CLINICAL PROTEOMICS:
TOWARDS PERSONALIZED MEDICINE AND HEALTH

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November 7 and 8, 2018

WELCOME

Dear participants,

On behalf of the Organizing Committee, it is with great pleasure that we welcome you to the 'Clinical Proteomics: towards personalized medicine and health' B·Debate.

Traditionally, medicine relied on the patient's examination, medical history and available clinical parameters for the diagnosis of diseases and the selection of treatments. However, this practice is currently evolving with the emergence of new imaging techniques and high-throughput molecular sequencing that generate large amounts of data per patient. These data can be converted to relevant clinical information, allowing patient stratification and the deciphering of pathological mechanisms, thus advancing in the paradigm of personalized medicine. Among the molecular sequencing techniques, proteomics provides functional information about the activity of proteins, which is often crucial for the understanding of cell physiology. During the last decade, the development of the field has facilitated the characterization of the main mechanisms of cell signaling, and the deciphering of protein-protein interaction that are essential in gene regulation and that govern the different phenotypes observed in cells and tissues. In addition, the consolidation of proteomics technologies have enabled new large-scope applications for clinical and biomedical research in which hundreds of samples can be analyzed by mass spectrometry. These applications allow the identification and quantification of proteins in biological fluids, biopsies and animal models, as well as the analysis of post-translational modifications, interactions and intracellular localization of proteins, in order to find markers of disease, understand the pathological molecular mechanisms, and provide new treatments for patients.

An initiative of Biocat and "la Caixa" Foundation, this B·DEBATE is co-organized by ProteoRed-ISCIII and four major research institutes in Barcelona: Bellvitge Biomedical Research Institute (IDIBELL), Vall d'Hebron Institute of Oncology (VHIO), Barcelona Science Park (PCB) and Centre for Genomic Regulation (CRG). By bringing together the world leaders in proteomics and the local clinicians and researchers, this B·Debate aims to introduce new applications, developments and recent innovations of the proteomics field to the biomedical community, to empower clinicians and translational researchers with latest generation proteomics technologies for personalized medicine, and to promote enriching scientific discussions among academic and medical communities, biotechnology industry and local citizens to foster new collaborations and synergies.

We thank you in advance for your input and participation in the discussion. We hope that the meeting will cover your expectations and we wish you a pleasant stay in Barcelona.

Yours sincerely,

Mercè Martí, Carolina de la Torre, Eliandre de Oliveira, Eduard Sabidó, Francesc Canals and B·DEBATE

PROGRAM

Wednesday, November 7, 2018

8:45	Registration
9:00	**Welcome** Jordi Portabella, "la Caixa" Banking Foundation Núria Martí, Biocat Jaume Reventós, Government of Catalonia José Manuel Menchón, Bellvitge Biomedical Research Institute Eliandre de Oliveira, Barcelona Science Park
9:15	**Opening Lecture** Chair: Fernando Corrales, National Center for Biotechnology-CSIC, Madrid Multi-Omics Research - Proteomics joins forces with Genomics to Advance Basic and Translational Cancer Research Henry Rodriguez, Center for Strategic Scientific Initiatives and National Cancer Institute, National Institutes of Health (NIH), USA
10:00	SESSION 1. **Proteomics in the National Health System** Chair: Jaume Reventós, Government of Catalonia, Barcelona The proteome quest to understand biology and disease Fernando Corrales, National Center for Biotechnology-CSIC, Madrid Adding Values to Healthcare System through Clinical Proteomics – A US perspective Y. Victoria Zhang, University of Rochester Medical Center, USA
11:30	Coffee break
12:00	SESSION 2. **Clinical Proteomics in Cancer Research** Chair: Jordi Barretina, Girona Biomedical Research Institute, Girona Epigenetics and the cancer proteome Manel Esteller, Bellvitge Biomedical Research Institute and Josep Carreras Leukaemia Research Institute, Barcelona Phosphoproteomics - an all-in-one tool for unraveling drug resistance, finding biomarkers and disease segmentation in breast cancer Miguel Quintela-Fandino, Spanish National Cancer Research Centre, Madrid
13:30	Lunch and poster session

14:30	SESSION 3. **Technology Innovations (I)** Chair: Alejandro Vaquero, Bellvitge Biomedical Research Institute, Barcelona The Human Protein Atlas - implications for human biology and precision medicine Cecilia Lindskog, Uppsala University, Sweden The target landscape of clinical kinase inhibitor drugs Bernhard Kuster, Technical University of Munich, Germany
16:00	Coffee break
	SESSION 4. **Clinical Proteomics in Cardio and Neurological diseases** Chair: Lina Badimon, IR Hospital Santa Creu i Sant Pau, Barcelona Protein-based Cardiogenic Shock Patient Classifier Antoni Bayes, Germans Trias i Pujol University Hospital, Badalona Clinical proteomics in the study of human neurodegenerative diseases with abnormal protein aggregates Isidro Ferrer, University of Barcelona, Barcelona The search for novel biomarkers of synapse degeneration as a diagnostic tool for dementia Olivia Belbin, Sant Pau Biomedical Research Institute, Barcelona
18:00	End of the session
18:00	Poster session and networking cocktail

Thursday, November 8, 2018

8:35	Registration
9:00	SESSION 5. **Clinical Proteomics in Immunology and Microbiology** Chair: Ricardo Pujol-Borrell, Vall d'Hebron University Hospital, Barcelona Unravelling the hidden universe of small proteins in bacterial genomes Luís Serrano, Centre for Genomic Regulation, Barcelona Organelle remodeling en route to virus replication: Integrated proteomics, lipidomics, microscopy and mathematical modeling Ileana M. Cristea, Princeton University, USA
10:30	Coffee break
11:00	SESSION 6. **Proteomics into personalized medicine** Chair: Paolo Nuciforo, Vall d'Hebron Institute of Oncology, Barcelona ProteOmics in Humans for Nutrition and Diagnostics Martin Kussmann, Frontiers Media S.A., Switzerland, and Interdisciplinary Nanoscience Center at Aarhus University, Denmark The Future of Precision Proteomics Emily Chen, Thermo Fisher Precision Medicine Science Center, USA

12:30	Lunch and poster session
14:00	SESSION 7. **Technology Innovations (II)** Chair: Oscar Yanes, IRB Barcelona and CIBERDEM, Barcelona Development and Application of the MasSpec Pen for Rapid Ex Vivo and in Vivo Cancer Tissue Diagnosis Marta Sans, The University of Texas at Austin, USA Spatial metabolomics in tissues and single cells Theodore Alexandrov, European Molecular Biology Laboratory, Germany
15:30	SESSION 8. **Proteomics Entrepreneurs Round Table** Chair: Jordi Naval, Biocat, Barcelona • Eva Colás, Vall Hebron Research Institute, Barcelona • Ralph Schiess, ProteoMediX AG, Switzerland
16:30	Coffee break
17:00	**Closing Lecture** Chair: Eduard Sabidó, Centre for Genomic Regulation, Barcelona Studying protein structural changes on a proteome-wide scale in health and disease Ilaria Piazza, ETH Zurich, Switzerland
18:00	End of the meeting

SCIENTIFIC COMMITTEE

Mercè Martí Gaudes, Head of CMRB-IDIBELL Core Facilities, Barcelona, Spain

Dr. Mercè Martí is the Head of the CMRB-IDIBELL Core Facilitiy (CMRB-IDIBELL CF). The CMRB-IDIBELL CF enhances cooperation between technical specialists and researchers. With this aim, the facility has been provided with sophisticated equipment and technology, as well as expert personnel. The CMRB-IDIBELL CF is composed by the following units: mouse, aquatic animals, cell and tissue models, histology, optical microscope, electron microscope, flow cytometry, molecular biology, molecular interactions, proteomics and genomic unit.

During these last 10 years, Dra. Martí has mainly collaborated into the field of stem cells and in studies of different animal models to understand a basic mechanism of initial development and organogenesis, as well as the high regenerative capacity of some of them. The CMRB team specifically demonstrate that after partial heart amputation in zebrafish, cardiomiocytes undergo first a dedifferentiation, and then a subsequent proliferation. Furthermore, recent studies have demonstrated that in Xenopus tail regeneration, there is a dedifferentiation of the myofibers. New data observed in the tadpoles regeneration study encouraged the team led by Dra. Martí to perform a thorough description of the post-natal myogenesis. As a result, they have described a new satellite cell division model. In addition, the large experience of her technical team in immunodetection technologies and different microscopies has been compiled in other papers related with the characterization of iPSC.

Carolina de la Torre Gómez, Head of Clinical Proteomics Unit at Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain

Carolina De La Torre, Ph.D., has studied Bacteriology at the Metropolitan University in Barranquilla (Colombia) and performed her PhD in the neuromuscular research group in Sant Pau hospital by the Barcelona University. There, she developed and applied proteomics techniques to answer the biological question in neuromuscular disorders. She has been working in various proteomic facilities developing and applying cutting-edge quantitative technologies to biomedical questions, with a more recently emerging interest and focus on clinical proteomics.
She has reached a key phase in her scientific career, in which has decided to leverage her combined skills in biology and proteomics into further sharpening and developing her personal scientific profile.
Currently, she is heading the Proteomics Facility at IDIBELL and the Bellvitge Hospital in Barcelona and she is involving in biomedical and biomarkers discovery projects according with the clinical background education.

Eliandre de Oliveira, Head of the Proteomics Unit at Barcelona Science Park, Barcelona, Spain

Eliandre de Oliveira has a degree in Chemistry from the University of São Paulo and a Ph.D. in Science from the Paulista School of Medicine. She did a postdoctoral stage at the University of Barcelona where she had the opportunity to collaborate on a project related to the development of synthetic peptide vaccines for Foot and Mouth disease and the Herpes simplex. The experience in peptide and protein chemistry led her to explore the field of proteomics where she has been working for over fifteen years.

During this time, she has managed the Proteomics Unit at the Barcelona Science Park whilst involved on several basic and clinical-related proteomics projects. She has both a strong interest and experience in developing bioanalytical research methodologies and applying them to projects thereby supporting basic and translational research. Such projects require and include protein identification, protein quantification with and without e.g. stable isotopic labelling, analysis of post-translational modifications.
Her current work is mainly focused on clinical proteomics applications based on high-resolution mass spectrometry. She has been working on projects that aim at finding candidates protein biomarkers for diseases' diagnosis (Shockomics) as well as projects related to the identification and characterization of proteins (Spanish Human Proteome Project, SHPP, ProteoRed-ISCIII) and projects dedicated to molecular analysis to better understand the mechanisms of bacterial resistance.

Eduard Sabidó, Head of the CRG/UPF Proteomics Unit at Centre for Genomic Regulation (CRG), Barcelona, Spain

Eduard Sabidó is the head of the Proteomics Unit of the Center for Genomics Regulation and the University Pompeu Fabra, and he is an associate professor at the Department of Experimental Sciences and Health of the University Pompeu Fabra. His group focuses on the development of innovative mass spectrometric methods for targeted protein quantification and the characterization of protein post-translational modifications from complex biological samples. E. Sabidó currently runs two national research projects as principal investigator, and he is part of the European consortium EPIC-XS. The group of E. Sabidó is part of ProteoRed, the reference proteomics platform of the Spanish National Health Institute, and he has been the main organizer of five EMBO Practical Courses on Targeted Proteomics (2014-2018).

Francesc Canals, Principal Investigator at the Proteomics Laboratory at **Vall d'Hebron** Institute of Oncology (VHIO), Barcelona, Spain

Francesc Canals graduated in Organic Chemistry from the Institut Químic de Sarrià, Barcelona, in 1982 from where he also obtained his PhD in 1989 working on organic photochemistry. He also obtained a degree in Biochemistry from the Universitat Autònoma de Barcelona in 1987. From 1989 to 1991 he worked as a postdoctoral fellow in the laboratory of J. Kyte, at the University of California San Diego (USA), and until 1995 in the laboratory of F. X. Avilés, at the Institut de Biotecnologia i Biomedicina (Universitat Autònoma de Barcelona). From 1995-2003 he was in charge of the Proteomics Facility at the Universitat Autònoma de Barcelon, where he also contributed to several studies on the biological applications of mass spectrometry.
From 2003 is principal investigator at the Proteomics Laboratory at the Vall d'Hebron Institute of Oncology (VHIO) at the Vall d'Hebron University Hospital in Barcelona. His main research is focused in exploring the role of metalloproteases of the ADAM and ADAMTS families in cancer through proteomic analysis, and pursues also the use of proteomic techniques for screening and validation of biomarkers for cancer diagnostic, treatment personalization and monitoring. He also leads the Proteomic Core facility, which is integrated in the spanish ProteoRed-ISCIII network. Within this framework, he has coordinated several multi-laboratory studies aimed to optimize, standardize and provide quality control tools for different proteomic workflows across the network laboratories.

DETAILED PROGRAM AND INVITED SPEAKERS

Wednesday, November 7, 2018

Opening Lecture

Fernando Corrales, Scientific Researcher at National Center for Biotechnology - CSIC, Madrid, Spain

Fernando J Corrales received the BSc degree in Biological Sciences (1986) and the PhD degree in Biochemistry and Molecular Biology (1992) from the University Autónoma of Madrid. After a Postdoctoral period at the University of Cambridge (UK), he joined the CIMA, University of Navarra, where he has been Professor of Biochemistry and head of the Proteomics, Genomics and Bioinformatics Facility since 1999. He is currently Senior Scientist and head of the Proteomics Laboratory at the Centro Nacional de Biotecnología. He is an active researcher in the field of Biochemistry. His interest is now focused on the study of the mechanisms associated to liver function as well as those involved in the progression of liver diseases using proteomics and genomics approaches, which are then combined with a systems biology-based strategy. His research activity has been regularly founded by regional, national and international grants and lead to the publication of 146 scientific articles H=28; more than 2400 cites/year). He is member of the editorial board of different journals specialized in proteomics and hepatology, General Coordinator of the Molecular and Bioinformatics resources Platform and ProteoRed-ISCIII (Spanish Proteomics Network) and is member of the Executive Councils of the European Proteomics Association and the BD and C-Human Proteome Project as well as PI of the Human Liver Proteome Project and the chromosome 16 Spanish Human Proteome Project.

Chair of the opening session.

Henry Rodriguez, Deputy Director (Acting) of the Center for Strategic Scientific Initiatives and Director of the Office of Cancer Clinical Proteomics Research at the National Cancer Institute, National Institutes of Health (NIH), Washington, D.C., USA

Henry Rodriguez, Ph.D, M.B.A., serves as the Deputy Director (Acting) of the Center for Strategic Scientific Initiatives, and is the founding Director of the Office of Cancer Clinical Proteomics Research, at the National Cancer Institute (NCI; Office of the Director), National Institutes of Health (NIH). Rodriguez also led the development of the International Cancer Proteogenome Consortium, and co-led the development of the Applied Proteogenomics OrganizationaL Learning and Outcomes network involving the DoD and VA healthcare system.

Dr. Rodriguez received his undergraduate degree in biology/chemistry and master's degree in biology/toxicology from Florida International University. He went on to pursue his doctorate degree in cell and molecular biology from Boston University, and Master of Business Administration in finance and management from Johns Hopkins University. Fellowships were conducted at The Scripps Research Institute and at City of Hope National Medical Center.

Dr. Rodriguez serves on the U.S. HUPO Board of Directors, and the Foundation for the NIH Biomarkers Consortium Cancer Steering Committee. Dr. Rodriguez is the recipient of numerous honors, and serves on the editorial boards of Scientific Data, Clinical Proteomics, and Annals of Laboratory Medicine. Dr. Rodriguez has authored more than 129 original scientific papers, including co-editing a best-selling book on oxidative stress and aging.

Dr. Rodriguez has made important contributions to understanding mechanisms of cancer and age-related diseases, including development of molecular-based technologies in basic and translational science.

Multi-Omics Research - Proteomics joins forces with Genomics to Advance Basic and Translational Cancer Research

Despite significant progress in understanding cancer through massively parallel sequencing genome programs, the complexity that comprises its diseases remains a daunting barrier. Today we know that molecular drivers of cancer are derived not just from DNA alterations alone, but from protein expression and activity at the cellular pathway level - proteomics. Key issues such as therapeutic resistance and the metastatic process fail to give single gene/mutation explanations. The new field of proteogenomics, where research pioneered recently from CPTAC using mass spectrometry demonstrated that the integration of proteomic profiles with genomic information, reveals new molecular subtypes of cancers that are inaccessible by NGS. The new field of proteogenomics provides an opportunity to generate new insights by melding the complexity of cancer genomics with cancer proteomics to more completely understand how somatic genomes activate aberrant signal transduction events that drive cancer pathogenesis. As such, a multi-omics (genomics, proteomics, even metabolomics) approach in clinical studies stands to fast become an essential part of laboratory medicine due to its tremendous potential to be a powerful clinical tool, allowing us to traverse the large knowledge gap between cancer genomics and clinical action. This seminar will discuss how genomics, transcriptomics, and proteomics are being combined in the quest to understand the etiology of cancer – in basic clinical sample studies and translational research (clinical trials).

Session 1. Proteomics in the National Health System

Fernando Corrales, Scientific Researcher at National Center for Biotechnology - CSIC, Madrid, Spain

Read bio in page 9.

The proteome quest to understand biology and disease. ProteoRed-ISCIII.

The last few decades have witnessed a tremendous technological development that greatly enhances our capacity to study living organisms. However, the generalized access to these resources might be compromised by the complexity of the infrastructures and the data generated, the necessity of multidisciplinary strategies or by budgetary restrictions, among others. Technological platforms emerge as an attempt to democratize the use of state of the art technology and integrate the new analytical capabilities in the routine biomedical and clinical research pipelines. The overall strategy developed by the Instituto de Salud Carlos III (ISCIII) leaded to the consolidation of PRB[2] and later PRB[3] that in addition to its own research offers support to research initiatives in genomics, proteomics, bioinformatics and biobanking. Within the PRB[2-3], ProteoRed has been a pioneer experience that has provided support to hundreds of projects, is currently leading a European standardization initiative and is one of the teams worldwide leading the Human Proteome Project. Special emphasis has been paid to the integration of the proteomics technology in the biomedical and clinical environments. To this end, a dissemination and training strategy has been designed and developed in close collaboration with the different structures of the Spanish Health System ISCIII, resulting in the consolidation of projects with a marked translational vocation. The workshop represents an excellent opportunity to discuss some of our next challenges, including the definition of a roadmap for biomarker qualification for clinical use, among others.

Y. Victoria Zhang, Vice Chair of Pathology and Laboratory Medicine and Director of Clinical Mass Spectrometry and Toxicology Laboratory at the University of Rochester Medical Center, Rochester, USA

Dr. Y. Victoria Zhang is Vice Chair and an Associate Professor of Department of Pathology and Laboratory Medicine at the University of Rochester Medical Center. She is Director of Clinical Mass Spectrometry and Toxicology Laboratory. Dr. Zhang is the Founding Chair of the American Association for Clinical Chemistry (AACC) Mass Spectrometry and Separation Sciences (MSSS) division and spearheaded the efforts in increasing the awareness and further improving applications of mass spectrometry in clinical diagnostics with the clinical community.

She is also the Faculty Chair for AACC Global Lab Quality Initiative Asia-Pacific Working Group to lead the initiative to develop workshops and frameworks for sustainable support for the Asia Pacific region to improve quality in lab medicine.

Dr. Zhang is the international leading expert in clinical applications of mass spectrometry. She has published extensively in this area with more than 100 peer-reviewed articles, book chapters and abstracts in this area with over 70 national and international presentations, and numerous media reports and interviews. Dr. Zhang has been also devoted her time in education and academic exchange in this area. She has organized about 20 regional and national conferences with similar number of international and national symposia, workshop and short courses. She is on several the Editorial Boards in the field of clinical chemistry and laboratory medicine.

Her research interests are in clinical mass spectrometry, translational research using "-omics" technology, test utilization particularly through laboratory formulary model, and laboratory management and leadership development.

Adding Values to Healthcare System through Clinical Proteomics – A US perspective

Clinical Proteomics through targeted mass spectrometry (MS) approaches for peptide and protein analysis are quickly becoming an essential part of laboratory medicine due to their tremendous potential in clinical application and clinical proteomics. Adoption of targeted MS to study clinical questions is well underway as these assays provide higher specificity, sensitivity, short development time, and allows for multiplexing analytes as compared to conventional platforms, further providing potential savings in a large volume environment.

However, establishing and validating the performance of these tests to make informed clinical and public health decisions pose significant clinical and scientific challenges. Most clinical laboratory are not familiar with the mass spectrometry platform. For those who have had experience in this area, they have been focusing on small molecular testing. Protein or peptide based targeted mass spectrometry assays requires different workflow and operational process. These skills are not readily available to the current laboratories. This presentation will discuss these challenges, the pitfalls and recommendations to implement the targeted mass spectrometry assays in a routine clinical laboratory to provide value to healthcare system and patient services.

Session 2. Clinical Proteomics in Cancer Research

Jordi Barretina, Director of the Girona Biomedical Research Institute (IDIBGI), Girona, Spain

Dr Barretina currently serves as the Director of the Girona Biomedical Research Institute (Institut d'Investigació Biomèdica de Girona, IDIBGI). Previously, he was a Laboratory Head in the Oncology Translational Research group at the Novartis Institutes of Biomedical Research (NIBR) in Cambridge (Massachusetts, USA). He joined this organization after leading an academia-industry collaboration at the Broad Institute of MIT and Harvard, also in Cambridge. That was after completing his postdoctoral research in the Department of Medical Oncology of the Dana-Farber Cancer Institute at Harvard Medical School in Boston (Massachusetts, USA). Before moving to the United States, he received his Ph.D. in Biochemistry and Molecular Biology from Universitat Autònoma de Barcelona.

Chair of the session 2.

Manel Esteller, Director of the Cancer Epigenetics and Biology Program (PEBC) at Bellvitge Biomedical Research Institute (IDIBELL) and Director-Elect of the Josep Carreras Leukaemia Research Institute (IJC), Barcelona, Spain

Manel Esteller (Sant Boi de Llobregat, Barcelona, Catalonia, Spain, 1968) graduated in Medicine from the Universidad de Barcelona in 1992, where he also obtained his Ph.D. degree specialising in molecular genetics of endometrial carcinoma, in 1996. He was an Invited Researcher at the School of Biological and Medical Sciences at the University of St. Andrews, (Scotland, UK) during which time his research interests focused on the molecular genetics of inherited breast cancer. From 1997 to 2001, Esteller was a Postdoctoral Fellow and a Research Associate at the Johns Hopkins University and School of Medicine, (Baltimore, USA) where he studied DNA methylation and human cancer. His

work was decisive in establishing promoter hypermethylation of tumour suppressor genes as a common hallmark of all human tumours. From October 2001 to September 2008 Manel Esteller was the Leader of the CNIO Cancer Epigenetics Laboratory, where his principal area of research were the alterations in DNA methylation, histone modifications and chromatin in human cancer. Since October 2008, Dr Esteller is the Director of the Cancer Epigenetics and Biology Program (PEBC) of the Bellvitge Institute for Biomedical Research (IDIBELL) in Barcelona, Chairman of Genetics in the School of Medicine of the University of Barcelona, and an ICREA Research Professor. His current research is devoted to the establishment of the epigenome and epitranscriptome maps of normal and transformed cells, the study of the interactions between epigenetic modifications and non-coding RNAs, and the development of new epigenetic drugs for cancer therapy.

Author of 503 original publications in peer-reviewed scientific journals, 24 of them categorized as "Highly Cited Paper" by Thomson Reuters. Dr Esteller has a Total Impact Factor of 4,508.212 and a Total Number of Citations of 58,860, having an h-Index of 119. He is also a Member of numerous international scientific societies, Editorial Boards and reviewer for many journals

Epigenetics and the cancer proteome

Normal cellular activity requires a precise regulation of the proteome. However, transformed cells have an aberrant protein profile. It is likely that intrinsic defects in protein homoeostasis contribute to human tumorigenesis, such as defects in de novo protein synthesis, or alterations in protein degradation, such as mutations in the von Hippel–Lindau ubiquitin ligase complex. In this last case, the ubiquitin proteasome system (UPS) targets a variety of proteins, including functional proteins that are no needed any more. Without adequate protein homoeostasis maintained by the UPS, normal cells can undergo malignant transformation, and this observation has been therapeutically exploited by the development of proteasome inhibitors as anticancer agents. Most of the cytoplasm UPS-degraded proteins are retrotranslocated from the endoplasmic reticulum (ER). In this regard, ER has a quality control mechanism, termed the ER associated degradation mechanism (ERAD), that is release in response to ER stress by a transcriptional program, known as the unfolded protein response, which leads to the accelerated degradation of unfolded proteins. We will explain how epigenetic defects acting in all these pathways shape the cancer proteome.

Miguel Quintela-Fandino, Clinical Program Director at Spanish National Cancer Research Centre (CNIO), Madrid, Spain

Miguel Quintela-Fandino was awarded his MD degree from the Universidad de Navarra in 2000 and trained as a medical oncologist at the Hospital Universitario 12 de Octubre. He then received his PhD from the Universidad Complutense de Madrid for his research on the impact of micrometastasis in patients with locally advanced high-risk breast cancer (2005). He also obtained a Master´s Degree in biostatistics from the Universidad Autónoma de Barcelona. He then joined Tak Mak's laboratory at the Ontario Cancer Institute, Canada, as a Postdoctoral Research Fellow for four years. After this period, he complemented his clinical training with a Fellowship in the Drug Development Program at the Princess Margaret Hospital for two more years focused on the development of several first-in-class, first-in-human drugs. He returned to Spain by mid 2010 to lead the Breast Cancer Clinical Research Unit supported by a "Beca de Retorno" grant awarded by the AECC Scientific Foundation. His research highlights are:

- Development of an individualized dose-titration system based on the assessment of the stimulated status of signaling pathways in peripheral blood cells for signal transduction inhibitors
- Definition and characterization of DNA-damage SNPs influencing the individual response to platinum compound
- Unraveling the dual escape pathway (hypoxic and normoxic) of tumors against antiangiogenic agents and exploiting the adaptive mechanisms for therapeutic purposes
- Elaboration of the first phosphoproteomic taxonomy of triple-negative breast cancer

Miguel has received several honours for his research, including the ASCO Young Investigator Award and the ASCO Merit Award (twice) and the Astra-Zeneca award. Since 2017 he is the director of the Clinical Research Program at CNIO.

Phosphoproteomics - an all-in-one tool for unraveling drug resistance, finding biomarkers and disease segmentation in breast cancer

Despite the advent of next generation sequencing, complex cancer phenotype traits such as response to chemotherapy or targeted agents or disease course have been difficult to fully understand and unravel. The task of defining simple biomarkers that were associated to specific complex traits has been frustrating besides the context of the presence of strong oncogenic addiction drivers (i.e., such as presence of EGFR activating mutations and response to erlotinib in lung cancer or BRAF activating mutations and response to vemurafenib in melanoma). The fact is that diseases without such drivers, such as HER2-negative breast cancer, are a result of the presence of multiple contributing low-penetrance genetic drivers, none of them necessary and none of them sufficient to drive a specific phenotype.

We have worked along the last 5 years under the hypothesis that all these combinations of different drivers would "collapse" into specific patterns of activation of the proteome, mainly in the form of protein phosphorylation. Such patterns, albeit highly complex (including in the order of 10^5-10^6 elements), would be driven by the action of a few hyperactive or hypoactive kinases.

By using a combined high-throughput mass-spectrometry-based phosphoproteomics in clinical samples with full annotation, and preclinical models of breast cancer, we have been able to achieve the following goals:

- Dissecting the two major pathways of escape against antiangiogenics, defining serveral actionable nodes that can abrogate or delay such clinical phenomenon.
- Elaborating the first kinase-based taxonomy of triple-negative breast cancer, which has also elucidated six top-targets that, when pharmacologically modulated, induce profound tumor regression effects
- Defining kinase-based biomarkers of response to the most widely used agent in clinical oncology in breast cancer: taxanes.

We will discuss during the talk the main methodology issues and bottlenecks in clinical proteomics, main results and clinical applications of our research.

Session 3. Technology Innovations (I)

Alejandro Vaquero, Group Leader of the Chromatin Biology Lab at Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain

Alejandro Vaquero (Barcelona, 1971) received his PhD from the University of Barcelona (UB) for his work on Drosophila GAGA factor on transcription. He performed his postdoctoral stage in Dr Danny Reinberg's lab (HHMI, USA) pioneering the study of the role of the mammalian NAD+-dependent deacetylases Sirtuins, in chromatin dynamics upon stress. His work demonstrated a key role for SirT1 in global chromatin organization (Mol Cell, 2004; Nature, 2007), the first direct link between Sirtuins and cancer (PNAS, 2006) and a role for SirT2 in H4K16Ac regulation during mitosis (Genes Dev 2006). In 2006, Dr Vaquero returned to Spain as ICREA Researcher at the IBMB-CSIC institute, and in 2008 he established his laboratory at the Bellvitge Biomedical Research Institute (IDIBELL) in Barcelona), within the Cancer Epigenetics and Biology Program (PEBC). Vaquero's group aims to understand the role of Sirtuins in the regulation of genome stability in response to stress, and their implication in cancer and aging. Over the years, the lab has described relevant epigenetic-dependent mechanisms involved in genome stability protection such as the role of SIRT1 in Suv39h1 stability and heterochromatin dynamics (Mol Cell, 2011), the key role of SIRT2 in the deposition of H4K20me1 in G2/M transition (Genes & Dev, 2013), SIRT6-dependent control of NF-kB signaling through cysteine ubiquitination (Nat Commun, 2018), and a distinctive role for HP1 isoforms in heterochromatin dynamics (Epigenetics, 2017, Cell Rep, 2018). The lab has also contributed to uncovering the role of SirT7 in DNA repair and aging (EMBOJ 2016) and its functional interplay with SirT1 (PNAS, 2017), the discovery of the embryonic histone H1 bigH1 in Drosophila (Dev. Cell 2013), and a functional link between AID and H4K20me3 in class-switch recombination (Sci Reports 2017).

Chair of the session 3.

Cecilia Lindskog, Director of the Tissue Atlas, Human Protein Atlas at Uppsala University, Uppsala, Sweden

Dr. Lindskog is a group leader at Uppsala University, Uppsala, Sweden. Her research focuses on protein science, understanding the biology and functions of different organs, and the underlying mechanisms leading to cancer and other diseases. She joined the Human Protein Atlas project in 2006 and has a PhD in pathology from the Faculty of Medicine, Uppsala University. Since 2014, Dr. Lindskog is director of the Tissue Atlas. Her team creates a world unique atlas of spatial proteomics, showing the cell-type specific localization of all human proteins in a large set of normal and cancer tissues.

The Human Protein Atlas - implications for human biology and precision medicine

The spatial distribution of proteins determines the morphology and function of tissues, cells, and organelles. Knowledge of this spatial distribution is therefore essential to understand the healthy and diseased human body. The Human Protein Atlas project is a knowledge-based resource (www.proteinatlas.org) focusing on an integrated omics approach for in situ detection of human proteins down to the single cell level. All human protein coding genes have been classified using a combination of genomics, transcriptomics, proteomics and antibody-based profiling, and used for studying global protein expression patterns. The data is open source and published together with 10 million high-resolution immunohistochemistry and immunocytochemistry images. The database is divided into three main parts: A Tissue Atlas was launched in 2014 (Uhlen et al, Science, 2015), a Cell Atlas in 2016 (Thul et al, Science, 2017) and a Pathology Atlas in 2017 (Uhlen et al, Science, 2017). In the Pathology Atlas, RNA-Seq data and clinical metadata from the Cancer Genome Atlas corresponding to 8,000 individual patients from 17 major cancer types was used for determining the correlation between RNA expression levels and overall survival time for each gene in each cancer type. The large-scale publicly available Human Protein Atlas data and images opens up for pursuing better diagnostic schemes and designing personalized cancer treatment regimes.

Bernhard Kuster, Full Professor and Chair of the Department of Biosciences at the Technical University of Munich, Freising, Germany

Bernhard Kuster is a chemist by training and obtained is PhD in Biochemistry from the University of Oxford. He went on to do a PostDoc funded by an EMBO long-term fellowship at the EMBL in Heidelberg and the University of Southern Denmark in Odense. After seven years as VP Analytical Sciences and Informatics at the biotech firm Cellzome (now GSK), he became full professor of Proteomics at the Technical University of Munich in 2007 where he is also Vice Dean of the School of Life Sciences, Chair of the Department for Biosciences, Co-Director of the Bavarian Biomolecular Mass Spectrometry Center and Carl von Linde Senior Fellow of the TUM Institute for Advanced Studies.

Bernhard's research focuses on mass spectrometry based proteomics and its application to chemical and systems biology. He is particularly interested in how drugs interact with proteins, signaling pathways and cellular systems in order to understand their often multiple modes of action. Bernhard has published over 150 papers on proteomics and bioinformatics with a recent focus on systematic protein-drug interaction profiling. Bernhard received a number of awards in recognition of his contributions to science, notably the Discovery in Proteomic Sciences Award of Human Proteome Organisation for mapping out a draft of the human proteome. His team continues to develop proteomic technologies and generates large-scale proteome studies that serve as a starting point for the exploration of the human proteome and its application to drug discovery and personalized medicine.

The target landscape of clinical kinase inhibitor drugs

Background: Kinase inhibitors have developed into important cancer drugs because de-regulated protein kinases are often driving the disease. Close to 40 such molecules have been approved for use in humans and several hundred are undergoing clinical trials. As most compounds target the ATP binding pocket, drug selectivity among the 500 human kinases is a recurring question. Clinically speaking, polypharmacology can be beneficial as well as detrimental. Therefore, knowing the full target spectrum of a drug is important but rarely available.

Methods: We have used a quantitative chemical proteomics approach to profile 240 clinical kinase inhibitors in a dose dependent fashion in cancer cell lysates to identify thousands of drug-protein interactions.

Results: The data revealed previously unknown targets for established drugs, offered a perspective on the druggable kinome, highlighted (non)kinase off-targets, and suggested potential therapeutic applications. Integration of phosphoproteomic data refined drug-affected pathways, identified response markers, and strengthened rationale for combination treatments. We exemplify translational value by discovering SIK2 (salt-inducible kinase 2) inhibitors that modulate cytokine production in primary cells, by identifying drugs against the lung cancer survival marker MELK (maternal embryonic leucine zipper kinase), and by repurposing cabozantinib to treat FLT3-ITD – positive acute myeloid leukemia.

Conclusions: The translational value of this project is apparent from the fact that the drug:target information generated in this project is now used in the molecular tumor board of the Comprehensive Cancer Center Munich in order to develop patient-specific recommendations for cancer patients.

Session 4. Clinical Proteomics in Cardio and Neurological diseases

Lina Badimon, Director of the Cardiovascular Science Program (ICCC) at the IR Hospital Santa Creu i Sant Pau, Barcelona, Spain

Prof. Lina Badimon is the Director of the Cardiovascular Science Program (ICCC) at the Hospital Santa Creu and San Pau, Director of the Cardiovascular Research Chair of the Autonomous University of Barcelona and Director of the UNESCO Chair in Biomedical Sciences Training and Research. She is the Chair of the Advocacy Committee and Board Member 2018-2020 of the European Society of Cardiolog

Her research activities focus on cardio-metabolic diseases, thrombosis, atherosclerosis and ischemic heart disease. She has published over 550 articles in highly qualified scientific journals with her work highly quoted in the scientific literature (Citations: 37.588; h-index 75). She has written more of 250 reviews and book chapters

Previous appointments include: Fellow in Cardiovascular Diseases at The Mayo Clinic, Rochester, MN, USA (1981-1983); Director of the Cardiology Basic Research Laboratory of the Division of Cardiology at the Mount Sinai Medical Center, New York, NY (1983-1991); Assistant Professor of Medicine (1983-1987) and Associate Professor of Medicine (1988-1991) at the Mount Sinai School of Medicine, NY; Lecturer in Medicine at Harvard Medical School, Boston (1991-1994); Consultant at the Cardiac Unit, at the Massachusetts General Hospital, Boston (1991-1994)

Positions of Trust: Vice-President for Scientific Affairs of European Society of Cardiology (2016-2018), Vice-President of the Spanish Society of Cardiology (2013-2015); Chairman of the Council on Basic Cardiovascular Science (2014-2016) and Chairman of the Working Group on Microcirculation (2012-2014) of the ESC; Past-President of the European Society for Clinical Investigation (2000-2002) and Past-President of the Spanish Society of Atherosclerosis (1996-2000); Member of the National Academy of Medicine and of the National Academy of Pharmacy of Catalonia and Spain.

Chair of the session 4.

Antoni Bayes Genis, Head of the Heart Institute at the Germans Trias i Pujol University Hospital, Badalona, Spain

Dr Bayes-Genis research is focused in two main areas, one more clinical and another basic-translational. From the clinical stand-point he is interested in precision medicine using novel biomarkers for diagnosis and prognosis in heart failure and sudden death as well as telemedicine. At the basic-translational level he is interested in stem cells (adipose tissue-derived, circulating progenitors and umbilical cord-derived) and cardiac tissue engineering to salvage and restore injured myocardium.

He has published over 405 SCI papers with more than 12000 citations. He is inventor of 9 international patents.

Summary of major scientific contributions:

1. Identification of a novel biomarker PAPP-A for the early identification of unstable angina and myocardial infarction.
2. Development of the elastin stent to reduce the risk of restenosis. This research pioneered the use of bioactive stents.
3. Characterization of the clinical use of natriuretic peptides and other cardiovascular biomarkers (ST2, hs-TnT …) for diagnosis, prognosis, monitoring and guided-therapy in heart failure. Development of the BCNbioHF calculator (bcnbiohfcalculator.org), as a first precision medicine approach for risk stratification using a multibiomarker panel.
4. Chimerism of the human heart. Pioneers in 2002 to identify the self-renewal capacity of the human heart and the presence of cardiac microchimerism.
5. Identification of a novel cell source for cardiac regeneration. The group identified and characterized cardiac adipose tissue-derived progenitor cells from biopsies of human adult cardiac fat. The research team has also performed translational research with other sources of stem cells.
6. Development of a novel interventional technique to salvage myocardium after infarction. Dr Bayes-Genis team has recently demonstrated that biological tissue engineering restores cardiac function in acute and chronic infarcts.

Protein-based Cardiogenic Shock Patient Classifier

Background. Cardiogenic shock (CS) is associated with high short-term mortality and a precise CS risk stratification could guide interventions to improve patient outcome. Here we aimed to develop a circulating protein-based score to predict short-term mortality risk among patients with CS in two independent prospective cohorts.
Methods. Mass spectrometry of 2662 proteins was used for screening in the discovery cohort. Targeted quantitative proteomics analyses were used in the validation cohort. The Barcelona discovery cohort is a prospective single-center study of CS of ischemic origin; the CardShock validation cohort is a European prospective, multicenter, multinational CS study of ischemic or non-ischemic origin. A 4-protein risk score (CS4P) was derived and validated for 90-day risk of mortality. C statistics and reclassification were used. Enzyme-linked immunosorbent assays (ELISA) were used to prompt clinical translation of the four selected proteins. The CardShock risk score was used as the baseline model.
Results. The combination of four circulating proteins, the CS4P, measured within 24 hours of admission, discriminated CS patients with low and high 90-day risk of mortality. Overall, the four proteins of CS4P reflect kidney, liver, and bowel injury, as well as systemic inflammation and immune activation. Within the validation cohort, the C-statistic was 0.78 for the CardShock risk score, 0.83 for the CS4P model, and 0.84 for the combination of CardShock risk score with the CS4P model (P=0.033 vs. CardShock risk score). The CardShock risk score with the CS4P model showed a marked benefit in patient reclassification, with an NRI of 0.49 (P=0.020) and an improved reclassification of 32% of patients compared to CardShock risk score. The CS4P was confirmed by ELISA.
Conclusions. A new protein-based (CS4P) CS patient classifier was developed for short-term mortality risk stratification. CS4P improved predictive metrics in combination with contemporary risk scores, which may guide clinicians in selecting patients for advanced therapies.

Isidro Ferrer, Professor of Pathology, Area of Neuropathology at the University of Barcelona, Barcelona, Spain

Isidro Ferrer, male, MD (1976), PhD (1978), gender: male, ORCID: 0000-0001-9888-8754 is Full Professor of Pathology at the University of Barcelona, Department of Pathology and Experimental Therapeutics; Senior Consultant Neuropathologist at the Bellvtge University Hospital; PI at the Institute of Biomedical Research Bellvitge (IDIBELL); and PI at the Institute of Neuroscience, University of Barcelona. He is also PI of the group Neuropathology in CIBERNED (Center of Biomedical Research of Neurodegenerative diseases) at the Institute of Health Carlos III. He has published more than 780 papers in international journals. H-factor: 73 (2017); 22 international book chapters; supervised 36 doctoral theses; produced 8 living patents and participates in the editorial board of several scientific journals focused on neuropathology and neurosciences.

Clinical proteomics in the study of human neurodegenerative diseases with abnormal protein aggregates

Proteomics are powerful tools to the large-scale study of proteins. Several methods can be employed with particular benefits and limitations in the study of human brain. This is a review of the rational use of current techniques with particular attention to limitations and pitfalls inherent to each one of the techniques, and more importantly, to their use in the study of post-mortem brain tissue. These aspects are cardinal to avoid false interpretations, errors and unreal expectancies. Other points are also stressed as exemplified in the analysis of human neurodegenerative diseases which are manifested by disease-, region-, and stage-specific modifications commonly in the context of aging. Information about certain altered protein clusters and proteins oxidatively damaged is summarized for Alzheimer and Parkinson diseases.

Olivia Belbin, Senior Associate Researcher at Sant Pau Biomedical Research Institute, Barcelona, Spain

Trained in Neurosciences, I received a doctorate from the University of Nottingham (UK) in 2008 for my thesis entitled "Haplotype Analysis of the genes involved in the amyloid cascade of Alzheimer's disease". I later spent two years as a post-doctoral researcher in the group of Professor Steve Younkin at Mayo Clinic (USA) where I continued my work to identify Alzheimer's disease genetic risk factors. My work on the VAMP1 gene led to my first publication as senior and corresponding author (published in Molecular Neurodegneration) and sparked my interest in the role of synapse degeneration in Alzheimer's disease. To continue this work, I relocated to the Neurobiology of Dementias laboratory led by Dr Alberto Lleó at IIB-SantPau in Barcelona (Spain) funded by a 3-year postdoctoral fellowship (Juan de la Cierva). Access to one of the largest collections worldwide of 1000+ cerebrospinal fluid samples and neuroimaging data from dementia patients has allowed me to develop my own research line focused on employing shotgun and targeted mass spectrometry to identify and validate biofluid synaptic biomarkers in neurodegenerative diseases. I am principal investigator on multiple research projects awarded by the Spanish and Catalan Governments and am a recipient of a tenure-track fellowhip (Miguel Servet Type I 2014-2018 and Type 2 2019-2021) awarded by the Spanish Government. I am lead inventor on a filed patent application to protect the intellectual property of the project, which has led to a license agreement for the generation of synaptic biomarker immunoassays suitable for the in vitro diagnostics market. I am co-author on 38 research publications in international journals and I participate in multiple international collaborations such as the Epistasis Project.

The search for novel biomarkers of synapse degeneration as a diagnostic tool for dementia

A biomarker of synapse loss, an early event in Alzheimer's disease (AD) pathophysiology that precedes neuronal death and symptom onset, would be a much-needed prognostic biomarker in living patients. With direct access to the brain interstitial fluid, the cerebrospinal fluid (CSF) is a potential source of synapse-derived proteins that should demonstrate changes that precede those of neuronal degeneration markers. In this study, we aimed to identify and validate novel CSF biomarkers of synapse loss in AD. Combining shotgun proteomics of the CSF with an exhaustive search of the literature and public databases, we identified 210 synaptic proteins detectable in CSF, from which we selected 10 for further study. We confirmed the specific expression of 9 of the remaining proteins (Calsynytenin-1, GluR2, GluR4, Neurexin-2A, Neurexin-3A, Neuroligin-2, Syntaxin-1B, Thy-1, Vamp-2) at the human synapse using Array Tomography microscopy and biochemical fractionation methods. Using Selected Reaction Monitoring (SRM), we monitored these synaptic proteins (22 peptides) in two independent cohorts of CSF from cognitively normal controls and all pre-clinical and clinical AD stages ($n=140$). Cross-cohort meta-analyses revealed a non-linear profile whereby, compared to controls, levels of a set of synaptic proteins were reduced 0.8-fold ($p<0.05$) in preclinical AD (reduced synaptic density) but elevated 1.2 to 1.4-fold ($p<0.04$) in clinical AD when neurodegeneration is widespread (neurodegeneration). This is the first study to demonstrate changes in CSF levels of synaptic proteins that precede markers of neurodegeneration in AD. These novel biomarkers could improve enrichment and monitoring of drug efficacy in clinical trials for AD.

Thursday, November 8, 2018

Session 5. Clinical Proteomics in Immunology and Microbiology

Ricardo Pujol-Borrell, Professor of Immunology at **Vall d'Hebron University Hospital,** Autonomous University of Barcelona, Barcelona, Spain

MD Universitat Autónoma de Barcelona 1979. PhD Immunology University College London 1990. Consultant and Professor of Immunology, Hospital Universitari Germans Trias i Pujol 1992 and 1994 respectively. Scientific Director of the Health Sciences Research Institute Germans Trias i Pujol (1999-200) and of the Blood and Tissue Bank (2007-2010).
Consultant Clinical Immunologist at Hospital Universitari Vall d'Hebron 2010-
Research Advisor to the Director of the Catalan Health Institute (ICS), 2008-
Contributions in the field of autoimmunity: to the hypothesis of organ specific autoimmune disease as a target tissue driven process (1983); in the role of central tolerance in preventing autoimmunity (1988); first transcriptomic profiling of the autoimmune thyroid and diabetic pancreas (2011), identification of the mechanism by which TSHR gene confers susceptibility to Graves' disease (2011) and a new proposal on the origin of TSHR stimulating antibodies generation (2016).

Chair of the session 5.

Luís Serrano, Director of the Centre for Genomic Regulation (CRG), Barcelona, Spain

Luis Serrano did his PhD at the CBM (Madrid, Spain) on Cell Biology. Then he spent 4 years in the laboratory of Prof. A.R. Fehrst (MRC, UK) working in protein folding. In 1993, he became Group Leader at the EMBL (Heidelberg, Germany) working in Protein Folding and design. Ten years later, he was appointed head of the Structural & Computational Biology programme at the EMBL and he started to work on Systems Biology. By the end of 2006 he moved back to Spain to lead a programme working on Systems Biology, where he was appointed vice-director before finally becoming the CRG director on July 2011. He is a member of the Spanish Society for Biochemistry and Molecular Biology (SEBBM), member of the European Molecular Biology Organization (EMBO), and member of the Royal Spanish Academy of Sciences (Spain). In 2003 he received the Marie Curie Excellence Award, in 2009 he was awarded the City of Barcelona prize (science category), an annual award organized by Barcelona City Council and in 2018 the Francisco Cobos award (http://fundacionfranciscocobos.org/). In recent years he has won four prestigious grants from the European Research Council, two ERC Advanced Grants and two ERC Proof of Concept grants. He is Professor of ICREA and has directed 18 PhD thesis. He has published more than 350 papers in international journals. He was involved in the creation of one of the first Spanish Biotech Companies (Diverdrugs) in 1999. And co-founder of Cellzome, EnVivo and TRISKEL companies. He has been Director and Founder of the association of European Institutes of Excellence EU-LIFE, as well as of the equivalent association at Spanish level, SOMMA .

Unravelling the hidden universe of small proteins in bacterial genomes

Identification of short open reading frames (smORFs) encoding small proteins (≤100 amino acids; SEPs) is a contemporry challenge in the fields of genome annotation and protein discovery. Here, by combining a novel bioinformatics tool (RanSEPs) with "-omics" approaches, we were able to describe 109 bacterial small ORFomes. Predictions were validated and compared with other tools using 124 "-omics" datasets from Mycoplasma pneumoniae and five related species, targeted proteomics, and SEPs validated in the literature. We found that up to 25% of proteins in a bacterium could be classified as SEPs. Integration of RanSEPs predictions with transcriptomics data from 11 bacterial species showed that some annotated non-coding RNAs could in fact encode for SEPs. A functional study of SEPs highlighted an enrichment in the membrane, translation, metabolism and nucleotide binding categories. Additionally, ~10% of the predicted SEPs include a secretion signal, indicating that they could participate in quorum sensing and/or signaling. This work represents the first comprehensive annotation of bacterial genomes and provides a tool to unmask the hidden universe of small bacterial proteins.

Ileana M. Cristea, Professor at Princeton University, Princeton, USA

Ileana Cristea is a Professor in the Department of Molecular Biology at Princeton University. Her laboratory focuses on characterizing mechanisms of cellular defense against viruses, as well as mechanisms used by viruses to manipulate these critical cellular processes. Towards these goals, she has promoted the integration of virology with proteomics and bioinformatics. She has developed methods for studying virus-host protein interactions in space and time during the progression of an infection, which have allowed her group to bridge developments in mass spectrometry to important findings in virology. For example, her laboratory has contributed to the emergence of the research field of nuclear DNA sensing in immune response, and has discovered sirtuins as broad-spectrum antiviral factors. Dr. Cristea is the President of US HUPO, chairs the Infectious Disease initiative of the Human Proteome World Organization, and has acted on the Education Committee of the American Society for Mass Spectrometry. She has taught the Proteomics Course at Cold Spring Harbor Laboratory for over ten years, and is Senior Editor for mSystems, Associate Editor of the Journal of Proteome Research, and on the Editorial Boards of Molecular Systems Biology and Molecular & Cellular Proteomics. She was recognized with the Bordoli Prize from the British Mass Spectrometry Society (2001), NIDA Avant-Garde Director Pioneer Award for HIV/AIDS Research (2008), Human Frontiers Science Program Young Investigator Award (2009), Early Career Award in Mass Spectrometry from the American Chemical Society (2011), the American Society for Mass Spectrometry Research Award (2012), the Molecular Cellular Proteomics Lectureship (2013), the Mallinckrodt Scholar Award (2015), and the Discovery Award in Proteomic Sciences at HUPO (2017).

Organelle remodeling en route to virus replication: Integrated proteomics, lipidomics, microscopy and mathematical modeling

The coexistence and coevolution of hosts with pathogens is intrinsic to our ecosystem. Pathogenic infections induce an array of changes in the hosts that are tightly linked to the progression of infection and establishment of disease. At the cellular level, this is reflected in alterations in host cell composition, organization, and ability to communicate with other cells. Thus, changes in the host proteome, metabolome, lipidome, and secretome have started to be recognized as signatures of infectious or disease states. These alterations function to either induce host defenses that counteract the infection or promote pathogen replication for spread of infection. Consequently, the discovery and characterization of these signature changes are essential for both understanding the biology of infection and identifying novel targets for therapeutic interventions. This presentation will highlight the value of advanced mass spectrometry-based proteomics for defining the dynamics of proteome organization and understanding mechanisms of cellular defense during viral infections. Examples will be given from our studies of spatial-temporal remodeling of subcellular organelles during infection. We will show how the integration of proteomics with lipidomics, live cell microscopy, mathematical modeling, and genetic knockouts has allowed us to discover a novel function for peroxisomes in the assembly of infectious particles. Additionally, the contribution of localization-dependent posttranslational modifications will be discussed, with a focus on the role of protein acetylation in cellular host defense against infection.

Session 6. Proteomics into personalized medicine

Paolo Nuciforo, Head of the Molecular Oncology group at **Vall d'Hebron Institute of** Oncology (VHIO), Barcelona, Spain

Paolo Nuciforo MD, PhD, board certified Pathologist, Principal Investigator of the Molecular Oncology group at Vall d`Hebron Institute of Oncology (VHIO, http://www.vhio.net/en/molecular-oncology-group). He head a group of 12 fully trained personnel specialized in different histopathology and molecular pathology areas. The group is one of the cutting-edge core technology laboratory of VHIO which supports the different preclinical and clinical research programs. As part of the institution prescreening program, it performs molecular profiling in over 1500 patients per year as candidates for enrolment in early phase clinical trials. The laboratory is ISO15189-accredited and serves as central laboratory in several national and international clinical trials. Main research activities include discovery and validation of novel biomarkers using tissue-based technologies, development and

application of novel molecular pathology strategies to basic, translational and clinical oncology. He has 10+ years of experience in oncology translational medicine and drug development both in academic and pharmaceutical environment. He co-authored over 80 publications in peer-reviewed journals with a main focus on discovery and validation of novel biomarkers using tissue-based technologies.

Chair of the session 6.

Martin Kussmann, Editorial Director at Frontiers Media S.A. (Switzerland) and Adjunct Professor at iNANO, Aarhus University (Denmark), Switzerland

Prof. Martin Kussmann, PhD, has been appointed Editorial Director at Frontiers Media S.A. (Switzerland) and holds an Adjunct Professorship at the Interdisciplinary Nanoscience Center at Aarhus University (Denmark).

From 2016-2018 he was 'Professor of Systems Biology in Nutrition and Health' at the Liggins Institute, University of Auckland, New Zealand; and Chief Scientist of the NZ National Science Challenge on 'High-Value Nutrition'. His research focus laid on early-life health and food innovation.

In February 2011, Martin joined the Nestlé Institute of Health Sciences (NIHS) on the campus of the Ecole Polytechnique Fédérale Lausanne (EPFL), Switzerland, as Head of the "Molecular Biomarkers Core", which he has built from scratch. This core facility and program covered five platforms and teams, i.e. proteomics, metabonomics, lipidomics, micronutrient analysis and diagnostics. His team developed and conducted systems biology-oriented nutrition and health research in the context of healthy ageing with a focus on cognitive, metabolic and intestinal health.

In June 2009, Martin was appointed Honorary Professor for Nutritional Science at the Faculty of Science, Aarhus University, Denmark, an adjunct position which he still holds. From 2012 to 2016, he was Lecturer at the Faculty of Life Sciences, EPFL. From 2003 to 2011, Martin built and led the Functional Genomics Group at the Nestlé Research Centre, Lausanne, and was responsible for proteomics and genomics in nutrition.

Being educated and trained as an analytical biochemist, Martin has acquired research experience in the pharmaceutical, biotech start-up and nutritional industry. Martin holds a B.Sc. from the Univ. Aachen, Germany, and a M.Sc. from the Univ. Konstanz, Germany. He performed his doctoral research in Konstanz and at the University of California, San Francisco, USA. During his doctorate and post-doctorate, he specialised in mass spectrometry, proteomics and genomics.

ProteOmics in Humans for Nutrition and Diagnostics

The omics downstream of genomics, i.e. mainly proteomics[1] and metabolomics[2], have matured into a suite of technologies that enable refined molecular phenotyping of human subjects enrolled in clinical (observational or interventional) studies. Such phenotyping extends beyond classical clinical assessment and facilitates our understanding of human individuality and its response to environment: genotype x environment + omics → molecular phenotype.

With these premises in mind, I will present recent developments in proteomic and metabolomic technologies that (i) advance the clinical compatibility of omics in terms of robustness and throughput1; and (ii) enhance the exploitation of

complex mass spectral data as typically obtained from human peripheral body fluids sampled by minimally invasive means, as it is typically required for nutrition research[3].

With these platforms being introduced, I will show how we deploy them in clinical studies:

(i) We have performed differential display human plasma proteomics in a large dietary intervention study, derived protein signatures predictive and (in parts) explanatory for weight loss and maintenance[4]. We could largely replicate our findings in a second clinical study, with an independent cohort comparable in size and ethnic composition. Such large-scale clinical replication in nutritional proteomics is to the best of our knowledge a first of its kind[5].

(ii) We have adapted our differential display clinical proteomics workflow to human cerebrospinal fluid (CSF)[6] and complemented it by multiplexed targeted, multiple reaction monitoring-based metabolomics to capture changes in one-carbon metabolism[7,8]. The objective was to derive predictive models and biomarkers for cognitive decline in elderly. Our proteomic and metabolic signatures outperformed classical models for predicting disease progression, informed about the disease implication of the blood/brain barrier, and both confirmed known and identified new (candidate) biomarkers for Alzheimer's disease[9,10].

In a nutshell, my talk should give you a good idea of today's performance and tomorrow's potential of omics in clinical nutrition and health science.

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Emily Chen, Senior Director at Thermo Fisher Precision Medicine Science Center, Cambridge, USA

Emily Chen has over 10 years of experience on mass spectrometry-based shotgun proteomics, oncology, and translational research. She led the proteomics biomarker discovery efforts as the director of Herbert Irving Comprehensive Cancer Center Proteomics Shared Resource at Columbia University Medical Center and interacted directly with physicians to support Precision Medicine projects prior to joining Thermo Fisher.

The Future of Precision Proteomics

Recent advances in mass spectrometry have skyrocketed the capabilities in translational proteomics, impacting our understanding of health and disease. Translational proteomics complements other omics disciplines (genomics, transcriptomics, and metabolomics/lipidomics), delivering new workflows that produce clinically relevant results that are quantitative and more informative. Under this new model, not only clinical profiles of patients but also their molecular profiles could be personally managed to drive for advanced treatment. However, a key challenge is to break the technical bottleneck and bridge the gap between early-stage discovery and next-stage, routine quantitative application of biomarker assays in the clinical research setting.

Thermo Fisher Precision Medicine Science Center (PMSC) is established to develop turnkey solutions for precision proteomics based on the extensive expertise of mass spectrometry. As the focus moves from identification to quantitation, success criteria for precision proteomics shift to factors such as reproducibility, standardization and scalability. Access to curated references, standards, as well as the need for reliable statistical analyses, becomes increasingly important. Future precision proteomics studies require robust high-throughput solutions to deliver accurate and reproducible peptide and

protein quantitation. PMSC is unique in that it collaborates within its parent organization, Thermo Fisher Scientific, to develop and integrate the latest tools and techniques such as consumables, instrumentation, and data interpretation software for MS-based workflows. Furthermore, PMSC will deploy these integrated technologies to collaborate extensively with clinical research and translational centers. Ultimately, our goal is to deliver robust, reproducible, and scalable proteomics discovery workflow solutions based on high-resolution mass spectrometers and light the path for precision medicine.

Session 7. Technology Innovations (II)

Oscar Yanes, Scientific Coordinator & Associate Professor at CIBERDEM and Universitat Rovira i Virgili, Tarragona, Spain

Oscar Yanes received his Ph.D. degree in Biochemistry (2006) from the Universitat Autonoma de Barcelona. In 2007 he became Research Associate in Gary Siuzdak's lab at The Scripps Research Institute. Since 2011 Dr. Yanes coordinates the Metabolomics Platform of the CIBERDEM-URV, he is affiliated member at the IRB Barcelona and Assistant Professor at the URV where he also leads his own research group (www.yaneslab.com).

The two major aspects of Dr. Yanes research are: (i) the development of new methodology and computational tools in mass spectrometry (MS) and NMR-based metabolomics; and (ii) the study of fundamental biological processes (e.g., health and disease) using metabolomics in combination with other omic platforms.

Such efforts have led to the development of new methodology in mass spectrometry (Nature, 2007; Nature Protocols, 2008; Analytical Chemistry, 2009; Analytical Chemistry, 2010), and novel strategies for compound spectra extraction, peak annotation and de novo identification and characterization of known and unknown metabolites by LC-MS (Analytical Chemistry, 2015; Analytical Chemistry, 2017), GC-MS (Analytical Chemistry, 2016) and NMR (Angewandte Chemie Int Ed. 2017) for global metabolite profiling.

Dr. Yanes is involved in multi-disciplinary studies combining metabolomics with other omic approaches including proteomics, epigenomics and metagenomics, and novel molecular biology techniques to interrogate relevant areas such as stem cell biology (Nature Chemical Biology, 2010; Cell Research, 2011; Nature Cell Biology, 2018), diabetes (Scientific Reports, 2016; Molecular Metabolism, 2016; International Journal of Obesity, 2018), neuropathic pain (Nature Chemical Biology, 2012), cancer (Scientific Reports, 2017; Nature Communications, 2016) and other fundamental biological processes in disease (Science, 2016; Nature Communications, 2016; Nature Structural and Molecular Biology, 2017) involving animal models and human samples.

Chair of the session 7.

Marta Sans, Doctoral Candidate at Livia S. Eberlin Group, The University of Texas at Austin, Austin, USA

Marta Sans is a doctoral candidate and fourth year graduate student in the Livia S. Eberlin Research Group at the University of Texas at Austin. Marta is originally from Castellar del Valles (Barcelona), and moved to the United States to pursue her college degree in Chemistry at the University of New Orleans. Since she moved to Austin (Texas), her PhD work has been dedicated towards developing and applying mass spectrometry methods, such as DESI-MS or the MasSpec Pen, for improved human cancer tissue diagnosis.

Development and Application of the MasSpec Pen for Rapid Ex Vivo and in Vivo Cancer Tissue Diagnosis

Conventional methods for histopathologic tissue diagnosis can delay decision-making during diagnostic procedures. Ambient ionization mass spectrometry techniques have been widely used to characterize the metabolic profiles from tissue samples and create statistical models predictive the disease, showing potential for clinical use and cancer diagnosis. Yet, technical incompatibilities have traditionally prevented their use for fresh tissue and *in vivo* analyses. A few approaches, such as the iKnife or SpiderMass, have been developed for fresh and *in vivo* tissue analyses. As a gentler alternative for

direct tissue analysis, we report the development of an automated and biocompatible handheld device, called the MasSpec Pen, for direct, real-time non-destructive sampling and molecular diagnosis of tissues. Differently than other techniques, based on electrothermal or laser sources, the MasSpec Pen uses a single water droplet to gently extract molecules from tissues upon contact, which are then analyzed by an orbitrap mass spectrometer, resulting in a total analysis time of 10 seconds or less. We have tested the device for *ex vivo* molecular evaluation of human tissue samples including normal and cancerous tissues from breast, lung, thyroid, ovary, pancreas and brain. The mass spectra obtained presented rich molecular information including diagnostic metabolites, lipids and proteins species. Statistical analysis using the least absolute shrinkage and selector operator (Lasso) technique allowed prediction of cancer with an overall accuracy >96% for over 700 tissue samples. We have also demonstrated that this technology is suited for *in vivo* use using a murine model of breast cancer.

To further evaluate the performance of our technology and move towards clinical translation, we have more recently worked on validating our results for ovarian cancer diagnosis by introducing new samples, tissue and histological subtypes, as well as evaluating performance in an ion trap mass analyzer, more suitable for translation into the operating room. Our results show improvements in classification performance over previously published results for high-grade ovarian carcinomas (96.2%) and serous cancer (SC) overall (94.7%) when compared to normal ovarian tissue. Variations in the mass spectra from normal tissue, low-grade and high-grade serous ovarian cancers were also observed, suggesting potential for cancer subtyping. Discrimination between ovarian cancer and fallopian tube or peritoneum tissue was also achieved with high accuracy, and 100% specificity, which can aid in surgical resection of the disease. Using ion trap data, excellent results for high-grade serous cancer vs normal ovarian differentiation were also obtained, further showcasing the validity and robustness of the metabolic features detected with this approach. Overall, our results indicate that the MasSpec Pen, together with machine learning, provides robust molecular models for ovarian serous cancer prediction, and thus has potential for clinical use for rapid and accurate diagnosis of ovarian cancer.

Theodore Alexandrov, Team Leader at the European Molecular Biology Laboratory (EMBL), Heidelberg, Germany

Theodore Alexandrov is a group leader at the European Molecular Biology Laboratory in Heidelberg, the head of the EMBL Metabolomics Core Facility and an Assistant Adjunct Professor at the Skaggs School of Pharmacy, University of California San Diego. The overarching aim of the Alexandrov team is to develop computational biology tools to picture metabolism in time and space across spatial scales from organism to tissues to single cells. Theodore Alexandrov is a grantee of an ERC Consolidator project focused on studying metabolism in single cells. He coordinated two European projects, particularly METASPACE, an initiative to push metabolite imaging to a new level through big data analytics. He has co-founded two startups, including the scientific software company SCiLS. He has over 60 journal publications and several patents in the field of spatial -omics.

Spatial metabolomics in tissues and single cells

Metabolites, lipids, and other small molecules exhibit complex and cell-specific spatial localization in tissues supporting tissue homeostasis in health and metabolism reprogramming in disease. Our team develops novel tools for spatial metabolomics to detect and interpret the roles of these molecules in tissues and single cells. We will present a recently developed cloud platform METASPACE for spatial metabolomics in tissues which provides a comprehensive community-populated resource for metabolism research and for spatial systems biology. We will also present a spatial single-cell metabolomics method which, by correlative in situ imaging of cell monolayers, provides for each cell its metabolic profile and assesses its optical, morphological, and fluorescent phenotype. These tools open novel avenues for understanding metabolism in tissues and on the single-cell level.

Session 8. Proteomics Entrepreneurs Round Table

Jordi Naval, CEO at Biocat, Barcelona, Spain

In February 2018, Jordi Naval joined Biocat as CEO.
Over the past 18 years, he has built a number of start-ups, successfully creating and developing new business concepts in the biopharmaceutical industry. He has also been involved in philanthropic and educational ventures, which he still leads today.
In 2014, he joined the world-class team at HIVACAT and co-founded AELIX Therapeutics, which aims to develop immunotherapies to cure HIV infection globally. AELIX raised €11.5 million in 2016 from several international investors.
In his position at the Bosch i Gimpera Foundation, his mission was to transform the world-class research at University of Barcelona into projects that benefit society as a whole.
He is the chairman of the Entrepreneurs School Foundation (Fundació Escola Emprenedors,) which provides entrepreneurial education to more than 3,000 young people (www.escolaemprenedors.org).
Previously, Jordi Naval held several executive roles in companies in a wide variety of subsectors in the life sciences: co-founder and scientific advisor at Genocosmetics, where he developed the concept of personalized cosmetics based on the consumer's genetic profile in 2011 (www.genocosmetics.com); co-founder and CEO of Anaxomics (2007-2013), providing drug-discovery services using advanced biocomputing and systems biology techniques, where he managed a team of 25 experienced professionals conducting operations worldwide; and global head of Post-Marketing Trials at Research Pharmaceutical Services (Philadelphia), now PRA, where he managed an international team of 20 people conducting clinical trials globally.
In 1997, he founded Infociencia, which would go on to become the biggest Spanish clinical research organization (CRO). He was CEO of the company, growing it from 2 employees in 1998 to 120 in 2008, with total sales of €9 million. In 2006, he created IMITIS, a European partnership of CROs from 5 countries that merged successfully with Research Pharmaceutical Services in 2008, in a deal valued at €25 million.

Chair of the session 8.

Eva Colás, Principal Investigator at Vall Hebron Research Institute (VHIR), Barcelona, Spain

Dr. Eva Colás has been fully dedicated to endometrial cancer research during the last 12 years, with a special focus in the search of biomarkers to improve management of EC patients, although also investigating on the molecular basis of this disease and the development of new therapeutic approaches. From 2006 to 2014, she did her Ph.D. thesis and a first postdoctoral period in the Group of Biomedical Research in Gynecology at the Vall Hebron Research Institute. After a 2-year postdoc in the Group of Dr. Xavier Matias-Guiu (IRBLleida), she returned to the Group of Biomedical Research in Gynecology at VHIR and become principal researcher of the Endometrial Cancer Translational Research Line. During her PhD, she participated in the development of the diagnostic kit GynEC-DX®, in collaboration with Oryzon S.A. and Reig Jofre S.A. In the last years, Dr. Colás has lead the conception and development of a new molecular diagnosis of endometrial cancer, the CEMARK project, based on protein biomarkers analyzed in a sample of uterine fluid. The CEMARK project is now on the prototype development phase and is expected to reach the market in the next years.

Ralph Schiess, CEO at ProteoMediX AG, Zurich, Switzerland

Dr. Ralph Schiess is a biochemist by training and received his Ph.D. from the ETH Zurich. During his doctoral studies his research was focusing on mass spectrometry based proteomics with a special interest in biomarker discovery. Since 2010, he is CEO and co-founder of ProteoMediX AG, a company dedicated to enable personalized cancer medicine by bringing together diagnosis and therapy.

Serum biomarkers for improved prostate cancer diagnosis

Prostate cancer is the most frequently diagnosed cancer in men and the second leading cause of male cancer-related deaths. The current standard test for prostate cancer detection measures levels of prostate-specific antigen (PSA). The drawback

with the PSA test is that it has a high false positive rate. The consequences are that many men, despite having no prostate cancer, undergo biopsies with potential side effects such as infections, bleeding and incontinence.

The presentation will cover the early discovery of protein biomarkers linked to prostate cancer employing proteomics technology. This will be followed by highlighting the process of demonstrating analytical and clinical validity resulting in a diagnostic product with the potential to impact physicians' decision-making process and ultimately reduce overdiagnosis and overtreatment.

Closing Lecture

Eduard Sabidó, Head of the CRG/UPF Proteomics Unit at Centre for Genomic Regulation (CRG), Barcelona, Spain

Read bio in page 8.
Chair of the closing lecture.

Ilaria Piazza, Research Associate at ETH Zurich, Zurich, Switzerland

Ilaria Piazza received her doctorate from the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany and is currently a postdoctoral research associate in the group of Paola Picotti at ETH Zurich. There she focuses on the application of chemoproteomic methods in complex biological systems. Using these technologies, she dissected how small molecules compounds can coordinate the regulation and activity of proteome networks, and drafted a global map of a protein-metabolite interactome that uncovered new allosteric and enzymatic protein functions. Ilaria is continuing her scientific research engineering tools to investigate drug targets in the native cellular environment. With these approaches she aims to identify structural biomarkers to fingerprint healthy conditions and human diseases.

Ilaria Piazza is the recipient of the European Proteomics Association young investigator prize for the year 2018 and of an EMBO long-term fellowship that recognize her research and involvement in the scientific community.

Studying protein structural changes on a proteome-wide scale in health and disease

Mass spectrometry (MS)-based proteomic techniques are routinely used to measure global changes in protein abundance, post-translational modification and protein-protein interactions but much less is known about protein structural changes. Signal transduction, binding of natural and artificial small molecule compounds cause variation in protein structures that can profoundly influence protein activity and thus modulate cellular physiology.

In the Picotti lab at ETH Zurich we recently developed multiple structural proteomics methods that enable the analysis of protein structural changes on a proteome-wide scale and directly in complex biological extracts. I will focus on LiP-SMap a proteomic workflow for the systematic identification of small molecule protein-interactions directly in their native environment. LiP-SMap combines limited proteolysis (LiP) with DIA (Data Independent Acquisition) mass spectrometry in the presence of unmodified small molecule compounds to enable a systematic analysis, unbiased with regard to both chemical compounds and proteins.

With LiP-SMap we identified a network of known and novel protein-metabolite interactions and binding sites in Escherichia coli, and we demonstrated the functional relevance of a number of newly identified protein-metabolite interactions. Our data enabled identification of new enzyme-substrate relationships, novel regulatory events and cases of metabolite-induced remodeling of protein complexes. I will further describe how the LiP method can be applied to the study of cellular pathways and I will present our latest applications for drug target deconvolution on a cell-wide scale.

POSTERS

1. Ada Soler-Ventura, Marina Gay, Mar Vilanova, Laura Villarreal, Gianluca Arauz-Garofalo, Josep Lluís Ballescà, Judit Castillo, Meritxell Jodar, Marta Vilaseca and Rafael Oliva. Top-down proteomic approach for the study of basic proteins in the human sperm nucleus.

2. Alba Garin-Muga, Claudia Mazo, Andoni Beristain, Ignacio Zabalza, Maria d.M. Vivanco and Iván Macia. Personalized breast cancer treatment based on Sox2 protein expression.

3. Albert Casanovas, Oscar Gallardo, Joaquin Abian and Montserrat Carrascal. Global analysis of ubiquitinome, acetylome and phosphoproteome dynamics reveals post-translational regulatory events in T-cell activation.

4. Antonio Serna, Joerg Dojahn, Dietrich Merkel, Rebekah Sayers, Ben C. Collins, Christie L. Hunter, Yansheng Liu, Birgit Schilling, George Rosenberger, Samuel L. Bader, Daniel W. Chan, Bradford W. Gibson, Anne-Claude Gingras, Jason M. Held, Mio Hirayama-Kurogi, Guixue Hou, Christoph Krisp, Brett Larsen, Liang Lin, Siqi Liu, Mark P. Molloy, Robert L. Moritz, Sumio Ohtsuki, Ralph Schlapbach, Nathalie Selevsek, Stefani N. Thomas, Shin-Cheng Tzeng, Hui Zhang and Ruedi Aebersold. Multi-laboratory Assessment of Performance of SWATH® Acquisition Mass Spectrometry.

5. Antonio Serna, Joerg Dojahn, Dietrich Merkel, Rebekah Sayers, Nick Morrice, Tom Knapman, Christie Hunter, Julie Brazzatti, Robert Graham and Tony Whetton. Standardizing and Harmonizing Multiple TripleTOF® systems for DDA and DIA using a Dedicated Performance Kit.

6. Carlos Lopez-Gil, Elena Martinez-Garcia, Antoine Lesur, Eva Coll, Silvia Cabrera, Xavier Matias-Guiu, Marc Hirschfeld, Jasmin Asberger, Jan van Oostrum, María de los Ángeles Casares de Cal, Antonio Gómez-Tato, Bruno Domon, Antonio Gil Moreno and Eva Colas. Targeted proteomics identifies proteomic signatures in liquid-biopsies of the endometrium to diagnose endometrial cancer and assist in the prediction of the optimal surgical treatment.

7. Christopher Hughes, Lee Gethings, Florian Marty, Sebastian Müller, Jose Castro-Perez and Robert Plumb. Rapid Qualitative and Absolute Quantification of Plasma based proteins using a Novel Scanning Quadrupole DIA Acquisition Method.

8. Clara Matas-Nadal, Joan Josep Bech-Serra, Marta Guasch, Josep Manel Casanova, Rafael Aguayo, Carolina de la Torre Gómez and Eloi Garí. Evaluation of tumor interstitial fluid-extraction methods for proteome analysis: comparison of biopsy elution versus centrifugation.

9. Cristina Chiva. Internal calibration curves for accurate quantitation in clinical proteomics.

10. E. Diaz-Riera, M. Garcia-Arguinzonis, L. Lopez, X. Garcia-Moll, L. Badimon and T. Padro. Differential urine proteomic signature for early diagnostic of renal insufficiency in patients with acute heart failure.

11. Esther Rodríguez-Gallego, Laura Tarancón-Diez, Felipe García, Jorge del Romero, Jose Miguel Benito, Verónica Alba, Pol Herrero, Anna Rull, Beatriz Dominguez-Molina, Onofre Martinez-Madrid, Luisa Martin-Pena, Federico Pulido, Agathe León, Carmen Rodríguez, Norma Rallón, Joaquim Peraire, Consuelo Viladés, Manuel Leal, Francesc Vidal and Ezequiel Ruiz-Mateos. Proteomic Profile Associated with Loss of Spontaneous HIV1 Elite Control.

12. Eva Coll, Irene Campoy, Cristian P. Moiola, Marc Hirschfeld, Jasmin Asberger, Silvia Cabrera, Xavier Matias-Guiu, Eduard Sabidó, Antonio Gil Moreno, Pierre Thibault and Eva Colás. Exosome-like vesicles of uterine aspirates permit the identification of diagnostic and stratification biomarkers of endometrial cancer.

13. Ferran Moratalla and Victor Moreno. Serum proteome analysis profiling to identify biomarkers associated with colorectal cancer and high risk adenomas.

14. Heiner Koch, Gary Kruppa, Scarlet Koch, Thomas Kosinski, Markus Lubeck, Florian Meier, Andreas-David Brunner and Matthias Mann. Highly Reproducible and Accurate Label Free Quantification using the PASEF method on a TIMS-QTOF mass spectrometer.

15. J. Bauzá, B. Bollen Pinto, F. Aletti, A. Odena, R. Díaz, K. Bendjelid and E. Oliveira. A Proteomics Study on Septic Shock Patients: an Overview on Sepsis-Induced Myocardial Dysfunction.

16. John P. Wilson and Darryl J. Pappin. Universal, reproducible and high-throughput workflows with S-Trap sample processing for clinical proteomics and metabolomics.

17. José-Ángel Robles-Guirado, Elena González-Paredes, Alex Mas-Ciurana, Miguel-Ángel Palacios-Pedrero, Carolina Franco-Herrera, Victoria Longobardo, Antonio Lario, Ana-Belén Jodar, Francisco J. Blanco, Vivian de los Ríos, Ignacio Casal, Mercedes Zubiaur and Jaime Sancho. Proteomic analyses of exosome fractions present in peritoneal exudates from mice with pristane-induced lupus.

18. Juanma Ramirez, Benoit Lectez, Nerea Osinalde, Monika Sivá, Nagore Elu, Kerman Aloria, Michaela Procházková, Coralia Perez, Jose Martínez-Hernández, Rosa Barrio, Klára Grantz Šašková, Jesus M. Arizmendi and Ugo Mayor. Quantitative proteomics reveals neuronal ubiquitination of Rngo/Ddi1 and several proteasomal subunits by Ube3a, accounting for the complexity of Angelman syndrome.

19. Laura Carreras-Planella, Sara Inés Lozano-Ramos, Ioana Bancu, Marta Monguió-Tortajada, Laura Cañas, Javier Juega, Marcella Franquesa, Josep Bonet, Ricardo Lauzurica and Francesc Enric Borràs. Urinary extracellular vesicles protein biomarkers for the non-invasive diagnosis of rejection in kidney transplanted patients.

20. Laura Pont, Fernando Benavente, Estela Giménez, Roger Pero-Gascon, Montserrat Mancera Arteu, José Barbosa and Victoria Sanz-Nebot. High sensitivity analytical platforms for the characterization of proteins and glycoproteins by high performance separation techniques coupled to mass spectrometry.

21. Lee Gethings, Adam King and Robert Plumb. Multi-Omic Characterisation of Bladder and Lung Carcinomas using a Novel Scanning Quadrupole DIA Acquisition Method.

22. M. Martin-Perez, T. Ito, A. Grillo, M. Kaeberlein and J. Villen. Protein kinase C is a key target for attenuation of inflammation and neurodegeneration by rapamycin during severe mitochondrial disease.

23. Míriam Díaz-Varela, Armando de Menezes-Neto, Daniel Perez-Zsolt, Ana Gámez-Valero, Joan Seguí-Barber, Nuria Izquierdo-Useros, Javier Martinez-Picado, Carmen Fernández-Becerra and Hernando A. del Portillo. Proteomics analysis of human reticulocyte-derived exosomes reveals more than a garbage-disposal mechanism in reticulocytes.

24. Nicolai Bache, Philipp E. Geyer, Erik Verschuuren, Dorte B. Bekker-Jensen, Ole Hoerning, Lasse Falkenby, Peter V. Treit, Sophia Doll, Igor Paron, Florian Meier, Jesper V. Olsen, Ole Vorm and Matthias Mann. Evaluation of a novel LC system that embeds analytes in pre-formed gradients for rapid, ultra-robust proteomics.

25. Olga de la Caridad Jorge Torres, Laura Solé, Jordi Serra, Carolina de la Torre, Joan Josep Bech-Serra, Aida Obiols Guardia, Sonia Guil Domenech and Manel Esteller Badosa. Unravelling the proteins forming Gsk3b complex in Rett syndrome models mice.

26. Patricia Fernández-Puente,Valentina Calamia, Lucía González-Rodriguez, Lucía Lourido, María Camacho, Rocio Paz-Gonzalez, Antonio Gonzalez, Cristina Ruiz-Romero and Francisco J. Blanco. Targeted analysis of protein biomarkers associated with Rheumatoid Factor and citrullinated protein antibodies in rheumatoid arthritis patients.

27. Serge Desmoulins (Agilent). An automated and reproducible workflow for human cancer cell line phosphopeptide analysis.

28. Yago Arribas, Roc Farriol, Lucía Labeur, Vanessa Casas, Joaquín Abián, Carol Guitart, Aura Muntasell, Montserrat Carrascal and Dolores Jaraquemada. Influence of invariant chain and HLA-DM on the HLA-DR3 peptidome in epithelial cells.

29. Yue Xuan, Yue Zhou, Sebastien Gallien, Pedro Navarro, Oleksandr Boychenko, Joshua Nicklay, Jenny Ho, Claire Dauly, Scott Peterman and Ken Miller (Thermo Fisher Scientific). A streamlined workflow for high-throughput, precise, and comprehensive large-scale quantitative proteomics analysis.

PRACTICAL INFORMATION

Venue: CosmoCaixa Barcelona

CosmoCaixa Barcelona
C/ Isaac Newton, 26
08022 Barcelona, Spain

Conference room
Auditori (-2 floor)

Free wifi
1. Select wifi_cosmocaixa_bcn
2. Open an Internet Browser
3. The page of CosmoCaixa will appear. Follow the instructions

Security issues:
The conference room will remain open. Please take care of your personal belongings, specially in the breaks. The Organizers won't be responsible of any loss or robbery occured in the context of B·Debate.

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SUGGESTED READING

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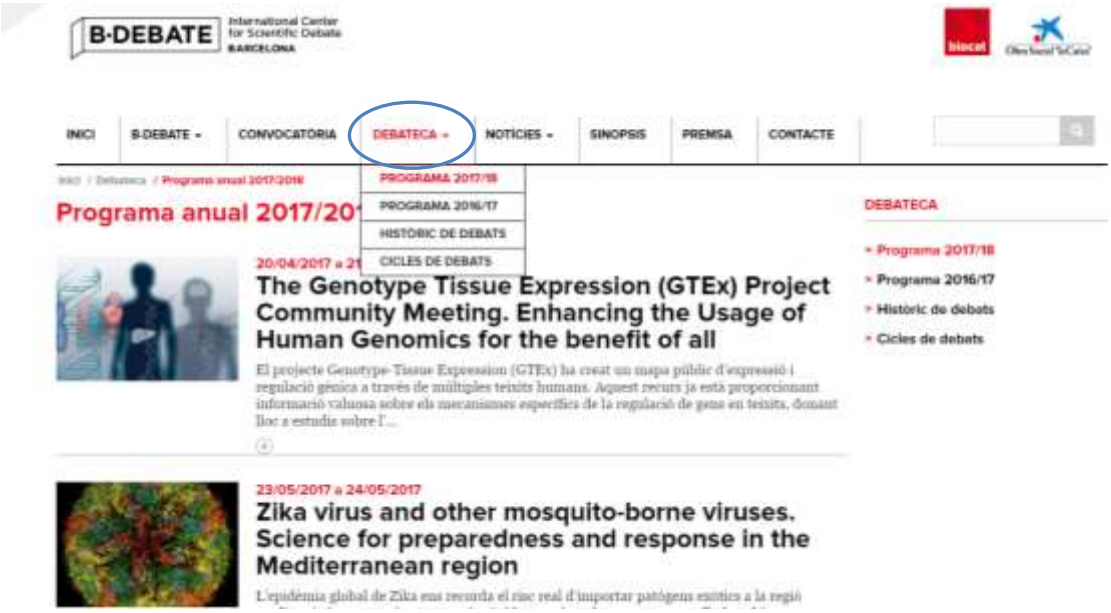
  Nature methods 12.4 (2015): 366-372.

OUTCOMES

B·Debateca

On the website of B·Debate, you will find all the information related with the celebration of the meeting that includes reports, conclusions, scientific documents, interviews with the experts, speaker's CVs, videos, images, press documentation and other related materials. We invite you to visit the section B·Debateca on www.bdebate.org

Contents of the meeting: "Clinical Proteomics: towards personalized medicine and health"



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The debates are top-notch international scientific meetings featuring a selection of experts of renowned international prestige and scientists that work in Barcelona and Catalonia, moderated by scientific leaders. Since 2009 B·Debate has invited about 1750 recognized speakers and over 13.000 attendees. B·Debate seeks out answers to the challenges and needs of society in the field of life sciences, taking into account the complex, ever-changing conditions of this global world. The debates foster the integration of different disciplines of science and deal with such diverse topics as ageing, new therapeutic approaches to various diseases, innovative technology to improve knowledge of the human genome, food resources, new tools to integrate knowledge management, clinical genomics, neurosciences, climate change, and new energy sources, among others. The knowledge and results obtained through these events is spread throughout both the scientific community and general society through the various B·Debate channels and instruments.

More info: www.bdebate.org

The Bellvitge Biomedical Research Institute (IDIBELL) is a biomedical research center for cancer, neurosciences and translational medicine established in 2004 in L'Hospitalet de Llobregat, south of Barcelona. Its stakeholders are the Bellvitge University Hospital (HUB) and the Viladecans Hospital, both part of the Catalan Institute of Health (ICS), the Catalan Institute of Oncology (ICO), the University of Barcelona (UB) and the town council of L'Hospitalet de Llobregat. In 2009, it became one of the first five Spanish research centers accredited as a health research institute by the Carlos III Institute of Health. IDIBELL also carries out high-level basic, epidemiological, translational and clinical research though its nine research programs, aiming at an effective translation of scientific advances into the prevention, diagnosis, prognosis and treatment of health problems and promoting innovation in health research. IDIBELL is an institute committed to bring research –based solutions to the clinical practice; we have the position of being able to conduct state of the art basic research with a view towards application to clinical application and exploitation of the results.

More info: www.idibell.cat

Established in 2006, the **Vall d'Hebron Institute of Oncology** (VHIO) is a leading comprehensive cancer center of excellence where its scientists and research physicians adopt a purely translational research model, working together as multidisciplinary teams to both accelerate and advance personalized and targeted therapies against cancer. Undertaking

one of Spain's most dynamic cancer research programs, VHIO is dedicated to delivering on the promise of 'precision' medicine in oncology – turning cancer discovery into more effective treatments and better practice for the care of our patients.

Organized into four main programs: Preclinical, Translational, Clinical, and Core Technologies, VHIO´s team of some 200 researchers and physician scientists focus on understanding the fundamental biology of human cancer, from cellular and molecular biology and genetics through to therapeutics.

Its optimal organizational structure, coupled with its privileged location within the campus of the Vall d´Hebron University Hospital – affording direct access to patients as well as the entire spectrum of oncology professionals who care for them, allows VHIO to tackle the many unresolved questions in ultimately outsmarting the multifaceted, heterogeneous and complex disease that is cancer.

More info: www.vhio.net

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Barcelona Science Park is one of the leading European ecosystems in research, technology transfer and innovation in life sciences. Located in Barcelona, in the knowledge Campus, the Park has more than 100,000 m2 available to an active Community of almost 2,700 professionals.
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- Mission: To promote research, knowledge transfer and innovation in the public and private sectors via smart space, technology and relations management as well as PCB discourse.
- Vision: To become the international benchmark in public/private research to enhance Catalonia's role as a scientific leader, its economic growth and its potential to attract talent.

More info: www.pcb.ub.edu

CRG
Centre for Genomic Regulation

The Centre for Genomic Regulation (CRG) is an international biomedical research institute of excellence, founded in December 2000 whose mission is to discover and advance knowledge for the benefit of society, public health and economic prosperity. The CRG believes that the medicine of the future depends on the groundbreaking science of today. This requires an interdisciplinary scientific team focused on understanding the complexity of life from the genome to the cell to a whole organism and its interaction with the environment, offering an integrated view of genetic diseases. Research at the CRG falls info four main areas: gene regulation, stem cells and cancer; cell and developmental biology; bioinformatics and genomics; and systems biology.

More info: www.crg.eu

ProteoRed
Carlos III Networked Proteomics Platform

ProteoRed-ISCIII, integrates 25 laboratories in a networked proteomics initiative of the Spanish National Institutes of Health ISCIII. The mission of ProteoRed is to consolidate and maintain a competitive proteomics technological resource to provide a service of excellence to academic and industrial partners.
ProteoRed general aim is to contribute to the design and development of projects in the biotechnology and biomedicine areas to establish new concepts in biology, to identify new diagnostic and therapeutic targets to promote the development of new biopharmaceutical products and to dissect the mechanism of action of drugs and their selective effects in specific individuals.

More info: www.proteored.org

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SCIEX is dedicated to placing the power of life-changing answers into the hands of those who care, everywhere. SCIEX provides integrated, reliable analytical tools to advance scientific understanding and safeguard health. The company's technology leadership spans across 40 years of innovations in state-of-the-art instrumentation, workflow solutions and support for mass spectrometry and separations science.

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Bruker is strongly committed to further fully meet its customers' needs as well as to continue to develop state-of-the-art technologies and innovative solutions for today's analytical questions.

More info: www.bruker.com

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More info: www.thermofisher.com

Evosep aims to improve quality of life and patient care by radically innovating protein based clinical diagnostics. Making sample separation before MS analysis 10 times faster and 100 times more robust will enable truly large cohort studies for biomarker validation and provide the foundation for precision medicine.
In current state of the art MS-based proteomics workflows, robustness and long duty cycles of the nano-LC systems have proven to be major bottlenecks. With a growing awareness for the need to optimize the use of valuable MS-time, LC downtime and duty cycles have come to the focus of attention. Evosep One is purposely designed to eliminate these bottlenecks.
With Evosep One, we have introduced an entirely novel concept based on the use of sample clean-up pipette tips as disposable trap columns. The tips are eluted by a gradient at relatively high-flow and low-pressure. In order to be able to focus the peaks on the top of the analytical column, we lower the %B in the elution gradient prior to storing it in a holding loop. This stored gradient, with the analytes embedded and pre-separated is then moved across to a high-resolution column by an isocratic, high-pressure pump.
Quick elution of the tip and other highly optimized elution and washing procedures reduce the system overhead to maximum 3 min per injection. Due to the use of disposable trap columns, Evosep One has been demonstrated to have minimal or absent cross contamination, greatly reducing the need for blank runs. Furthermore, we have found very reproducible chromatography as well as a very high consistency of label-free quantitation results across numerous injections.
The new concept of the Evosep One has the capability to change the way many proteomics experiments are done today and opens the door for fast, robust, yet sensitive clinical protein assays.
Evosep aims to improve quality of life and patient care by radically innovating protein based clinical diagnostics.

More info: www.evosep.com

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I&L Biosystems

I&L Biosystems is a leading, experienced and respected supplier of innovative laboratory equipment since 1991. The French site was founded during summer 2015 and has been growing ever since. The company's core business is the distribution of complex and exclusive technologies applicable in microbiology, cell biology and biotechnology within France and southern Europe (Spain, Italy and Portugal). I&L Biosystems France stands out from its competitors by offering rapid, customer-oriented and high-quality service offered by a team of highly educated and motivated employees. Technical support can be offered at customer's site or in house.

Here we present the Barocycler Technology from Pressure BioSciences Inc., an innovation that serves by its Pressure-Cycling Technology (PCT) for the extraction of proteins and for the accelerated enzymatic digestion for the sample preparation in the Proteome Analytics. The cooperation with Prof. Aebersold from the ETH Zürich did lead in the past years to a new developed method based on PCT which gives an acceleration and standardization in the sample preparation of biopsy tissue before the mass spectrometric analysis.

More info: https://il-biosystems.com/

ProteoMediX

ENABLING PERSONALIZED MEDICINE

ProteoMediX AG is a privately held diagnostic company that was founded in March 2010 as a spin-off company from ETH Zurich. ProteoMediX enables personalized medicine by developing non-invasive diagnostic tests to detect and assess the prognosis of cancer, as well as to match patients with safer and more effective therapies. The first products are focusing on prostate cancer, the most frequently diagnosed cancer in men, where neither the detection nor the effective treatment is currently guaranteed. ProteoMediX owns the exclusive commercial rights on a set of protein-based biomarkers that were discovered with state-of-the-art proteomics technology developed at the ETH Zurich. These biomarkers are directly linked to the origin of cancer on a molecular level and allow to capture the complexity of the disease by combining multiple biomarkers. A combination of these showed superior results for the accurate diagnosis of prostate cancer when compared to the current standard PSA test in several clinical studies.

More info: www.proteomedix.com

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