying small molecule probes to the field of drug discovery. Dr. Bogyo then joined the Department of Pathology at Stanford University in July 2003 and was promoted to Associate Professor in 2009 and to full professor in 2013. His laboratory works on the development of new chemical probe technologies that are applied to study the role of proteases in complex biological pathways associated with human disease. Dr. Bogyo has published over 200 primary research publications and currently serves on the Editorial Board of several prominent research journals. He was the President of the International Proteolysis Society from 2007-2009 and is the chair of the Gordon Research Conference on Proteolytic Enzymes and Their Inhibitors in 2018 and the Imaging in 2020 meeting in 2016. Dr. Bogyo is a consultant for several biotechnology and pharmaceutical companies in the Bay Area, including the company that he co-founded, Akrotome Imaging.

Vincent Dive, Head of the Section of Molecular Engineering of Proteins at the **Institute of Biology and Technology CE-Saclay (CEA)**, Saclay, France.

Dr V. Dive is the head of the "Section of Molecular Engineering of Proteins" at the CEA Life Science Division in Saclay and the leader of a group which has a long-standing expertise in the chemistry of phosphorus-containing peptides as potent inhibitors of zinc-metalloproteinases and evaluation of their in vivo activity. Labelling of inhibitors with 3H and 14C in combination with digital autoradiography is routinely used to study the in vivo biodistribution of corresponding compounds. Dr. Dive's group has been involved in multiple European integrated projects (FP4, FP5, FP6 and FP7) dealing with the development of inhibitors of zinc proteases (MMPs, ACE, ACE2) for cancer and cardiovascular applications. The group has published more than 100 peer-reviewed articles and 8 patents on protease inhibitors. The team has been selected in 2011, as a member of the "Laboratory of Excellence in Research on Medication and Innovative Therapeutics" (LERMIT). (http://www.cea.fr/drf/ibitecs/Pages/services/simopro.aspx and www.labex-lermit.fr)

Oliver Plettenburg, Director, Institute of Medicinal Chemistry at the **Helmholtz Zentrum München GmbH, German Research Center for Environmental Health**, Munich, Germany.

Oliver Plettenburg is Director of the Institute of Medicinal Chemistry at the Helmholtz Center for Environmental Health in Munich and Professor for Medicinal Chemistry at Leibniz Universität Hannover. Previously he held various positions within the pharmaceutical industry, last as Head of Biosensors & Chemical Probes in Sanofi's Diabetes Division. The group's main responsibility was to support evaluation of validity of novel targets, provide tools to visualize pathologically relevant processes, to develop new methods to quantify important biomarkers and to explore new treatment options at the drug-device interface. Oliver was with Sanofi for 14 years. Before joining the Diabetes Division he worked as a project leader in several medicinal chemistry projects in the area of Diabetes and Cardiovascular Diseases and was deeply involved in the Chemical Biology approach within Aventis. After receiving his PhD in organic chemistry, he joined The Scripps Research Institute as a postdoctoral fellow, working in the group of Chi-Huey Wong on the total synthesis of glycosyl sphingosides.

Markus Rudin, Professor at the **University of Zurich and ETH Zurich**, Zurich, Switzerland.

Markus Rudin studied chemistry at ETH Zürich, Switzerland, and graduated in the Physical Chemistry Laboratory working on electron-nuclear double resonance (ENDOR) of transition metal complexes. After post-doctoral stays at ETH and the Biocenter of the University of Basel, he joined Sandoz Pharma AG in Basel, Switzerland, in 1983 to establish one of the first MRI imaging labs in pharmaceutical industry world-wide. Within Sandoz, to become Novartis AG in 1996, he became head of the global Analytical and Imaging Science Unit and deputy head of the Core Technology Area, before he moved to academia in 2005 to become full professor for Molecular Imaging and Functional Pharmacology at the University of Zürich and ETH Zürich.
His research topics are the development of small animal imaging techniques, in particular MRI, fluorescence imaging as well as the combination of fluorescence molecular tomography and MRI, with application of these techniques in the field of neuroscience and oncology. Primary focus in neuroscience is the study of brain function under normal and pathological conditions and the elucidation of mechanisms underlying the hemodynamic fMRI signal. In oncology, the principal research topic is the development of imaging assays to study tumor hypoxia, hypoxia signaling and its downstream effects on angiogenesis, metabolism and tissue invasion.

INVITED SPEAKERS

Tuesday, November 8th, 2016

Session 1: State of the Art in in-vivo Imaging, Approaches and Challenges

María García Parajo, ICREA Research Professor and Group Leader, **Institute of Photonic Sciences (ICFO)**, Barcelona, Spain.

Dr. Maria Garcia-Parajo received her MSc in Solid State Physics at Imperial College London, UK and PhD in Physical Electronics in 1993 at the same Institute. After a two-years postdoc at the L2M-CNRS, Bagneux, France, she moved in 1996 to the Applied Optics group of the University of Twente, the Netherlands, where she worked in the fields of nanophotonics, single molecule fluorescence detection, photophysics and dynamics. In 2005 se moved to Barcelona as ICREA Research Professor, first hosted at the IBEC - Institute for Bioengineering of Catalonia and since July 2011 at the institute of Photonic Sciences, ICFO, leading the Single Molecule Biophotonics group. Her research focuses on the development of advanced optical techniques to the study of biological processes at the single molecular level on living cells. She has co-authored more than 120 publications in peer-reviewed international Journals and delivered more than 140 talks at international conferences and workshops upon invitation. She coordinates several international research projects and is a member of the executive board of the Spanish Biophysical and the International Fluorescence Societies. She has been teaching several specialized courses in fluorescence microscopy and single molecule detection in the Netherlands, Portugal, France, Germany, UK and Spain.

Chair of the SESSION 1

Matthew Bogyo, Professor, **Stanford University**, Stanford, USA.

(See his CV at the Scientific Committee section)

Chair of the SESSION 1

Markus Rudin, Professor at the **University of Zurich and ETH Zurich**, Zurich, Switzerland.

(See his CV at the Scientific Committee section)

Functional and structural connectivity of the normal and diseased mouse brain

Functional magnetic resonance imaging (fMRI) in rodents is attractive in many regards. Information on the biophysical basis of the hemodynamic response to neural activity can be obtained by combining fMRI with established invasive readouts of neuronal function. The use of genetically engineered mouse lines allows assessing the impact of specific molecular entities involved in signal processing. E.g., the availability of photoreceptors that allow controlling electrical excitability via photon absorption, is attractive for targeted interventions into the neuronal circuitry. The relatively simple morphology of the rodent brain facilitates the analysis of functional topology and its rearrangement following CNS injury. Modern fMRI techniques allow for full 3D brain coverage essential for the study of large-scale networks. Challenges in rodent fMRI are imposed by the small dimensions of the brain and correspondingly high demands on spatial resolution, and

by animal physiology, which should be stable enough to allow for detection of the weak activity related signals.
We will discuss the use of fMRI to derive 1) mechanistic information on the neurovascular coupling, 2) on structural and functional connectivity in mouse brain, as well as 3) on dynamic aspects of functional connectivity, and finally 4) the use of fMRI in assessing alterations in connectivity under pathological conditions.

Rainer Kneuer, Senior Investigator I, **Novartis Institutes for Biomedical Research**, Basel, Switzerland.

Rainer Kneuer, Ph.D. studied chemistry at the University of Würzburg, Germany and graduated at the Department of Organic Chemistry in the research group of Dr. J. Hartung. He joined Novartis 2001 as postdoctoral fellow being involved in the set-up of the Near-infrared Fluorescence (NIRF) imaging technology by designing fluorescently labeled target specific ligands for this application. One year later he moved into a permanent position as Labhead in the preclinical imaging group. His current work focuses on the design, synthesis, physicochemical and in vitro/vivo characterization of novel tracers for Near-Infrared Fluorescence, PET/SPECT, contrast agents for MR in vivo (molecular) imaging and reagents for Mass Cytometry. These probes are applied to visualize and quantify the distribution of compounds on the cellular/in vivo level and to study the effect of drugs on key cellular functions and mechanisms. In addition suitable delivery vehicles for tracers and contrast agents (e.g. nanoparticles, liposomes, biocompatible polymers) are developed in this lab.

Imaging Biologics & Biologics for Imaging

In this presentation it is demonstrated how a multi-modality/scale molecular imaging platform (fluorescence microscopy, Near-infrared fluorescence, PET & ex vivo tissue imaging) can be used to study the distribution, trafficking, tissue targeting and clearance of biotherapeutics on the (sub)-cellular level and non-invasively in vivo ("therapeutic imaging"). On the other hand, biologics with potential for reformatting would be a rich source for the design of tailored highly specific molecular imaging agents from scratch in a diagnostic fashion by optimizing the targeting scaffold, circulation PK and site-specific labeling technology ("diagnostic imaging"). In an outlook it is shown how metal-labeled biologics, in particular antibodies are used in conjunction with novel highly multiplexed single cell analysis tools such as Imaging Mass Cytometry to enable deep phenotypic analysis of cell-cell interactions on tissue sections in unprecedented details.

María J. Vicent, Head of Polymer Therapeutics Lab, **Centro de Investigación Príncipe Felipe (CIPF)**, Valencia, Spain.

Dr. María J. Vicent received her Ph.D. degree in 2001 in chemistry on solid supports from University Jaume I after several scientific stays in Prof. Fréchet's lab. at University California, Berkeley (USA). Then, she moved to more biomedically oriented research, initially with a Spanish company Instituto Biomar SA., and subsequently at the Centre for Polymer Therapeutics with Prof. R. Duncan after the award of a Marie Curie Postdoctoral Fellowship in 2002. In 2004, María joined Centro de Investigación Príncipe Felipe (CIPF) as research associate through a Marie Curie Reintegration contract and was promoted to her current position, head of Polymer Therapeutics Laboratory at CIPF, in 2006. Currently she is also the responsible of the Screening Platform and the Advance Therapies Program Coordinator at CIPF. She also coordinates the Valencian Community Strategy on Innovative and Precision Medicine. Her research group focused on the development of novel nanopharmaceuticals, in particular Polymer Therapeutics, for different therapeutic anddiagnostic applications and has been funded by national and European grants (several acting as coordinator including a recently awarded ERC Consolidator grant-MyNano). María co-authored >80 peer reviewed papers and 7 patents, 2 of them licensed to the pharmaceutical industry and a third one used as foundation of the spin off company 'Polypeptide Therapeutic Solutions SL' in 2012.

Well-defined Polypeptide-based architectures: applications in drug delivery and molecular imaging

Polyglutamates are highly biocompatible, biodegradable and multifunctional polymers, which have been effectively used as building blocks in polymer drug conjugates and polymeric micelles for various medical applications ranging from cancer to ischemic processes. In addition, polypeptides are envisaged to achieve a major impact on a number of different relevant areas such as biomedicine and biotechnology. Acquired knowledge and the increasing interest on amino acids, peptides and proteins is establishing a large panel of these biopolymers whose physical, chemical and biological properties are ruled by their controlled sequences and composition. The development of new and more defined architectures with higher Mw, predictable structure and conformation, lower heterogeneity, higher drug loading capacity and greater possibility for multivalency are main research lines in polymer therapeutics.
We have developed novel constructs to be used as drug delivery systems/ imaging probes after an adequate labelling with fluorescence/NIR probes or/and complexing agent for MRI and/or PET techniques. It is evident that, there is a wide range of therapeutic opportunities for these novel and interesting polypeptidic architectures.

Arndt Asperger, Applications Team Leader MALDI-TOF at Applications and Demo Center, **Bruker Daltonik GmbH**, Bremen, Germany.

Arndt Asperger, PhD studied chemistry at Leipzig University. Arndt received his diploma in chemistry from Leipzig University in 1995. He received his PhD in Analytical Chemistry from Leipzig University in 1999. In 2002, Arndt joined Bruker Daltonik GmbH as a MALDI-TOF applications scientist working at the Bruker Daltonik applications and demo center in Leipzig. Currently, Arndt is working at Bruker Daltonik as an applications team leader MALDI-TOF at the applications and demo center in Bremen.

MALDI mass spectrometry imaging - latest advances and current potential

Over the last decade, MALDI mass spectrometric imaging has evolved into a powerful tool being utilized in various branches of lifescience research, including preclinical analytics. The talk will provide a brief introduction to the principle of MALDI imaging, and will outline the latest technological and methodical advances as well as the current state of the art of the method in terms of its application to various fields of research. To illustrate the latter, application examples will be presented describing the MALDI imaging analysis of various compounds, f.e. lipids, proteins, peptides, various small molecules, in a variety of biological tissues. The talk will introduce two complementary high-performance MALDI imaging platforms: The Bruker rapiflex MALDI Tissuetyper, an imaging solution based on next-generation MALDI-TOF technology, allows for maximum acquisition speed (up to 50 pixels/sec) and high-definition imaging (maximum spatial resolution 5µm). The Bruker solarix XR II, a high-performance MALDI-FTICR based imaging platform, is capable of generating ultimate-level convidence imaging data relying on unparalleled mass resolution and accuracy enabling direct identification of compounds when analyzing their spatial distribution in tissues. Finally, the talk will address the topic of imaging data analysis applying statistical methods, which represents a critically important step in the workflow.

James Sharpe, Program Coordinator and Group Leader, **Center for Genomic Regulation (CRG)**, Barcelona, Spain.

James Sharpe entered biology from a passion about computer programming and electronics, wondering: How is the complexity of life encoded in our genes? After his Biology degree at Oxford University (1991), he pursued in a PhD in developmental genetics at the MRC National Institute for Medical Research (1997). Then, during his postdoc at the Human Genetics Unit in Edinburgh, he invented a new technology, called Optical Projection Tomography, which allows tissues and organs to be imaged in 3D (2002). Since that time he has been building dynamic computer models of limb development, which his research group continues to pursue since moving to the Centre for Genomic Regulation in Barcelona (2006), where James is now the coordinator of the Systems Biology Program.

OPTiSPIM: Getting the best of both worlds

Light-sheet microscopy is becoming an essential tool for imaging in the life sciences. Compared to confocal microscopy, it allows researchers to image deeper, faster and with less phototoxicity/bleaching. Various technical improvements have been described over recent years, however one artifact is intrinsically difficult to overcome. Arbitrary distributions of absorption interfere with quantitative imaging, but cannot be directly addressed by LSFM due to its dependence on fluorescent signals. Optical Projection Tomography (OPT) is another imaging technique suitable for specimens in a similar size range. OPT can produce 3D images of fluorescent signals, but can also operate in transmission mode, where it records the 3D distribution of attenuation. We have now developed OPTiSPIM – a hybrid scanner in which the absorption artifacts seen in LSFM/SPIM are mathematically corrected by using the 3D map of attenuation created by OPT. We believe that this valuable combination will become a standard approach for mesoscopic imaging in the future.

Session 2: Subcellular, Cellular and Small Animal Imaging

Anna M. Planas, Researcher at **IIBB-CSIC, IDIBAPS,** Barcelona, Spain.

Anna M. Planas graduated at the University of Barcelona and carried her Ph.D. on cerebral blood flow and metabolism at the Medical Research Council, Toxicology Unit in Carshalton (UK) (1984-1987). She carried out a postdoctoral stage at the Service Hospitalier Frédéric Joliot (SHFJ) PET Centre of the Commissariat à l'Énergie Atomique (CEA) in Orsay (France) (1990-1992). She is now a researcher of the Spanish Research Council (CSIC) and leads the Laboratory for Cerebrovascular Research at the Institute for Biomedical Research (IIBB-CSIC) in Barcelona where she is Head of the Department of Brain Ischemia and Neurodegeneration. She coordinates the area of Neurosciences at the Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) in Barcelona. Her current main research interests are to underscore the contribution of inflammatory and immune responses to stroke brain damage. She has published more than 150 papers in international peer-reviewed scientific journals. Dr Planas is currently member of the Board of Directors of the International Society for Cerebral Blood Flow and Metabolism (ISCBFM). She was the local host for the Brain 2011 meeting of ISCBFM and for the meeting of the European Molecular Imaging Society (ESMI) in 2009. She is member of the Editorial Board of scientific journals in the field of stroke and neurosciences and Section Editor of the journal Stroke.

Chair of the SESSION 2

Vincent Dive, Head of the Section of Molecular Engineering of Proteins at the **Institute of Biology and Technology CE-Saclay (CEA)**, Saclay, France.

(See his CV at the Scientific Committee section)

Chair of the SESSION 2

María García Parajo, ICREA Research Professor and Group Leader, **Institute of Photonic Sciences (ICFO)**, Barcelona, Spain.

(See her CV at the Session 1)

Nanoscale imaging and spectroscopy of living cell membranes using single molecule optical nanotools

A hot topic in current cell biology is to understand the specific nanometer-scale organization and distribution of the surface machinery of living cells and their role controlling cellular processes. For many years, fluorescence microscopy has been one of the most prominent and versatile research tools used in modern cell biology. Unfortunately, the major drawback of conventional light microscopy is its limited spatial resolution, around 300nm. In recent years, major technical developments have demonstrated that the diffraction limit of light can be broken so that the entire cell machinery becomes accessible with an unprecedented level of detail and resolution. In this contribution, I will overview most recent technological advances on super-resolution nanoscopy and will discuss how these approaches are now being exploited to reveal the existence of pre-assembled nanoplatforms of multi-molecular components on the cell membrane. Furthermore, I will discuss how these techniques are progressing beyond cell nanoimaging to more sophisticated applications, providing unique insights into the spatial organization, dynamics and functions of cell surfaces.

Francisca Mulero, Head, Molecular Imaging Unit, **Spanish National Cancer Research Center (CNIO)**, Madrid, Spain.

Francisca Mulero, obtained her MD degree from the Universidad de Alicante and was awarded her MIR as a Fellow in Nuclear Medicine at the Hospital Universitario Virgen de la Arrixaca in Murcia. She obtained her First Class Honours PhD degree from Universidad de Murcia for her research focusing on the differential diagnosis of breast injuries using MIBITc-99m Scintigraphy.
Since 1994 she has worked as Nuclear Medicine Specialist at the Nuclear Medicine Department, the Hospital Virgen de la Arrixaca, focusing on imaging diagnosis.Since 2007 she is head of the Molecular Imaging Unit at CNIO.
She published a number of papers, see few of them:
- 18F-fluoromisonidazole PET and activity of neoadjuvant nintedanib in early HER2-negative breast cancer: a window-of-opportunity randomized trial. Quintela-Fandino M, Lluch A, Carrato , Carrasco EM, Palacios J, Mulero F*, Colomer R*. *Senior Author. Clin Cancer Res. 2016.
- Targeting MT1-MMP as an immunoPET-based strategy for imaging gliomas. A.G. de Lucas, A.J. Schuhmacher, M. Oteo, M. Á. Morcillo, M. Squatrito, J.L. Martinez-Torrecuadrada and F. Mulero. PLOS ONE 2016
-Targeting Tumor Mitochondrial Metabolism Overcomes Resistance to Antiangiogenics. Navarro P, Jimenez-Renard V, Mulero F, Quintela-Fandino M. Cell Rep. 2016 Jun 21;15(12):2705-18.
- Analysis of Murine Lung Tumors by Micro PET-CT Imaging. Chiara Ambrogio, Juan Antonio Cámara, Patricia Nieto, David Santamaría and Francisca Mulero. Bio-Protocol. 2015, 5(24)

Assessing tumoral microenvironment: hypoxia with F18-MISO PET-CT in Cancer Research

Hypoxia is rare in normal tissues, but is common in cancers and is a prognostic factor for many types of cancer. Clinically, patients with tumours having low oxygenation levels have a poor prognosis, with strong evidence showing that this is due to the effects of hypoxia on therapy resistance and malignant progression. With PET-CT, radiolabeled hypoxia avid compounds can be applied to evaluate oxygenation status in experimental or human tumours. 18F-fluoromisonidazole (18F-MISO) is the most widely used nitroimidazole derivative in PET studies it has been used for non-invasive evaluation of hypoxia, and is related to patient prognosis. The aim of this study was to predict and evaluate tumour response to an angiomodulator treatment in advanced breast carcinoma and pancreatic carcinoma according to baseline 18F-MISO PET-CT uptake in those patients. We studied 150 patients with locally advanced breast carcinoma and 50 with pancreatic carcinoma. Each patient was underwent 2 PET 18F MISO scans one pretreatment and the second one 15 days after the treatment. All images were acquired at 3 h after MISO injection of 250 MBq for 20 minutes in prone position to separate breast tissue from thoracic structures and in the case of pancreatic carcinoma only supine position was performed. The results shown that the hypoxic volume has no correlation with tumor response but there is a significant reduction in the SUV max in patients that showed good response to treatment. Conclusions: FMISO PET has a value in assessing and predicting response to treatment in a number of carcinomas.

Oliver Plettenburg, Director, Institute of Medicinal Chemistry at the **Helmholtz Zentrum München GmbH, German Research Center for Environmental Health**, Munich, Germany.

Oliver Plettenburg is Director of the Institute of Medicinal Chemistry at the Helmholtz Center for Environmental Health in Munich and Professor for Medicinal Chemistry at Leibniz Universität Hannover. Previously he held various positions within the pharmaceutical industry, last as Head of Biosensors & Chemical Probes in Sanofi's Diabetes Division. The group's main responsibility was to support evaluation of validity of novel targets, provide tools to visualize pathologically relevant processes, to develop new methods to quantify important biomarkers and to explore new treatment options at the drug-device interface. Oliver was with Sanofi for 14 years. Before joining the Diabetes Division he worked as a project leader in several medicinal chemistry projects in the area of Diabetes and Cardiovascular Diseases and was deeply involved in the Chemical Biology approach within Aventis. After receiving his PhD in organic chemistry, he joined The Scripps Research Institute as a postdoctoral fellow, working in the group of Chi-Huey Wong on the total synthesis of glycosyl sphingosides.

Molecular Imaging in Drug Development

Success rates in current drug development are unsustainably low. In order to improve on this, thorough target validation and demonstration of target engagement are hallmarks of successful drug development and need to be addressed already at early project stages. Different aspects and applications of molecular imaging based approaches to facilitate preclinical drug development will be discussed. This will particularly include illustrating examples for in-vivo imaging of enzymatic activity and design and characterization of targeted imaging reagents to improve characterization of distinct disease stages. Consequent implementation of similar target validation approaches will lead to an improved understanding of disease pathogenesis and of the employed animal models and thus ultimately reduce attrition rates.

Julien Colombelli, Microscopy Facility Manager at the **Institute for Research in Biomedicine (IRB Barcelona)**, Barcelona, Spain.

Julien Colombelli is the Head of the Advanced Digital Microscopy Core Facility (ADMCF) at IRB Barcelona since 2008. He obtained his degrees in physics at the University of Paris and in Optics engineering at the École Centrale de Marseille.
He worked as research Engineer at Corecom (Politecnico di Milano - Italy), and at the European Molecular Biology Laboratory (EMBL- Germany) in the Light Microscopy Group. Mr. Colombelli manages advanced microscopy and image analysis resources for more than 200 users per year, a wide range of BioImaging applications with 15 microscopy systems, and is in charge of custom instruments development, e.g. Lightsheet-based microscopy or Laser Nanosurgery technologies. Mr Colombelli chairs, since 2016, a new COST Action: NEUBIAS, Network of European BioImage Analysts, and also provides services to European scientists through EuroBioimaging, the future European Infrastructure for Biological and Biomedical Imaging.

Imaging Model Diseases in Transparent Organs

In 3D Fluorescence imaging, two important methods have been subject to intensive developments in the past years: Optical Clearing and Lightsheet Microscopy. However, the overwhelming speed at which their latest developments are being released does not necessarily facilitate that both methods converge towards being always compatible. In particular, new clearing methods involve different refractive indices of the imaging medium, a crucial parameter for 3D imaging which must be taken into account and corrected for, when hardware enables it. We have worked in the past years on developing a custom Lightsheet Macroscope system in our Facility to image optically cleared samples of fairly large dimensions (beyond a centimeter), for any clearing/imaging medium (i.e. any refractive index) and which includes rotation of the sample for full 360º access, easy mounting of the sample, and 3D tiling. The system also features "Intelligent Imaging" to enable automated imaging of the relevant parts of a sample, which ultimately tackles two important bottlenecks inherent to Lighsheet Imaging in Core facilities: reduce acquisition duration and data storage. I will illustrate biomedical applications where in toto organ imaging can address present questions in Biomedical research, e.g. in the context of Alzheimer disease, angiogenesis/cancer or metastasis tissue invasion. Our results enable to challenge stereology (the 3D interpretation of 2D histological images) and demonstrate when imaging an organ at full depth significantly improves data interpretation and opens new scientific challenges in the study of human disease. Imaging Whole mount organs also offers economical benefits in mouse biology, and even becomes a technical requirement for specific tissue imaging quantifications assays, where the inherent architecture of tissues and distribution of disease hallmarks is not always homogeneous in 3D.

Simó Schwartz Jr, Director, **CIBBIM-Nanomedicine. Vall d'Hebron Institut de Recerca (VHIR),** Barcelona

Director of CIBBIM-Nanomedicine and Team leader of the "drug delivery and targeting group" focused on new biomedical nanotechnology-based applications. Member of the Science Advisory Board of the Vall d'Hebron Research Institute (VHIR) and Science Advisor of the European Nanotechnology Characterization Laboratory (EU-NCL). He is also Science Advisor of SOM BIOTECH and CELGENE, member of the Advisory Board of NANOCAN, Southern Denmark University, and has been recently appointed as President of the European Society of Nanomedicine and Executive Board member of the International Society of Nanomedicine. He helds 13 patents, most transfered to leading companies of the biotech and pharma sectors and coauthors more than 80 papers in high impact factor journals. Dr Schwartz Jr was also appointed as Deputy Director and technology transfer coordinator of "CIBER de Bioingeniería, Biomateriales y Nanomedicina" (CIBER-BBN) of the Spanish Health Institute CarlosIII (ISCIII) which gathers a total of 45 research groups of national excellence in the field of nanotechnology and nanomedicine. Dr Schwartz was also Co-founder and Science Advisor of ARGON Pharma SL and is also member of the editorial Board of the journals Nanomedicine-NBM and the Eur. J. Nanomedicine.

New bioluminiscent models to target cancer stem cells with nanomedicine

Cancer Stem Cells (CSC) are a subset of tumor cells responsible of tumor repopulation after chemotherapy. Since current therapies do not specifically target CSC, the overall survival of cancer patients is poor. In this scenario, the use of specific drug delivery systems and tailor-made nanomedicines to increase the dose of anticancer agents reaching tumor and metastatic sites rise expectations for more effective and less toxic treatments. However, active tumor targeting, using antibodies or peptides as director moieties, do not seem to significantly improve retention of delivered drugs or their overall efficacy in animal cancer models. Further, evaluation of active targeting in CSC populations is hampered by technical difficulties and questioning CSC targeting feasibility. Here, we report new fluorescent CSC models, in which tdTomato reporter vectors under the CSC specific promoter are used for preclinical validation of PLGA-co-PEG micelles loaded with

paclitaxel. We validate targeting against CD44 and EGFR receptors, in breast and colon cancer cell lines. Accordingly, active CSC targeting sensitizes CSC to paclitaxel based chemotherapy. Further, finding new molecular targets to eliminate CSC is an additional goal which will greatly improve patient survival. Inhibition of specific kinases seems to be effective in CSC and inhibit CSC growth and spread. SiRNA strategies can therefore be applied also together with active targeting as new selective cancer treatments.

Wednesday, November 9th, 2016

Session 3: Combining Different Imaging Approaches

Oliver Plettenburg, Director, Institute of Medicinal Chemistry at the **Helmholtz Zentrum München GmbH, German Research Center for Environmental Health**, Munich, Germany.

(See his CV at the Scientific Committee Section)

Chair of the SESSION 3

Manel Sabés, External collaborator at **ALBA Synchrotron (UAB)**, Barcelona, Spain.

Alba Synchrotron-Universitat Autònoma de Barcelona (UAB, Experimental Division. Dr. in Biochemistry University Lecturer since 1989. Publications in 3 years:
S. Gil, et.al. A comparative study of the effectiveness of cisplatin and 5-fluorouracil on cutaneous squamous human carcinoma cell line. Der. Ther. in press .
Sabés-Alsina, M.; et.al 2016. Metabolic activity of sperm cells: correlation with sperm cell concentration, viability and motility in the rabbit. Zygote. doi:10.101.. 1
Gil S., et.al. 2015 Analysis of platinum and trace metals in treated glioma rat cells by X-ray fluorescence emission . Biol. Trace Elem. Res.. 163. p. 177
L G. Hermida, et al 2014. Characteristics and behaviour of liposomes when incubated with natural bile salt extract: implications for their use as oral drug delivery systems. Soft Matter. p. 1 -
S. Gil; et.al 2014. Double-strand breaks on F98 glioma rat cells induced by minibeam and broad-beam synchrotron radiation therapy. Clinical and translational Oncology. 16. p. 696 -
M. Cócera, et.al 2014. Synchrotron Radiation for Diagnosis of Skin Conditions. AA.VV.. Advances in Dermatological Sciences. 1 ed. Cambridge. Royal Society of Chemistry,; p. 53 -
Currently he is involved in 3 projects: Alba, UAB, I3PT Taulí and Clínic.

Chair of the SESSION 3

Vincent Dive, Head of the Section of Molecular Engineering of Proteins at the **Institute of Biology and Technology CE-Saclay (CEA)**, Saclay, France.

(See his CV at the Scientific Committee Section)

Sensitivity, resolution and long-term biodistribution studies by 3H and 14C digital autoradiography : moving from 2D to 3D imaging

Introduction of digital autoradiography with a new generation of radioimagers over classical autoradiography on film has provided major improvements in terms of acquisition time (1 h instead 1 month), sensitivity (50 attomoles 3H-drugs) and absolute quantification of drug biodistribution in animal tissue sections. Performance of this imaging modality will be illustrated by reporting recent data on the translocation of 14C-labelled carbon nanotubes from lung to peripheral organs and the ability of a natural 3H-toxin to cross physiological barriers (intestinal, blood brain and placental barriers). By

moving from 2D to 3D imaging by processing autoradiographic and corresponding histological tissue section, we will show how subtle drug biodistribution can be observed in rat embryos.

Cancer Stem Cells (CSC) are a subset of tumor cells responsible of tumor repopulation after chemotherapy. Since current therapies do not specifically target CSC, the overall survival of cancer patients is poor. In this scenario, the use of specific drug delivery systems and tailor-made nanomedicines to increase the dose of anticancer agents reaching tumor and metastatic sites rise expectations for more effective and less toxic treatments. However, active tumor targeting, using antibodies or peptides as director moieties, do not seem to significantly improve retention of delivered drugs or their overall efficacy in animal cancer models. Further, evaluation of active targeting in CSC populations is hampered by technical difficulties and questioning CSC targeting feasibility. Here, we report new fluorescent CSC models, in which tdTomato reporter vectors under the CSC specific promoter are used for preclinical validation of PLGA-co-PEG micelles loaded with paclitaxel. We validate targeting against CD44 and EGFR receptors, in breast and colon cancer cell lines. Accordingly, active CSC targeting sensitizes CSC to paclitaxel based chemotherapy. Further, finding new molecular targets to eliminate CSC is an additional goal which will greatly improve patient survival. Inhibition of specific kinases seems to be effective in CSC and inhibit CSC growth and spread. SiRNA strategies can therefore be applied also together with active targeting as new selective cancer treatments.

J Raul Herance, Researcher-Principal Investigator at **Vall d'Hebron Research Institute (VHIR),** Barcelona, Spain.

J Raul Herance is a Miguel Servet researcher who is a Principal Investigator in the Medical Molecular Imaging Group at Vall d'Hebron Research Institute beginning 2015. There, he mainly explores the utility of positron emission tomography (PET) technology for the study of metabolic disorders, personalized medicine and the development of nanomedicine. He obtained his BA degree in Chemistry at the Autonomous University of Barcelona in 2000 where he also obtained his PhD with honours in the field of organic chemistry and nanotechnology in 2005. He then joined High Technological Institute Foundation at Barcelona Biomedical Research Park, where he received his expertise in molecular imaging. In 2006 Dr. Herance took the lead of the Chemistry and Radiochemistry Research Unit in the above Foundation. For the next seven years he has been working in several molecular imaging projects related to PET both in clinical and preclinical trials for drug discovery and development. During this period, he was also an exchange researcher in several International centers including Turku PET Center and the Clinical Imaging Center-Imperial College London. In 2014, Dr. Herance has been awarded a Miguel Servet grant änd expanded his research line in nanomedicine in connection to clinics (diabetes) by working in Dr. Peset Hospital (Valencia) after which he moved to Vall D´Hebron Research Institute (2015) to organize the Medical Molecular Imaging Group.

PET in drug discovery and development: an overview

Medical Imaging is the group of techniques that are used to view the human body in order to diagnose, monitor, or treat medical conditions. Anatomical, physiological or molecular information is taken according to the imaging modality used. Thus, the group of techniques with high resolution, radioactive and optical, can be used to get only molecular and physiological information but not anatomical one. On the other hand, the techniques with high sensibility, radiological, allow obtaining much more anatomical information with a lack of molecular one. Therefore, radioactive techniques, mainly positron emission tomography (PET) and single-photon emission computed tomography (SPECT), have been selected for molecular imaging to view the expression of biological target or functional analyses as well as metabolic pathways in humans and other living systems by using radiopharmaceuticals aka radiotracers. Besides, these radiotracers have a similar behaviour in animals and humans thus allowing translational research. The most powerful technique for molecular imaging is PET that is used in nuclear medicine to obtain 3D images of processes inside the body by applying radiopharmaceuticals with PET isotopes. PET changed the management of patients in some medical areas such as oncology, neurology, and cardiology. It has been proposed as an indispensable tool for patient selection in personalized medicine and for validation of other tools in a similar are. In addition, this technique is amenable for drug discovery and development because it covers all the R&D stages including target identification, screening of compounds, preclinical and clinical trials as well as follow up studies. Nowadays, PET is an indispensable tool for research and clinical diagnosis.

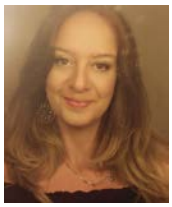
Tim Wokrina, Market Manager Fundamental Markets at **Bruker BioSpin MRI,** Ettlingen, Germany.

Dr. Tim Wokrina is the Product Marketing Manager for preclinical MRI and PET/MRI products at Bruker BioSpin Preclinical Imaging. He acquired his background in EPR and NMR technology and physics at the Technical University in Karlsruhe, Germany. As a PostDoc, he conducted clinical MRI studies on major depression, ageing, and the metabolic syndrome using MR spectroscopy methods at the Central Institute of Mental Health in Mannheim, Germany. He began his industry career in 2007 when joining Bruker BioSpin MRI as an Application Scientist for preclinical applications. In 2010, he took over Project and Product Management tasks, and was later responsible for the ICON, BioSpec/PharmaScan and CryoProbe MRI products. Since 2013 he is

responsible for the Product Management and Strategic Product Marketing for the MRI product lines at Bruker BioSpin PreClinical Imaging, and since 2016 also for the PET/MRI combined modality instruments.

Multimodality Imaging - The Ideal Solution to Advance Molecular Imaging?

The merging of distinct technologies and procedures in molecular imaging research is typically considered to be a practicable path to integrate scientific insights and make them more meaningful for the understanding of the underlying biological processes, new therapeutics, and treatment approaches – and this is the promise – to ultimately enable faster translation into clinically viable tools and treatments. The presentation discusses recent technological advances in integrating complementary modalities to make scientific outcomes more rich and meaningful from a preclinical vendor's perspective. Multimodal molecular imaging involves a wide range of technologies, skills, and challenges in general when merging them into multimodal devices. The integration of Bioluminescence-, Fluorescence-, Cherenkov-, Radioisotopic-, and X-ray imaging to detect most molecular probes, agents, and tracers in one compact instrument is discussed as well as recent technological breakthroughs that enable simultaneous PET and MRI measurements at high field, opening up new avenues for basic research in oncology, stroke, cardiac imaging, and others.



Ana Paula Candiota, Senior Researcher CIBER at **Centro de Investigación Biomédica en Red (CIBER) /UAB)**, Barcelona, Spain.

Dr. Candiota (b. 1971, Rio Grande do Sul, Brazil). Presently working in the biomedical applications of nuclear magnetic resonance (NMR/MRI/MRS/MRSI), with a special focus in the evaluation of glial brain tumours from preclinical mice models. Main efforts are actually devoted to the noninvasive therapy response follow-up in preclinical glioblastoma. For this, MRSI- based molecular imaging techniques and pattern recognition strategies are being applied to generate nosological maps of therapy response with translational potential. Finally, besides conventional therapeutic agents, novel therapeutic strategies are also being evaluated in preclinical glioblastoma. Dr. Candiota graduated (BSc) in Pharmacy in 1997 (UCPel, Brazil). Awarded three times with stage grants to Spain from the Agencia Española de Cooperación Internacional (AECI) between 1997 and 1999. PhD in Bioquímica, biologia molecular i biomedicina awarded at Universitat Autònoma de Barcelona, Spain in 2005. Since 2007, she is a permanent researcher of Centro de Investigación Biomédica en Red (CIBER) Bioingeniería, Biomateriales y Nanomedicina (http://www.ciber-bbn.es/). She is also Profesor Asociado at Universitat Autònoma de Barcelona, at the Biology BSc and the Master of Nanotechnology .

Unraveling therapy response in preclinical glioblastoma using MRSI-based molecular imaging and source analysis

Characterization of Glioblastoma (GB) response to treatment is a key factor for improving patient survival and prognosis. Magnetic Resonance Imaging and Spectroscopic Imaging (MRI/MRSI) provide morphologic and metabolic profiles of GB but usually fail to produce unequivocal surrogate biomarkers of response. Ideally, we would like to provide clinicians with early therapy response follow-up and an improved time frame for changing or adapting therapy schemes. This talk focuses in the capability of advanced pattern recognition techniques, such as semi-supervised signal source extraction, to produce nosological images with robust recognition of response to temozolomide (TMZ) in preclinical GB (GL261 tumour-bearing in immunocompetent C57/BL/6mice) through the information contained in MRSI grids. These techniques have a clear translational potential and could improve future patient management and care.

Session 4: Towards Translational Imaging and Theranostics

Markus Rudin, Professor at the **University of Zurich and ETH Zurich**, Zurich, Switzerland.

(See his CV at the Scientific Committee Section)

Chair of the SESSION 4

Carles Arús, Professor of Biochemistry and Molecular Biology at **Universitat Autònoma de Barcelona and CIBER-BBN,** Barcelona, Spain.

Born in 1954, BSc 1976, PhD 1981 (Barcelona, ES). First involved with protein NMR in 1979 in Naples (IT). Postdoctoral work in muscle NMR with Michael Bárány and John L. Markley (1982-1985, USA). Since 1985 at the Department of Biochemistry and Molecular Biology of UAB (Barcelona, ES), now as Full Professor. Also, leading the GABRMN group since then (http://gabrmn.uab.es/). About 140 publications, "h" number of 30 (http://www.researcherid.com/rid/C-2361-2009). Present interests in the field of MR-basedmolecular imaging of brain tumours, for diagnosis, prognosis and therapy planning.

Chair of the SESSION 4

Matthew Bogyo, Professor, **Stanford University**, Stanford, USA.

(See his CV at the Scientific Committee section)

Small molecule protease probes for imaging cancer and infectious diseases

Proteases are enzymes that often play pathogenic roles in many common human diseases such as cancer, asthma, arthritis, atherosclerosis and infection by pathogens. Therefore tools that can be used to dynamically monitor their activity can be used as diagnostic agents, as imaging contrast agents for intraoperative image guidance and for the identification of novel classes of protease-targeted drugs. In this presentation, I will describe our efforts to design and synthesize small molecule probes that produce a fluorescent signal upon binding to a protease target. In the first part of the presentation, I will discuss probes targeting the cysteine cathepsins that show tumor-specific retention, fast activation kinetics, and rapid systemic distribution. These probes are useful for real-time fluorescence guided tumor resection and other diagnostic imaging applications. In the second half of the presentation, I will present our efforts to develop imaging probes that are specific for protease targets in the pathogenic bacteria Mycobacterium tuberculosis. These probes are being developed as optical and radiological imaging tracers to non-invasively track disease progression and response to therapeutic interventions.

Kevin P Francis, Fellow, **PerkinElmer,**, Alameda, CA, USA.

Dr Kevin Francis joined Xenogen, now part of PerkinElmer, in January 1999 as Director of Infectious Disease Research, subsequently becoming Head of Biology R&D. He is currently a PerkinElmer Fellow, helping to direct scientific innovation within the company and steer collaborative research externally with its extensive customer base. In February 2008 Kevin was awarded an Honorary Professorship in the Department of Surgery at the University Medical Center Groningen, and served as Visiting Professor in the Faculty of Natural Sciences at Imperial College between January 2013 and August 2015. He is currently a Visiting Professor in the Department of Orthopaedic Surgery at UCLA, helping to develop clinically relevant models of orthopaedic implant infection. Kevin received his Ph.D in Molecular Biology from the University of Edinburgh in 1994, and has been involved in the development of novel bioluminescent reporter systems and in vivo models of disease for the past 25 years.

Optical Tomography and Its Role in Multimodality Imaging and Translational Disease Research

PerkinElmer is a global leader in the development of instrumentation and probes for small animal non-invasive imaging, including optical, PET and μCT imaging. Through optical imaging, we have developed a technology which allows biological processes, including gene expression that is temporally and spatially defined, to be non-invasively monitored both longitudinally and in real-time. Genes encoding optical reporters, luciferases and fluorescent proteins, are engineered into cells (e.g., cancer cells, stem cells) and pathogens (e.g., bacteria, viruses), or directly into animals (e.g., monitoring host responses) to enable the generation of light that can be visualized through the tissues of a live animal. PerkinElmer is the only company to have optimized this technique to allow true three-dimensional optical imaging and tomographic multimodality imaging (e.g., through co-registration of optical imaging with μCT and MRI). Furthermore, this technique is equally applicable to imaging of fluorescent dyes and particles, allowing fluorescently tagged biological events (e.g., tracking of antibodies, peptides and viral capsids) to be monitored both independently and in combination with genetically

tagged events. PerkinElmer has also recognized the importance of moving optical imaging beyond monitoring small animals, allowing its fluorescent probes to be seamlessly translated from preclinical to diagnostic and surgical applications in large animals (e.g., veterinary), with the view of eventually moving this technology into routine clinical settings. An overview of optical imaging in a range of disease backgrounds will be presented, showing how this approach can be used to refine and improve fundamental biological research, as well as drug development strategies and surgical procedures.

Quyen T. Nguyen, Associate Professor, **University of California San Diego (UCSD)**, San Diego, USA.

Dr. Nguyen is an Associate Professor in the Department of Surgery at the University of California San Diego (UCSD). She received her combined MD/PhD degree from Washington University, School of Medicine in St. Louis, MO. She completed her General Surgery Internship at Barnes Jewish Hospital in St. Louis and residency/subspecialty fellowship training at the UCSD.She is board certified in both Head and Neck Surgery and Neurotology/Skull Base Surgery. Her clinical practice is at UCSD Health Systems is she supervises students, residents and fellows and cares for patients with diseases the facial nerve, ear and skull base. She is Director of the Facial Nerve Clinic and co-director of the Cancer Imaging Program at the Moores Cancer Center.

Precision Markers for Color-Coded Surgery - Imaging tumors and nerves

Cancer is the leading cause of death among adults 40 to 79 years. Although treatment algorithms vary, surgery is the primary treatment modality for most solid cancers. The fundamental goal of a curative oncologic surgery is complete cancer removal but equally important from the patient's point of view is function preservation and pain control. Currently, there is an increasing trend to adopt minimally invasive technologies such as endoscopic and robotic surgery in order to decrease patient morbidity. However, the ability for surgeons to distinguish between normal and diseased tissue by texture or consistency is significantly reduced with these techniques (due to lack of ability to physically touch the tissue) and is limited to visual inspection alone. Using white light reflectance which is the current standard mode of illumination in operating rooms, the visual difference between normal and cancerous tissue can be imperceptible. The inability of surgeons to visually distinguish between tumor and normal tissue leads to residual cancer cells left behind at the edges of resection, i.e. positive surgical margins and can be as high as 20-40% in breast cancer lumpectomy, 21% for radical prostatectomy, and 13% for HNSCC. Molecular imaging with fluorescence provides enhanced visual definition between diseased and normal tissue and have been shown to decrease PSM in both animal models and patients. Molecular imaging with fluorescence can also provide enhanced visualization of important structures such as nerves to improve preservation and minimize inadvertent injury. Our laboratory has extensive experience in development of both nerve and tumor injectable markers for surgical visualization. In presentation we will discuss the development of nerve and tumor markers combinations to improve intraoperative visualization – aka color-coded surgery.

Ramon Mangues, Research Professor, **Research Institute, Hospital de Sant Pau**, Barcelona, Spain.

Ramon Mangues is a Full Professor at the Biomedical Research Institut Sant Pau (IIB-Sant Pau) of the Hospital de Sant Pau in Barcelona. He held a 6 year position as Clinical Pharmacist at the Navarra University Clinic, and a postdoctoral and Senior Researcher positions, for 10 years, at the New York University Medical Center. He is Head of the Oncogenesis and Antitumor Drug Group, member of the Biomedical Research Network for Excellence in Nanomedicine (CIBER-BBN). Ramon Mangues is also a board member of the IIB-Sant Pau Executive Committee, borad member and Translational Research Coordinator of CIBER-BBN and of theJosep Carreras Research Institute Scientific Committee. He is an Expert Reviewer of the Swedish Research Council and the Scientific Evaluation Committee of the French National Cancer Institute. He is a member of the European Technology Platform on Nanomedicine, the American Association for Cancer Research and the New York Academy of Sciences. He is coordinator and principal investigator of research projects funded by the Spanish Government and the EU focused on targeted drug delivery in oncology, involving basic and clinical groups and small biotechnology companies. Ramon Mangues was co-founder and Scientific Advisor of Argon Pharma SL, a spin-off of the Hospital de Sant Pau. He has collaborated or currently holds Research Contracts with Merck and Co., PharmaMar/Zeltia, Esteve Laboratories, Lilly and Roche.

Imaging targeted drug delivery in colorectal cancer models

We are combining fluorescence and bioluminescent imaging with the most classical flow-cytometry, histology and immunohitochemistry methods to follow the in vivo biodistribution and anticancer effect of an actively targeted drug-protein nanoparticle conjugate in an orthotopic model of colorectal cancer. The nanoconjugate contains a GFP domain,

whereas tumor cells are bioluminescent and highly express a specific receptor in their membrane as compared to normal tissues. We first selected a specific ligand for the receptor to be incorporated to the nanoparticle to achieve high level of receptor-mediated internalization. We achieve selective biodistribution to the tumor, and target cell uptake, which is compited with a specific receptor antagonist. We also describe the capacity of the nanoconjugate, after its intravenous injection, to increase DNA damage and apoptosis induction in target cells, leading to their selective elimination. We also describe differential regulation of the target receptor in cancer cells at different organs, leading to differential target cell internalization and antimetastaic effect. Finally, we report absence of toxicity of the nannoconjugate and a high therapeutic window because of low level of biodistribution and lack of histological alterations on o normal tissues. We are now defining the threshold of target receptor overexpression in cancer models for candidate patient selection.

Boris Turk, Professor of Biochemistry at **Jozef Stefan Institute & University of Ljubljana,** Ljubljana,Slovenia

(See his CV at the Scientific Committee section)

Cysteine cathepsins as targets for noninvasive whole body imaging and targeted drug delivery

Inflammation plays an important role in disease onset and progression in a vast number of diseases, called also inflammation-associated diseases including various cancers, psoriasis, dermatitis, inflammatory bowel diseases, pancreatitis, various forms of arthritis, osteoarthritis, osteoporosis/bone resorption, septic shock, atherosclerosis, ischaemia-reperfusion injury, coronary heart disease, vasculitis, amyloidosis, pulmonary fibrosis, viral infections, systemic lupus erythematosus, and asthma. Proteases play a major role in a number of these diseases. However, understanding the precise role of an individual protease in a disease remains a major challenge for successful therapeutic applications. There are several ways how to address this issue, including the chemical biology approaches including small molecule inhibitors and activity-based probes, as well as by engineered macromolecules (e.g. DARPins). These approaches offer a major potential for noninvasive optical imaging by monitoring protease activities in situ, i.e. on disease site. Moreover, they enable also validation of proteases as drug targets, in vivo validation of drug candidates and evaluation of the diagnostic potential of the target proteases. Among the proteases found to be tightly linked with inflammation-associated diseases are also cysteine cathepsins that can be found at the sites of inflammation. Furthermore, since they are heavily upregulated in a number of inflammation-associated diseases, they are therefore perfect targets for such approaches. There is increasing evidence that monitoring cathepsin activity in vivo may be applicable to diagnostic imaging, such as demonstrated primarily for cancer, arthritis and inflammatory bowel diseases. Moreover, cathepsins can be also used as targets for targeted drug delivery approaches combined with diagnostics, thereby offering a theranostic potential.

PRACTICAL INFORMATION

Venue: CosmoCaixa Barcelona

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Conferences
Agora room on -3 floor

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SUGGESTED READING

Journals & books

-American Journal of Nuclear Medicine and Molecular Imaging (Century Publishing Corp.)

(http://www.ajnmmi.us)

-International Journal of Clinical and Medical Imaging

(http://imagejournals.org)

-Journal of Molecular Biology and Molecular Imaging (Austin Publishing Group)

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OUTCOMES

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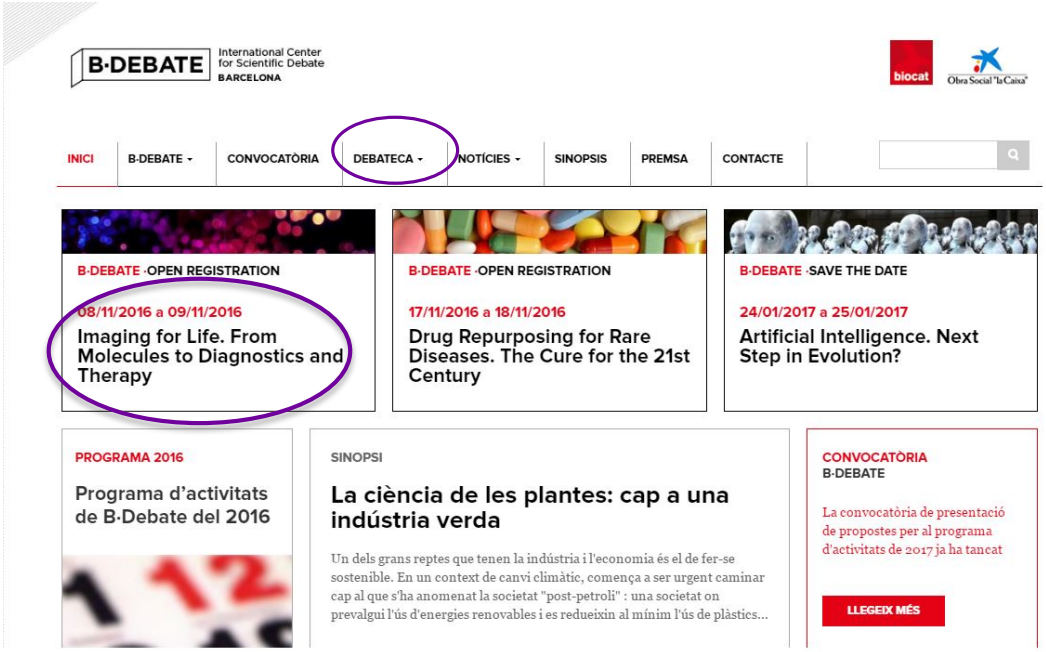
Contents of the meeting "Imaging for Life. From Molecules to Diagnostics and Therapy"



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