Dear Participants,
On behalf of the meeting organizers, we would like to welcome you and thank you very much for your participation in the **Women’s Cancer B-Debate** conference. The conference is an initiative of the “La Caixa” Foundation, Biocat, Bellvitge Institute for Biomedical Research (IDIBELL), Catalan Institute of Oncology (ICO), and Catalan Institute of Health (ICS).

Cancer has an obvious major impact in health care activity and, particularly, it has differential social, professional and familial consequences when affecting women. Therefore, in addition to improving prevention, treatment and cure, the patient’s voice is critical for better direct research efforts and funds. To address these questions, the designed conference aims at to present, discuss and enhance the latest basic and translational research advances in women’s cancer, and give voice to patients for discussing their view and needs. The aim is to bring together in one space and time “clinical-research-patients-associations” towards improving women’s cancer care. The conference highlights will include the latest advances in cancer biology, risk estimation, prevention (including the successful impact of HPV vaccination) and treatment. The afternoon of the second day will be open (free access) for a debate including patients, representatives of patient associations, medical oncologists, and experts in bioethics and scientific communication. The debate will be focused on the future of personalized and participative medicine.

Catalonia is a hub of biomedical research and, particularly, in cancer research for the assessment of novel therapies through robust oncology programs and clinical trial units. The conference-invited talks by internationally renowned investigators together with the open debate will stimulate the discussion and provide novel ideas and guidelines for improving cancer care. We encourage you to actively participate in the discussions and wish you a fruitful meeting over the next two days.

We hope that the meeting will cover your expectations and we wish you a pleasant stay in Barcelona.

Yours sincerely,

“La Caixa” Foundation, IDIBELL, ICO, ICS, B-DEBATE
PROGRAM

Thursday, November 16th, 2017

8:45  Registration

9:00  Welcome
   Ángel Font, La Caixa Foundation
   Marta Soler, Biocat
   Ramón Salazar, Catalan Institute of Oncology
   Gabriel Capellà, Bellvitge Biomedical Research Institute

9:15  SESSION 1: Advances in Cancer Biology
     Chairperson: Eva González-Suárez, IDIBELL, Barcelona, Spain
     The last 15 year of the big killer: turning points in advanced disease
     Silvia Novello, University of Turin, Turin Italy
     Short talk:
     Therapeutic opportunities for RANK pathway in breast cancer
     Eva González-Suárez, IDIBELL, Barcelona, Spain
     Short talk:
     Targeting p38α increases chromosome instability and enhances the anti-tumoral response
to taxanes in breast cancer cells
     Begoña Canovas, IRB Barcelona, Barcelona, Spain

11:10  Coffee break

11:35  Deconstructing and reconstructing the ovarian cancer microenvironment
      Frances Balkwill, Barts Cancer Institute, London, UK
     Short talk:
     Tumor-associated macrophages (TAMs) depend on ZEB1 for their cancer-promoting roles in
human ovarian cancer
     Marlies Cortés, IDIBAPS, Barcelona, Spain

12:45  Poster session

13:10  Lunch

14:20  Telomeres as therapeutic targets for cancer
      Maria Blasco, CNIO, Madrid, Spain

15:10  SESSION 2: Advances in Cancer Susceptibility
     Chairpersons: Conxi Lázaro and Miquel Ângel Pujana, ICO-IDIBELL, Barcelona, Spain
     Breast and ovarian cancer susceptibility: what have we learned from large international
consortia?
     Antonis Antoniou, University of Cambridge, Cambridge, UK
     BRCA testing in ovarian tumors initiated by a pathologist: a pre-screen for germline testing
and therapy choice
     Nicoline Hoogerbrugge, Radboud University Medical Center, Nijmegen, Netherlands
     Short talk:
     Pathogenic variants (PVs) detection in a 19-gene core panel and yield of opportunistic
screening in BRCA1/2 and MMR genes in a cohort of 1242 hereditary cancer
     Judith Balmaña, VHIO, Barcelona, Spain
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<tr>
<td>17:10</td>
<td>Coffee break</td>
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<td>17:35</td>
<td>Clinical Assay of Endometrial Cancers</td>
<td>Elaine Mardis, Nationwide Children’s Hospital,</td>
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<td>Pål Møller, Norwegian Radium Hospital, Oslo,</td>
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**Friday, November 17th, 2017**

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<td>9:00</td>
<td><strong>SESSION 3: Advances in Cancer Prevention</strong></td>
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<td>Chairperson: Silvia de Sanjose, ICO-IDIBELL,</td>
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<td>**Progress in Therapeutic Prevention of Breast</td>
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<td>Jack Cuzick, Queen Mary University of London,</td>
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<td>HPV faster: searching for the optimal combination</td>
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<td>Francesc X Bosch, ICO-IDIBELL, Barcelona, Spain</td>
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<td>Short talk: The diagnostic value of cervico-vagal</td>
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<td>cytology in endometrial carcinoma: a systematic</td>
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<td>Laura Costas, ICO-IDIBELL, Barcelona, Spain</td>
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<td>**Novel strategies for early detection and</td>
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<td>prevention of breast and ovarian cancer in BRCA</td>
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<td>Martin Widschwendter, UCL EGA Institute Women's</td>
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<td>Health, London UK</td>
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<td>Short talk: Characterization of Nigerian Breast</td>
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<td>Cancer Reveals High Rates of Homologous</td>
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<td>Jordi Barretina, IDIBGI, Girona, Spain</td>
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<td>12:35</td>
<td>Buffet lunch</td>
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<td>14:00</td>
<td><strong>SESSION 4: Advances in Cancer Cure</strong></td>
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<td>Chairperson: Aleix Prat, Hospital Clínica de</td>
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<td>Treating Triple-Negative Breast Cancer: From</td>
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<td>Biology to the Clinic</td>
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<td>Carey Anders, UNC Lineberger Cancer Center, Chapel</td>
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<td>Daniela Quail, McGill University in Montreal,</td>
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<td>Daniel Massó, VHIO, Barcelona, Spain</td>
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<td>16:00</td>
<td>Coffee break</td>
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16:25 Open session:

**Why Don't We Get More Cancer: The significant role of ECM in normal breast function and breast cancer.**

*Mina Bissell*, Lawrence Berkeley National Laboratory, Berkeley, USA

17:15 Open debate:

**Medicina participativa i personalitzada** (This session will be held in Catalan)

Chairperson: *Lara Bonilla*, Diari ARA

- *Victoria Camps*, Fundació Víctor Grifols i Lucas/UAB/Comitè de Bioètica de Catalunya
- *Pere Estupinyà*, periodista i divulgador científic
- *Laura Sancho*, actriu i pacient
- *Clara Rosàs*, Federació Catalana d'Entitats Contra el Càncer (FECEC)
- *Rosa Gasà*, investigadora i pacient
- *Joan Brunet*, oncòleg i conseller genètic (ICO)

19:15 Conclusions and closing of the meeting

19:30 End of the meeting
Eva Gonzalez Suarez is Principal Investigator of the Transformation and Metastasis Group at the Bellvitge Institute for Biomedical Research in Barcelona, Spain. She obtained her Master degree in Biochemistry in the University of Oviedo (1998) and her PhD in Molecular Biology at the Autonoma University of Madrid, Spain (2003). During her Doctoral Thesis in M Blasico laboratory (National Center of Biotechnology/CSIC, Madrid, Spain), she made important contributions clarifying the role of telomerase in cancer and aging. Subsequently, Dr Gonzalez Suarez joined Amgen Inc, Seattle, USA, as a postgraduate fellow before assuming her current role in 2008. Her research focuses on the mechanisms leading to cell transformation, the metastatic capabilities of epithelial cells, and the identification of novel therapies and resistance mechanisms. She has made important contributions to the field of mammary gland development and breast cancer research, highlighting the key role of RANK signalling pathway and its potential as therapeutic target. Research in her laboratory exploits primary cell cultures, organoids, genetic mouse models, patient derived xenografts and clinical samples. She is a member of the European Network of Breast Development and Cancer committee; she has been awarded multiple national and international competitive projects including the prestigious Susan G Komen career catalyst grant and an ERC Consolidator grant. She is a frequently invited speaker in national and international congresses and coordinates a clinical trial with RANKL inhibitors in breast cancer patients. She has supervised nine PhD students, five postdoctoral scientists, several technicians and master students. She has authored over 35 articles published in international peer-reviewed journals including Nature, Nature Genetics, EMBO J, Molecular and Cellular Biology, Cancer Research, Stem Cells, Stem Cell Reports and she is a reviewer for several international journals and research agencies.

Conxi Lázaro studied biology in the University of Barcelona. Her PhD thesis was completed in the Genetics Department of the Institut de Recerca Oncològica (IRO) under the supervision of Dr. Estivill. She worked as a Molecular Geneticist at the Genetics Service of Hospital Clinic and after that she returned to IRO to lead the Neurofibromatosis 1 group as well as to participate in several research projects related to common multifactorial disorders (asthma and psoriasis). During 2003/04 she was a visiting scientist in the Cancer Center of the Massachusetts General Hospital (Harvard, Boston). In 2006 she obtained her current position as a director of the Molecular Diagnostics Unit for Hereditary Cancer at ICO. In addition to the routine clinical work, Dr. Lázaro leads two research lines, one focus on deciphering the genetic basis underlying the Hereditary Breast and Ovarian Cancer Syndrome, and another mainly focus in the development of new therapeutic strategies for Neurofibromatosis Type 1. Currently she is also involved in several projects aimed to use Next Generation Sequencing (NGS) for genetic testing purposes. She is a member of the Center of Reference on Neurofibromatosis in Spain and a close collaborator of the different local and international NF Associations.

Silvia de Sanjosé is a Medical doctor, Family Practitioner and Epidemiologist. She has been involved in the research of infections and cancer since 1998 after her PhD at the London University. She has been involved in multiple international studies that led to the identification of Human Papilloma Virus to be considered as the necessary cause of cervical cancer and that helped to identify the most relevant worldwide HPV genotypes for the construction of the existing HPV vaccines. She coordinates the evaluation of the introduction of HPV testing as primary screening tool in cervical cancer screening in Catalonia since 2006. She has been involved in guidelines and position papers related to HPV within the WHO. She is now the President of the International Papillomavirus Society. She has published over 350 peer reviewed papers.
Miquel Àngel Pujana, Independent Group Leader and Director of the Program Against Cancer Therapeutic Resistance (ProCURE) at the Catalan Institute of Oncology (ICO, IDIBELL), Barcelona, Spain

BSc in Biology and PhD in Human Genetics (Prof. Xavier Estivill) at the Cancer Research Institute, l’Hospital de Llobregat (Barcelona). Postdoctoral studies at the Center for Cancer Systems Biology, Dana-Farber Cancer Institute, Harvard Medical School (Prof. Marc Vidal). His research focuses on comprehensively understand breast cancer development and progression through the integration and modeling of different biological data levels. He currently applies systems-biology approaches and uses in vivo xenograft models to decipher resistance to endocrine and other targeted therapies, and to evaluate novel strategies to overcome resistance. He is member of the Spanish National Research Network on Breast Cancer and of the international Consortium of Investigators of BRCA1/2 modifiers.

Aleix Prat, Head of Medical Oncology Department at Hospital Clinic of Barcelona, Barcelona, Spain

Dr. Aleix Prat is currently the Head of the Medical Oncology of Hospital Clinic of Barcelona (Spain), Associate Professor of the University of Barcelona and the Head of the Translational Genomics and Targeted Therapeutics in Solid Tumors Group at August Pi i Sunyer Biomedical Research Institute (IDIBAPS). He obtained his MD degree in 2003 from the University of Barcelona and completed a medical oncology fellowship in 2008 at Vall d’Hebron Institute of Oncology (VHIO). In 2008, Dr. Prat became a postdoctoral research associate at the Lineberger Comprehensive Cancer Center (University of North Carolina at Chapel Hill, USA) in the Laboratory of Prof. Charles M. Perou. In 2012, he returned to Barcelona as the Head of the Translational Genomics Group at VHIO and more recently, he moved to Hospital Clinic and IDIBAPS. Dr. Prat is a clinical scientist with a longstanding research interest in the clinical application of laboratory findings in breast cancer, with a particular interest in gene expression and the clinical implications of different intrinsic molecular subtypes of breast cancer. He designs and leads clinical trials of novel drugs and approaches, and is currently the scientific coordinator of SOLTI, a Spanish breast cancer cooperative group. Recently he has been recently named as a Member of Executive Committee of the The Breast International Group (BIG), an international non-profit organization that includes more than 56 cooperative groups from around the world, more than 10,000 experts and it is linked to more than 3,000 hospitals. Its main goal is to promote clinical and translational research in breast cancer. Dr. Prat received the International Prize for Breast Cancer Research (Padova, Italy) for his scientific discoveries regarding the characterization and clinical value of the intrinsic subtypes. Since 2007, he has actively taken part in a total of 110 publications (H-score of 33), with a total of 5,486 citations and 45 communications.
Thursday, November 16th, 2017

Session 1: Advances in Cancer Biology

Eva González-Suárez, Principal investigator at Bellvitge Biomedical Research Institute (IDIBELL), Bellvitge, Spain

Read bio in page 7

Chair of the SESSION 1

Silvia Novello, Full Professor of Medical Oncology at the Department of Oncology at the University of Turin, Turin, Italy

Professor Novello graduated in Medicine at the University of Turin, Italy in 1995. She then did a Postgraduate Course in Respiratory Medicine which she completed in 1999 summa cum laude. In 2006 she achieved a PhD in Human Oncology and went on doing a Postgraduate in Medical Oncology in 2010.

Professor Novello is presently Full Professor of Medical Oncology at the Department of Oncology at the University of Turin, Italy and Chief of the Thoracic Oncology Unit at the San Luigi Hospital in Orbassano, Italy. Her previous positions include: Fellow at S. Luigi Hospital, Clinic of Respiratory Diseases, Orbassano, Turin, from 1995 to 1999 and Clinical Fellow at the same hospital, Thoracic Oncology DH, from 1999 to 2000. From 2000 to 2001 she was Resident A at the Institut Gustave Roussy, Villejuif, France. From 2001 to 2003, Research Fellow in the Medical Experimental and Clinical Sciences area at the Thoracic Oncology Division (University of Turin), and attending Physician at the Thoracic Oncology Division, from 2004 to 2010.

Professor Novello was also Thoracic Oncology Division tutor of Educational Classes in Thoracic Oncology and Educational Classes supported by AIPO (Hospital Pulmonologist Italian Association) for Specialised Doctors in Respiratory Diseases, Thoracic Surgery, Radiology, Radiotherapy and Medical Oncology. Professor Novello is a Member of the American Society of Clinical Oncology (ASCO), Member of “Innovators in Lung Cancer”, Member of IASLC and Board of Director Member, Member of NLCP (National Lung Cancer Partnership) Scientific Committee, Member of IASLC Young Investigators Awards Scientific Committee, Board of Director of AMO (Italian Association of Medical Oncology) and Board of Director Member and President of the European Association - Women Against Lung Cancer in Europe (WALCE).

The last 15 year of the big killer: turning points in advanced disease

Abstract not available.

Short talk: Eva González-Suárez, Principal investigator at Bellvitge Biomedical Research Institute (IDIBELL), Bellvitge, Spain

Therapeutic opportunities for RANK pathway in breast cancer

RANK pathway, key in bone remodeling and metastasis, is essential for mammary gland development. Using genetic mouse models we have shown that RANKL is the main mediator of the protumorigenic role of progesterone in the mouse mammary gland. RANK overexpression in non-transformed human mammary cell lines induces epithelial to mesenchymal transition and stemness, and promotes tumorigenesis and metastasis in breast cancer lines. We have found that RANKL inhibition reduces breast cancer incidence, recurrence and metastasis in multiple mouse models evidencing a direct effect of RANK pathway on cancer cells and supporting the use of RANKL inhibitors for breast cancer prevention and treatment.
Targeting p38α increases chromosome instability and enhances the anti-tumoral response to taxanes in breast cancer cells

During the past years, the protein kinase p38α has emerged as an important regulator of tumorigenesis in normal epithelial cells. However, recent studies provided evidence for a function of p38α promoting tumor cell proliferation and survival in some cancer types. Moreover, p38α inhibition has been shown to cooperate with chemotherapeutic drugs such as cisplatin and sorafenib. We have used the Polyoma middle T mammary tumorigenesis model to study the role of p38α in breast cancer progression, and found that p38α is essential for tumor cell survival in vivo. To analyze the functions of this kinase in epithelial cancer cells, we established cell lines from PyMT-induced mammary tumors. We observed that p38α downregulation resulted in replication stress, elevated DNA damage, and increased chromosome missegregation, which correlated with decreased viability of PyMT-expressing cancer cells. Giving the compromised DNA integrity, we investigated the status of the DNA damage response in p38α-deficient cancer cells. We observed impaired single strand-DNA generation, ATR activation, and RAD51 recruitment after DNA damage, indicating that homologous recombination DNA repair was defective in p38α-deficient cells. Moreover, we identified CtIP, a key factor that promotes DNA-end resection, as a novel p38α substrate. De-regulation of CtIP activity could affect the DNA damage response and explain many of the observed phenotypes. Altogether, our results indicated that p38α was required for effective DNA damage response and repair, which impinges on DNA replication and maintenance of chromosome stability in breast cancer epithelial cells. The above results suggest that targeting p38α could increase tumor cell sensitivity to certain DNA damaging agents, as well as chromosome instability-inducing drugs such as taxanes. We validated these hypotheses using combinations of taxanes and p38α inhibitors both in vitro and in vivo, supporting the potential use of p38α inhibitors in breast cancer therapy.

Frances Balkwill, Professor of Cancer Biology at Barts Cancer Institute, Queen Mary University of London, London, UK

Frances Balkwill is Professor of Cancer Biology at Barts Cancer Institute, Queen Mary University of London where she leads the Centre for Cancer and Inflammation. She studies the links between cancer and inflammation being especially interested in translating knowledge of cancer biology into new biological treatments for cancer, the role that inflammatory cytokines play in cancer promotion and novel ways of modelling the human tumour microenvironment.

Deconstructing and reconstructing the ovarian cancer microenvironment

The tumor microenvironment (TME) is critical for cancer growth and spread. However, the relationships between molecular components of the TME and higher-order features, tissue stiffness, extent of disease and cellularity, are not known. Using clinical samples of metastatic high-grade serous ovarian cancer (HGSOC) that ranged from minimal to extensive disease, we have defined RNA and protein profiles that evolved with these higher order features.

We obtained a unique profile of the evolving metastatic microenvironment of HGSOC that includes data not only on gene expression and proteomics but also cytokine/chemokine expression, ECM organization and biophysical properties. This ‘deconstruction’ of a metastatic microenvironment provides a critical reference for our mouse model systems and a template for reconstruction of 3D multi-cellular human ovarian cancer models.

Although our work was conducted on omental metastases of HGSOC, we found evidence for a conserved mechanism that may be relevant to many human solid tumours: a pattern of matrix-associated gene expression, that we termed the matrix index. In the HGSOC samples, the matrix index significantly associated with various leukocyte signalling pathways of cells associated with poor prognosis including Th2 cells and macrophage-associated genes and correlated with extent of disease and tissue stiffness. Interrogating transcriptional datasets from a wide range of human solid cancers, including HGSOC, we found that the matrix index had prognostic significance irrespective of patient age, stage of disease or first response to therapy. This led us to suggest that there may be a common matrix response to human cancer.

Tumor-associated macrophages (TAMs) depend on ZEB1 for their cancer-promoting roles in human ovarian cancer

Background: Accumulation of tumor-associated macrophages (TAMs) associates to malignant progression in cancer. However, the mechanisms that drive the pro-tumor functions of TAMs in ovarian cancer are not fully understood. ZEB1 is best known for driving an EMT in carcinoma cells to promote tumor progression. Objective: To explore the role of ZEB1 in
TAMs in the microenvironment of ovarian cancer. Methods: Gene expression analyses (RNA-seq, real time PCR, Western blot) and functional assays (chemotaxis, tumor progression by bioluminescence, macrophage depletion and adoptive transfer) in TAMs and cancer cells using a mouse model of ovarian carcinoma. Gene expression analyses (immunohistochemistry) and survival data in human samples of serous ovarian carcinomas. Results: TAMs require ZEB1 for their tumor-promoting and chemotherapy-resistance functions in a mouse model of ovarian cancer. Only TAMs that expressed full levels of ZEB1 achieved tumor growth. Mechanistically, ZEB1 expression in TAMs induced their polarization toward an F4/80low pro-tumor phenotype, including direct activation of Ccr2. In turn, expression of ZEB1 by TAMs induced Ccl2, Ccl7 and a mesenchymal/stem-like phenotype in ovarian cancer cells. In human ovarian carcinomas, TAM infiltration and CCR2 expression correlated with ZEB1 in tumor cells, where along CCL2 and CD74 determined poorer prognosis. Importantly, ZEB1 in TAMs was a factor of poorer survival in human ovarian carcinomas. Conclusion: These data establish ZEB1 as a key factor in the tumor microenvironment of ovarian carcinomas where it maintains the tumor-promoting functions of TAMs.

Maria A. Blasco, Director at Spanish National Cancer Research Centre (CNIO), Madrid, Spain

Maria A. Blasco obtained her PhD in 1993 at the Centro de Biología Molecular “Severo Ochoa” under the supervision of M. Salas. That same year, Blasco joined the Cold Spring Harbor Laboratory in New York (USA) as a Postdoctoral Fellow under the leadership of C. W. Greider. In 1997 she returned to Spain to start her own research Group at the Centro Nacional de Biotecnología in Madrid. She joined the CNIO in 2003 as Director of the Molecular Oncology Programme and Leader of the Telomeres and Telomerase Group. In 2005 she was also appointed Vice-Director of Basic Research. Since June 2011, she is the CNIO Director.

Blasco has received the following awards, among others: Josef Steiner Cancer Research, Rey Jaime I, “Carmen and Severo Ochoa” Award in Molecular Biology, Swiss Bridge Award for Research in Cancer, Körber European Science Award, Fundación Lilly Preclinical Research Award, Prize “Alberto Sols” for Excellence in Research, as well as the Santiago Ramón y Cajal Research Award in Biology in 2010. Blasco has also been awarded the EMBO Gold Medal and has served on its Council since 2008. In 2014 received a Doctorate Honoris Causa from the Universidad Carlos III of Madrid, Spain. In January of 2017 received a Doctorate Honoris Causa from the Universidad de Alicante and on October of the same year she received the XIII Health Science Award of the Fundación Caja Rural de Granada (Spain) as well as the Scientific Merit Award of the Generalitat Valenciana (Spain).

With more than 245 scientific publications, her research has focused on demonstrating the importance of telomeres and telomerase in cancer as well as age-related diseases.

Telomeres as therapeutic targets for cancer

Telomeres are considered anti-cancer targets, as telomere maintenance above a minimum length is necessary for cancer growth. Telomerase abrogation in cancer-prone mouse models, however, only decreased tumor growth after several mouse generations when telomeres reach a critically short length, and this effect was lost upon p53 mutation. Here, address whether induction of telomere uncapping by inhibition of the Trf1 shelterin protein can effectively block cancer growth independently of telomere length. We show that genetic Trf1 ablation impairs the growth of p53-null K-RasG12V-induced lung carcinomas and increases mouse survival independently of telomere length. This is accompanied by induction of telomeric DNA damage, apoptosis, decreased proliferation, and G2-arrest. Downregulation of Trf1 in established p53-deficient K-RasG12V lung cell lines also impairs tumor growth and metastasis in xenograft models. Importantly, long-term whole-body Trf1 deletion in adult mice did not impact on mouse survival and viability. Moreover, inhibition of TRF1 binding to telomeres by small molecules blocks the growth of already established lung carcinomas without affecting mouse survival or tissue function. Thus, induction of acute telomere uncapping emerges as a potential new therapeutic target for lung cancer.
Session 2: Advances in Cancer Susceptibility

**Conxi Lázaro**, Head of the Molecular Diagnostics Unit at *Catalan Institute of Oncology (ICO) – IDIBELL*, Barcelona, Spain

Read bio in page 7

Chair of the SESSION 2

**Miquel Àngel Pujana**, Independent Group Leader and Director of the Program Against Cancer Therapeutic Resistance (ProCURE) at *Catalan Institute of Oncology (ICO) - IDIBELL*, Barcelona, Spain

Read bio in page 8

Chair of the SESSION 2

**Antonis Antoniou**, Professor of Cancer Risk Prediction at *University of Cambridge*, Cambridge, UK

Professor Antoniou studied at the London School of Economics and Political Science and the University of Cambridge before gaining his PhD in Genetic Epidemiology at Cambridge in 2001. In 2009 he was awarded a Cancer Research UK Senior Fellowship to establish an independent research group. In 2013 he was appointed a Reader in Cancer Risk Prediction and was promoted to Professor of Cancer Risk Prediction in 2017. He currently leads a research group within the Department of Public Health and Primary Care and he is the Academic Course Director for the MPhil in Epidemiology.

Professor Antoniou’s main research is the development and application of statistical modelling techniques for addressing clinical questions, and the development of risk prediction tools which are used in clinical practice.

Professor Antoniou heads up a research group of 10 which focuses on two broad areas: (1) The development and evaluation of risk prediction models for familial breast, ovarian, prostate and other common cancers. (2) The characterisation of cancer risks for genetically susceptible individuals, such as those carrying mutations in the the BRCA1, BRCA2, PALB2, RAD51C and RAD51D genes.

Specific ongoing projects include:

- CanRisk Programme, which aims to develop and validate quantitative tools for cancer risk stratification and prevention that take advantage of discoveries in both cancer genomics and epidemiology; the development of the BOADICEA risk prediction algorithm which can be used for predicting the risk of developing breast or ovarian cancer and the likelihood of carrying mutations in high risk genes; investigation of genetic modifiers of breast, ovarian and prostate risk for BRCA1 and BRCA2 mutation carriers using data from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA).

**Breast and ovarian cancer susceptibility: what have we learned from large international consortia?**

Advances in genomic technologies have enabled more rapid, less expensive genetic sequencing than was possible a few years ago. These technologies allow for the comprehensive genetic profiling for assessing risks to breast and ovarian cancers and include multiplex sequencing panels of several genes and panels of common single nucleotide polymorphisms (SNPs). However, the clinical utility of such multiplex gene and SNP panels depends on having accurate estimates of cancer risks for mutations in the genes included in such panels as well as cancer risk prediction models that consider the multifactorial aetiology to cancer susceptibility. Over the past decade international consortia, such as the Breast and Ovarian Cancer Association Consortia, the Consortium of Investigators of Modifiers of BRCA1/2 and the International BRCA1/2 Carrier Cohort Study have enabled us to accurately characterise the cancer risks for rare and common cancer susceptibility genetic variants; to understand how the genetic variants interact with each other; and how genetic variants interact with other lifestyle/hormonal risk factors for the disease. The presentation will review the key recent advances by these international consortia and how these are helping us to realise a more personalised risk-based cancer prevention and cancer control.
**Nicoline Hoogerbrugge**, Full Professor in Hereditary Cancer at Radboud University Medical Center, Nijmegen, The Netherlands

Prof. Hoogerbrugge is chairing the European Reference Network of Genetic Tumour Risk Syndromes (ERN GENTURIS). She has the ambition of improving detection, diagnosis and treatment of hereditary cancer and preventing cancer in relatives. Over the last 5 years her work has mainly focused on the implementation of current knowledge and finding new genetic factors for gastrointestinal cancer. Prof. Hoogerbrugge changed the diagnostic setting of hereditary colorectal cancer, by introducing Mismatch repair deficiency analysis (MSI/IHC) analysis for all newly diagnosed CRC or endometrial cancer patients diagnosed below a certain age limit. Since 2008 this was taken up in the Dutch guideline below age 50 and based on her research the guideline was changed to age 70 in 2016. This has led to an important increase in the recognition of Lynch syndrome (hereditary colorectal cancer). She now works on improving the effectiveness and efficiency of the diagnostic setting for hereditary ovarian cancer.

She was among the very first who made and studied the effects of Apps for successfully improving the recognition of hereditary cancer by doctors and patients themselves in current practice. She showed that patients and relatives themselves can act together with professionals for further improvement of the recognition of hereditary cancer. Together with Dr Marjolijn Ligtenberg and Dr Roland Kuiper she worked successfully on the detection of new genetic factors for CRC. They found a new cause for Lynch syndrome: EPCAM deletions. Other causes they found for hereditary colorectal cancer were: heterozygous mutations in BUB1, BUB3 and FOCAD. In 2015 a new recessive cause for polyposis was found in one of the BER-genes: NTHL1. Prof. Hoogerbrugge now implements dendritic cell vaccinations healthy carriers of a Lynch syndrome mutation. The first immunologic results are promising.

**BRCA testing in ovarian tumors initiated by a pathologist: a pre-screen for germline testing and therapy choice**

**Introduction:** Most guidelines recommend germline BRCA testing in all epithelial ovarian cancer (EOC) patients. Approximately 20% of all EOC patients have tumor DNA BRCA mutations of which 75% germline and 25% somatic. Both may benefit from PARP inhibitor therapy.

We aimed to implement Ovarian tumor DNA BRCA testing by a Pathologist (OPA) in all newly diagnosed EOC patients, as a pre-screen for germline BRCA testing and to enable timely genotype-based therapeutic choices.

**Materials and methods:** Pathologists were invited to submit Formalin Fixed Paraffin Embedded (FFPE) samples of newly diagnosed EOCs for tumor DNA BRCA testing by single molecule Molecular Inversion Probe (smMIP)-based targeted next generation sequencing (NGS) of BRCA1/2 and Multiplex Ligation-dependent Probe Amplification (MLPA) of BRCA1. Outcomes were communicated to patients by their gynecologist, who referred patients with tumor DNA BRCA mutations for genetic counseling and germline analysis of the identified mutation. OPA uptake is evaluated with data from PALGA (Dutch Pathology Registry) and patients and physicians experiences with questionnaires.

**Results:** From October 2015 to January 2017 OPA was initiated in 199 women. In 195 women with a median age of 65 years (range 21-87), OPA was feasible and 32 tumor DNA BRCA mutations were identified (16%). Median turnaround time was 14 days (8-29). Germline testing revealed 11 BRCA mutations in 18 women (61%).

**Conclusion:** OPA provides a feasible pre-screen for genetic testing and PARP inhibitor therapy shortly after EOC diagnosis. If evaluation by patients and physicians is positive, international implementation can be considered.

Short talk from selected abstracts: Judith Balmana, Medical Doctor at Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain

**Pathogenic variants (PVs) detection in a 19-gene core panel and yield of opportunistic screening in BRCA1/2 and MMR genes in a cohort of 1242 hereditary cancer patients**

**Background:** Multigene panels provide a powerful tool for analyzing several genes simultaneously and identifying cancer susceptibility beyond the suspected clinical phenotype. We evaluated the PVs frequency in customized pre-defined panels according to phenotype and extended the analysis to our 19-gene research panel. We also investigated the yield of opportunistic screening in the BRCA1/2 and MMR genes in all patients.

**Patients and methods:** Overall, 1242 unrelated probands underwent multigene testing with customized pre-defined panels according to their phenotype in addition to BRCA1/2 and MMR genes, and a 19-gene research panel from sept 2014-july 2017.

**Results:** Overall, 1033 female and 209 male were studied, mean age at cancer diagnosis was 47 years old (14), 579 had breast cancer (BC), 273 ovarian cancer (OC), 156 colorectal cancer, and the remaining 234 had other tumors. A BC, OC, or BC/OC panel was requested in 68% and a Lynch syndrome (LS) panel in 17%. One hundred and fifty-six (13%) probands carried at least one PV with the customized diagnostic panel. All BRCA1/2 carriers fulfilled BC, OC or BC/OC criteria, while among the MMR carriers, 51 (89%) PV were identified in the LS-panel and 6 (11%) were opportunistic,
all 6 in MSH6. The 19-gene research panel provided 45 additional PV beyond the customized panel according to the clinical phenotype, 22 monoallelic MUTYH, 5 BARD1, 4 NBN, 3 BRIP1, 3 CHEK2, 2 RAD51C, 2 ATM, 1 CDH1, 1 PTEN, 1 PALB2, 1 RAD51D. Twelve of these PV were in actionable genes (BRIP1, RAD51C, ATM, CHEK2, RAD51D, CDH1, PALB2, PTEN).

**Conclusions:** The yield of PV detection in different actionable genes identified by multiplex testing is clinically relevant. Eleven percent of MMR mutation carriers (all carrying MSH6 PVs) were identified through opportunistic screening. Identification of PVs in BARD1 and NBN genes by the research panel deserve further investigation.

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**Elaine Mardis**, Co-Executive Director, Institute for Genomic Medicine at [Nationwide Children's Hospital](#), Columbus, USA

Elaine R. Mardis is Co-Executive Director of the Institute for Genomic Medicine at Nationwide Children's Hospital. She is also Professor of Pediatrics at The Ohio State University College of Medicine. Educated at the University of Oklahoma with a B.S. in Zoology and a Ph.D. in Chemistry and Biochemistry, Dr. Mardis did postgraduate work in industry at BioRad Laboratories. She was a member of the faculty of Washington University School of Medicine from 1993-2016. She has authored over 330 articles in peer-reviewed journals, and serves as an associate editor for three peer-reviewed journals and is Editor-in-Chief of Molecular Case Studies, published by Cold Spring Harbor Press. Dr. Mardis was named the Morton K. Schwartz award recipient in 2016 from the American Association for Clinical Chemistry. She has been listed since 2013 as one of the most highly cited researchers in the world by Thompson Reuters. Dr. Mardis is a member of the American Association for Cancer Research (AACR) since 2007, serves on its Board of Directors, and is the program committee chair for the 2018 AACR Annual Meeting.

**Clinical Assay of Endometrial Cancers**

Large-scale studies of cancer genomics have enhanced our understanding of both somatic and germline contributions to cancer onset and susceptibility. In endometrial cancers, as in other cancer types, this information can provide important information to clinicians regarding treatment options and outcomes. To this end, we have developed a gene panel test that enables the assay of germline and somatic alterations from testing only tumor-derived DNA. By applying previously characterized endometrial cancer samples with clinical outcomes, we are developing a data set for clinical validation of this gene panel. Ultimately, we will offer the test state-wide to Ohio women with an endometrial cancer diagnosis, enabling the broad-scale application of this testing to community hospitals where most patients seek cancer care.

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Short talk from selected abstracts: [Pål Møller](#), Senior Scientist at [Norwegian Radium Hospital](#), Oslo University Hospital, Oslo, Norway

**Endometrial and ovarian cancer in carriers of inherited pathogenic MMR variants (Lynch Syndrome)**

**Background:** Carriers of path_MMR gene variants (Lynch Syndrome, LS) constitute besides the path_BRCA1/2 the most frequent inherited cancer syndrome.

**Objective and design:** This observational, international, multicenter study aimed to determine prospectively observed incidences of cancers and survival in path_MMR carriers up to 75 years of age.

**Results:** 3,119 patients were followed for a total of 24,475 years. Except for breast, prostate and gynaecological cancers, cancer incidences were similar for men and women. Cumulative incidences at 75 years (risks) for colorectal cancer were 46%, 43% and 15% in path_MLH1, path_MSH2 and path_MSH6 carriers; for endometrial cancer 43%, 57% and 46%; for ovarian cancer 10%, 17% and 13%; for upper gastrointestinal (gastric, duodenal, bile duct or pancreatic) cancers 21%, 10% and 7%; for urinary tract cancers 8%, 25% and 11%; and for brain tumors 1%, 5% and 1%, respectively. Ovarian cancer occurred mainly pre-menopaually. By contrast, upper gastrointestinal and urinary tract cancers occurred predominantly at older ages. Overall five-year survival for urinary bladder 93%, ureter 85%, duodenum 67%, stomach 61%, bile duct 29%, brain 22% and pancreas 0%. Path_PMS2 carriers had lower risk for cancer.

**Conclusion:** Female LS patients have a very high risk for endometrial cancers which by and large are cured with follow-up and early treatment. Also, they have a risk of premenopausal ovarian cancer similar to path_BRCA1/2 carriers which is usually cured. Risk estimates for counselling and planning of surveillance and treatment should be tailored to each patient's age, gender and path_MMR variant. We have updated our open-access website www.lsccrisk.org to facilitate this.
Progress in Therapeutic Prevention of Breast Cancer

Breast cancer is by far the commonest cancer in women, with an estimated 1.6 million new cases every year, and it is an ideal candidate in which to develop drug therapy for cancer prevention.

Two drugs, tamoxifen and raloxifene, are licensed for preventive therapy in the United States. More recently two other selective oestrogen receptor modifiers (SERMs), lasofoxifene and arzoxifen have been investigated in large prevention trials in osteoporotic women. In an individual patient overview of all these drugs, a 55% reduction in ER positive cancer in the five years of active treatment and a further 42% reduction in the next 5 years was seen. A long term follow up of the IBIS 1 study found an approximately constant 30% reduction of new cancers for 20 years after 5 years of tamoxifen. However no reduction in ER negative tumours has occurred.

Newer approaches are looking at the role of aromatase inhibitors. These are only appropriate for post-menopausal women whereas tamoxifen can also be used premenopausally. The MAP.3 trial evaluated exemestane and a 65% reduction in invasive tumours after a relatively short 30 months median follow up was seen. More recently the IBIS 2 trial using anastrozole has completed analysis of 3846 women with a median follow up of 5 years and reported a 53% reduction in all breast cancer, with a larger reduction in ER positive invasive breast cancer. Fracture rates were not significantly increased, and musculoskeletal and vasomotor symptoms were increased, but only by about 10%, with very high rates in the placebo arm. This has led to a recommendation from NICE in the UK that anastrozole should be offered to high risk post-menopausal women.

As both of these classes of drugs (SERMs and AIs) have common side effects and some rare more serious ones, it is important to focus their use among women most likely to benefit. Models have been developed to aid this decision and the Tyrer–Cuzick model appears to be one of the best at the moment. However newer results have shown that mammographic breast density is an important predictor and a risk score combining the 88 of the currently identified risk single nucleotide polymorphisms (SNPs) add to predictive accuracy. Initial data indicates both density and SNPs are sufficiently independent of other factors to make substantial improvements to risk prediction.

There is much interest in nonhormonal agents for breast cancer prevention including metformin, bisphosphonates, aspirin, and the NSAIDs, but there are no prevention trials currently and evidence is based on cohort and case control studies.
Francesc Xavier Bosch, Senior Researcher at Bellvitge Biomedical Research Institute (IDIBELL), Hospitalet de Llobregat, Spain

F. Xavier Bosch is Director Epidemiology, Public Health, Cancer Prevention and Palliative Care Program at IDIBELL and Honorary Consultant to the Cancer Epidemiology Research Program & Director of the e-oncologia at Catalan Institute of Oncology. Dr Bosch is the editor in chief of the journal Papillomavirus Research (PVR) and the editor of the international newsletter HPV Today (www.hpvtoday.com), served as guest editor for the HPV MONOGRAPH series (Vaccine, Elsevier) and is the organizer and current Director of and e-learning effort in oncology and notably on e-courses on cervical cancer prevention (www.eoncologia.net). He served as epidemiologist at the International Agency for Research on Cancer (Lyon, France 1982-1993) and as visiting scientist at the National Cancer Institute (Washington, USA 2002).

Dr Bosch has conducted epidemiological research on cancers linked to infectious agents notably on cancer of the liver, the cervix, the genital tract and of the oral cavity and oropharynx. Dr Bosch was at the origin of the IARC program of epidemiological studies that demonstrated causality in the HPV and invasive cervical cancer relationship, established the role of the environmental co-factors for carcinogenesis among HPV positive women, and described the international variation of HPV types in cervical cancer. Some of these studies have played a catalytic role for the initiation of the first vaccine trials for HBV and HPV and for the evaluation of HPV tests as screening tools. Current interest reside in dissemination of scientific information of clinical relevance and in studies that integrate HPV vaccination and screening in environments with limited resources.

Dr Bosch’s publications in relation to HPV and cervical cancer amount to over 500 original publications, over 25 monograph books and major reviews and over 900 scientific communications at medical meetings.

HPV faster: searching for the optimal combination of HPV screening and HPV vaccination of women in screening ages

Human papillomavirus (HPV)-related screening technologies and HPV vaccination offer great potential for cancer prevention, notably prevention of cervical cancer. However, the effectiveness of these approaches is suboptimal owing to limited implementation of screening programs and restricted indications for HPV vaccination. Trials of HPV screening have shown significantly better sensitivity and high specificity as compared to the standard cytology-based programs. Trials of HPV vaccination in women aged up to age 55 years have shown almost 90% protection from cervical pre-cancer caused by HPV16/18 among HPV16/18-DNA-negative women and no safety concerns. We propose extending routine vaccination programs to women of up to 30 years of age (and to age groups 45-50 in some settings), paired with at least one HPV-screening test at around age 30 years or older. Expanding the indications for HPV vaccination and much greater use of HPV testing in screening programs has the potential to accelerate the decline in cervical cancer incidence. Such a combined protocol should represent an attractive approach for many health-care systems, in particular for countries in central and Eastern Europe, Latin America, Asia, and some more-developed parts in Africa. Given the scarcity of diagnostic resources in many of these population, the specificity of the screening test and adequate combinations of screen and treat algorithms are of importance. The role of vaccination in women aged >30 years, and the lifetime number of HPV-screening tests required in vaccinated women, remain important research issues. Cost-effectiveness models will help determine the optimal combination of HPV vaccination and screening in public health programs and to estimate the effects of such approaches in different populations.

Short talk from selected abstracts: Laura Costas, Researcher at Catalan Institute of Oncology (ICO) – IDIBELL, Barcelona, Spain

The diagnostic value of cervico-vaginal cytology in endometrial carcinoma: a systematic review and meta-analyses

Objectives: To determine the sensitivity of cervico-vaginal cytology (Pap test) in detecting endometrial carcinoma and its relationship with clinicopathological factors.

Methods: We performed a systematic review of the literature with the following terms: PapaincovalgynMeans, liquid-based, “cervical, cytology”, endometrial carcinoma, Endometrial cancer. Reference lists from all included studies were also reviewed. We performed meta-analyses of proportions using random effects models with -metaprop. We included 35 articles in this review from North America (n=22), Europe (n=5) and Asia/Oceania(n=8).

Results: Abnormal Pap preceding the diagnosis or treatment of endometrial carcinoma were observed in 49% (95%CI=42%-55%) of study subjects. The percentage was significantly higher among those of non-endometrioid histologic subtypes compared with the endometrioid subtype (80%, 95%CI=69-90% vs 47%, 95%CI=39%-54%, respectively, p-heterogeneity<.01). There were no statistically significant differences between conventional or liquid-based methods (49%, 95%CI=40-57% vs 50%, 95%CI=26%-74%, respectively, p-heterogeneity=0.93). Several clinicopathologic factors were related to a higher percentage of abnormal Pap, including cervical invasion (64%, 95%CI=55%-72% vs 34%, 95%CI=28%-41%), lymph nodes (74%, 95%CI=57-89% vs 45%, 95%CI=30%-60%), myometrial invasion >50% (57%, 95%CI=48%-66% vs 43%, CI=33%-53%) and lymphovascular invasion (56%,
CI=49%-64% vs 40%, 95%CI=31%-50%; p<0.05 for all variables). Twelve studies specified that the Pap test was performed before diagnosis, while 14 studies that it was preoperative (48%, 95%CI=38%-58% vs 49%, 95%CI=39%-59%; respectively, p=eterogeneity = 0.85).

**Conclusions:** Cervico-vaginal cytology is primarily a screening test for cervical cancer. However, it may also play a role in the detection of endometrial carcinoma, especially for those of non-endometroid histology and higher stages. Available data was insufficient to evaluate if abnormal Pap usually precedes clinical symptoms of endometrial carcinoma. This information is relevant in order to estimate the value of routine Pap test in detecting endometrial cancers in a cervical cancer screening setting among the general population.

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**Martin Widschwendter**, Head of Department of Women's Cancer at University College London and Consultant Gynaecological Oncology Surgeon at University College London Hospital, London, UK

Prof Martin Widschwendter MD, FRCOG is Professor in Women's Cancer, Dept. of Women's Cancer Head, University College London (UCL) and Consultant Gynaecological Oncology Surgeon, University College London Hospital (UCLH). In 2001, having completed his training in Gynaecology & Obstetrics in Austria, Martin worked at the Norris Comprehensive Cancer Centre, LA, USA and spent 3 years as lead clinician/surgeon of a large breast cancer centre before embarking on a career at UCL/UCLH from 2005 where he undertook sub-speciality training in gynaec onc. As the Head of Department of Women's Cancer, EGA Institute for Women's Health, UCL, he established his research group focusing on the role of early detection, risk prediction and prevention of breast and gynaecological cancers. Martin is an author on > 155 papers in high impact journals, has contributed to numerous text books and secured more than £17M of grant income in the last 10 years. His work has been quoted > 11,000 times and his current H-Index is 51. He has lectured widely on his research and clinical experience in the UK and abroad. Martin leads on 3 major research programmes: H2020 FORECEE (Female cancer predictOn using ceRvical cell omics to individualise prevention) aims to develop individual risk predictors for cancers that are hormone-associated and specific to women (breast, ovarian, endometrial and cervical cancers); BRCA PROTECT (BRCA1/2: PReventOn of breast and sErous pelvIC cancers via systems medicine) aims to understand the molecular events that lead to the development of breast and ovarian cancer, so that effective prevention and ultimately prevention of the occurrence of these cancers can take place; and the European Research Council (ERC) Advanced Grant BRCA-ERC (Understanding cancer development in BRCA 1/2 mutation carriers for improved Early detection and Risk Control)--supporting BRCA PROTECT & BRCA PREVENT. Martin's particular clinical interest is in complex radical laparoscopic and open surgery.

**Novel strategies for early detection and prevention of breast and ovarian cancer in BRCA carriers**

Current approaches to cancer prevention in BRCA1/2 mutation carriers are based on the notion that these mutations elevate cancer risk in the epithelial lining of mammary ducts and of proximal segments of the female reproductive tract primarily because of the consequences on DNA repair specifically within these tissues (cell-autonomous effects). Risk reduction is primarily focused on surgical removal of these at-risk organs. A significant number of affected women delay or refuse these potentially life-saving procedures due to social or fertility concerns. Germline BRCA1/2 mutations also have important systemic consequences that indirectly influence those tissues cell-non-autonomously, significantly contributing to their elevated cancer risk. A better understanding of these cell-nonautonomous mechanisms could lead to non-surgical approaches for risk reduction in BRCA1/2 mutation carriers and also provide novel tools for their management, including the development of intermediate surrogate biomarkers of responsiveness in cancer prevention trials or of biomarkers to evaluate pathogenicity of BRCA1/2 mutations of unknown significance. These cell-nonautonomous mechanisms are mediated, at least in part, by the menstrual cycle, an important risk factor for these cancers in the general population. This knowledge might therefore also be applicable for evaluating cancer risk in individuals not carrying germline BRCA1/2 mutations.

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**Short talk from selected abstracts:** **Jordi Barretina**, Director at Biomedical Research Institute of Girona (IDIBGI), Girona, Spain

**Characterization of Nigerian Breast Cancer Reveals High Rates of Homologous Recombination Deficiency**

Using a combination of genome, exome, and RNA sequencing, we examined the molecular features of breast cancers across 194 patients from Nigeria compared to 1,037 patients from The Cancer Genome Atlas (171 Black, 753 White, 113 other). Triple Negative and HER2+ subtypes were enriched in Africans whose tumors were characterized by a greater prevalence of the homologous recombination deficiency (HRD) signature, higher TP53 mutation rate and increased structural variation. In contrast to Whites, hormone receptor positive tumors in Nigeria were also enriched for HRD, TP53, and GATA3 mutations, indicating more aggressive biology. Higher proportions of APOBEC-mediated substitutions strongly associated with PIK3CA and CDH1 mutations, which were underrepresented in Africans and Blacks. We also identified PLK2, KDM6A, GPS2, and B2M as novel significantly mutated genes in breast cancer. This unique dataset provides novel insights into potential mechanisms of de novo drug resistance and outcomes disparities in populations of African ancestry.
Session 4: Advances in Cancer Cure

Aleix Prat, Head of Medical Oncology Department at Hospital Clínic of Barcelona, Barcelona, Spain
Read bio in page 8
Chair of the SESSION 4

Carey Anders, Associate Professor of Medicine at The University of North Carolina, Chapel Hill, USA
Carey K. Anders, MD is an Associate Professor of Medicine at the University of North Carolina (UNC) School of Medicine and an active member of the UNC Lineberger Comprehensive Cancer Center (LCCC) and co-leader of the LCCC Breast Program. As a clinician-scientist, she is Section Leader for the UNC Breast Program, Leader of the UNC breast cancer clinical trials program, and co-Director of the multi-disciplinary brain metastases clinic at UNC. Dr. Anders' translational research program, which spans bench to bedside, focuses on the biology of triple negative breast cancer and brain metastases. She serves as the principal investigator for multiple clinical trials evaluating novel anti-cancer agents to more effectively treat patients with advanced triple negative breast cancer and brain metastases. In parallel, and supported by the UNC Chapel Hill Hematology Oncology K12, NIH/NCI K23, LCCC SPORE and Damon Runyon Clinical Investigator Award, she has developed multiple intracranial breast cancer tumor models to test novel therapies, including small molecule and nanoparticle chemotherapeutics in the laboratory. She is also devoted to uncovering the genetic and genomic underpinnings of triple negative breast cancer and brain metastases using Next Generation Sequencing, the focus of her American Society of Clinical Oncology Advanced Clinical Research Award. Her ultimate goal is to translate preclinical findings into rationally-designed therapeutic strategies to improve survival and enhance quality of life for the many patients facing a diagnosis of triple negative breast cancer brain metastases.

Treating Triple-Negative Breast Cancer: From Biology to the Clinic

Triple negative breast cancer (TNBC) is clinically-defined as breast cancer lacking expression of the estrogen and progesterone receptors and HER2. This subtype of breast cancer is associated with early, visceral recurrences and inferior survival when compared to non-TNBC subtypes. On a molecular level, TNBC is a heterogeneous disease that is comprised of multiple different subtypes, largely basal-like or claudin-low by the PAM50. Additional classification systems have identified subtypes driven by immune features, mesenchymal stem cells, and the androgen receptor, each with therapeutic implications. While the mainstay of therapy in the treatment of early stage TNBC remains chemotherapy, molecular analysis of TNBC has revealed several tractable targets in development in the metastatic setting. These include activation of the PI3K pathway through loss of negative regulators such as PTEN and INPP4B; the addition of an inhibitor of AKT to paclitaxel in the treatment of advanced TNBC revealed improvements in progression free survival. Associations of TNBC with germline mutations in the BRCA1 gene, and so BRCA2, have yielded therapeutic strategies targeting DNA repair pathways beyond homologous recombination, such as PARP which controls base excision repair. Inhibition of PARP, when compared to standard of care chemotherapy agents, resulted in an improvement in progression free survival for patients with germline BRCA-associated breast cancer. Augmenting the innate immune response against TNBC is gaining traction as a therapeutic strategy. Inhibitors of PD-1 and PDL-1 are yielding response rates of approximately 20% across unselected TNBC; development of biomarkers to enhance response are actively being explored. Targeting the androgen receptor in TNBC with agents such as bicalutamide and enzalutamide illustrate clinical-benefit in this subset of TNBC. Finally, the development of antibody-drug-conjugates (ADC's) to more effectively target and deliver cytotoxic agents directly to TNBC cells while sparing the host side effects are in active development. Specific ADC's include glembatumumab vedotin, sacituzumab govetecan among others. A combined approach of unraveling the biology of TNBC in the laboratory combined with strategic translation to clinical trials will continue to improve the outcome of the thousands of patients facing TNBC worldwide.
Daniela Quail, Assistant Professor at Goodman Cancer Research Centre, McGill University, Montreal, Canada

Daniela F. Quail is a newly appointed Assistant Professor at the Goodman Cancer Research Centre and the Department of Physiology (Faculty of Medicine, McGill University). She completed a BSc (2003-2007) and PhD (2008-2012) from the University of Western Ontario in London, Ontario (Canada), and completed her postdoctoral training (2012-2017) at Memorial Sloan Kettering Cancer Center in New York, New York (USA). Dr. Quail’s current research program is focused on how the microenvironment modulates cancer progression and prognosis. She has contributed to a body of research characterizing the effects of the microenvironment during brain and breast tumor progression. Her current research interests are focused on the role of obesity-associated inflammation during breast cancer metastasis.

Impact of obesity-associated inflammation on breast cancer progression

Metastasis is the leading cause of breast cancer-related mortality. Metastatic efficiency is determined in part by systemic factors, including inflammation, which can modify the composition of secondary microenvironments to be more/less accommodating to metastatic disease. Obesity is characterized by chronic, systemic inflammation, and is associated with elevated risk of multiple types of cancer. As a growing global epidemic, obesity now rivals smoking as the leading preventable risk factor for cancer incidence and mortality. Clinical studies have demonstrated that obesity is associated with an elevated incidence of breast cancer metastasis, particularly to lung and liver. We are particularly interested in lung metastasis, given the high frequency of metastasis to this organ in breast cancer patients, and the clinical association between obesity and inflammatory conditions of the lung (e.g. asthma). We recently demonstrated a causal link between obesity and breast cancer metastasis to lung that is reversible with weight loss. Specifically, we found that obesity-associated inflammation alters the myeloid cell landscape within the lung, leading to enhanced breast cancer metastasis to this site. This phenotype is driven by elevated levels of interleukin-5 (IL5) in blood, which causes expansion of circulating IL5-receptor alpha (IL5Rα)+ monocytes, upregulation of granulocyte-macrophage colony stimulating factor (GM-CSF) production, and a significant expansion of peripheral neutrophils that preferentially traffic to the lung. Importantly, we have found that reducing neutrophils either through targeted strategies (e.g. GM-CSF or Gr1 neutralizing antibodies) or weight loss interventions is sufficient to reverse obesity-associated lung inflammation and breast cancer metastasis. Our data suggest that monitoring GM-CSF, IL5, or absolute neutrophil counts in blood could have useful prognostic value to stratify obese patients, and identify those at highest risk of cancer progression who may benefit from obesity-specific adjuvant therapies or dietary interventions.

Short talk from selected abstracts: Daniel Massó, Postdoc at Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain

Targeting Myc in metastatic breast cancer by Omomyc: from proof-of-principle to pharmacological approach

Objectives: Breast cancer is a leading cause of cancer mortality in women due to the high frequency of metastatic disease. Using a Myc dominant negative termed Omomyc, we have demonstrated that Myc inhibition is a safe and effective therapeutic approach against several types of cancer, but Omomyc has only been tested in primary tumors. Since many steps of the metastatic cascade have been reported to depend on Myc, we hypothesized that Omomyc could be effective in both the prevention and treatment of metastasis too.

Methods: We induced transgenic expression of Omomyc in a panel of breast cancer cell lines and analyzed its effect on clonogenic capacity, proliferation, angiogenesis, migration and invasion. We also performed prevention and intervention studies in several human-derived and immunocompetent mouse models of metastatic breast cancer. In parallel, we are also validating the therapeutic utility of Omomyc-derived peptides as a pharmacological approach by testing them in vitro and in vivo.

Results: Omomyc expression has a dramatic effect on colony formation, proliferation, migration, invasion and the capacity to induce angiogenesis of breast cancer cells. In vivo, Omomyc reduces the growth of orthotopic tumors, induces regression of metastases after primary tumor resection and impairs the development of lung metastases after tail vein injection. In the MMTV-PyMT transgenic model, Omomyc expression dramatically delays tumor formation, thereby preventing the appearance of lung metastases. When administered exogenously, the Omomyc peptide causes remarkable growth inhibition that recapitulates its transgenic expression. When conjugated with a metastasis-targeting sequence, its cell penetrating capacity is increased. In vivo, treatment with the fusion peptide reduces growth of mammary primary tumors and lung metastases.

Conclusions: We have demonstrated for the first time the applicability of Omomyc against metastasis and have validated a metastasis-targeting fusion peptide as the first directly-deliverable Omomyc-based drug for the treatment of metastatic breast cancer.
Open session: Why don’t we get more cancer?

Mina Bissell, Distinguished Scientist at Lawrence Berkeley National Laboratory, Berkeley, USA

MINA J. BISSELL is Distinguished Scientist, the highest rank bestowed at Lawrence Berkeley National Laboratory (LBNL) and serves as Senior Advisor to the Laboratory Director on Biology. She is also Faculty of four Graduate Groups in UC Berkeley: Comparative Biochemistry, Endocrinology, Molecular Toxicology, and Bioengineering (UCSF/UCB joint program). Having challenged several established paradigms, Bissell is a pioneer in breast cancer research and her body of work has provided much impetus for the current recognition of the significant role that extracellular matrix (ECM) signaling and microenvironment play in gene expression regulation in both normal and malignant cells. Her laboratory developed novel 3D assays and techniques that demonstrate her signature phrase: after conception, “phenotype is dominant over genotype.”

Bissell earned her doctorate in microbiology and molecular genetics from Harvard Medical School, won an American Cancer Society fellowship for her postdoctoral studies, and soon after joined LBNL. She was the founding Director of the Cell and Molecular Biology Division and later the Associate Laboratory Director for all Life Sciences at Berkeley Lab where she recruited outstanding scientists and developed a strong program in cell and molecular biology and breast cancer.

Bissell has published more than 400 publications, received numerous honors and awards and is one of the most sought-after speakers in the field. She is not only an elected Fellow of most U.S. honorary scientific academies, but she also sits on many national and international scientific boards and continues to inspire, mentor and engage in full-time research, among other scientific activities.

Why Don’t We Get More Cancer?
The significant role of ECM in normal breast function and breast cancer

Our research in the last three decades has been focused on the crucial role of extracellular matrix (ECM), in particular laminin 111, as a fundamental regulator of normal breast function, milk production, polarity and quiescence. As well as breast cancer. This molecule plays an extremely important role in organ- and tissue-specificity and form and function. The ECM of each tissue dictates how normal remains normal and how aberration in its components or signaling or the loss of laminins will eventually lead to genomic instability and cancer.

I will discuss, the above as well as the important role of laminins and its receptors in drug resistance and therapy. Our current data connect laminin111 (formerly laminin1) and laminin 5 to regulation of p53 and many other transcription factors and negative and positive regulators of the differentiated state of breast in physiologically relevant 3D models (E. Life, in revision).

In addition, we have shown that the aberrant growth associated with cancer is due to lack of response to laminin111 signaling, where the level of nuclear actin (N-actin) increases and architecture is lost. Reversion to a normal phenotype corrects regulation of growth even in malignant cells (Cell Report, 2017). Finally, current findings indicate a direct mechanical connection between the ECM and the nucleus and this is consistent with our surprising discovery that nuclei contain a tunnel where cytoskeleton bundles traverse from cytoplasm to the other side of nucleus and where it appears that chromatin and lamins are in contact with each other in 3D. (JCS 2017, Cover Story)
Open debate: Medicina Participativa i Personalitzada

Lara Bonilla, Journalist (Health and Social topics) at Diari ARA, Barcelona, Spain

Journalist at ARA Newspaper specialized in Health and Social Topics. I've worked in ARA Newspaper for seven years since it was launched in 2010. Before that, I worked in New York as a correspondent for AVUI Newspaper and Com Ràdio covering politics, economics, social and cultural topics in US. I have wrote with Joan Serra the book "Viure. Jo també tinc càncer" (Editorial UOC) about cancer survivors.

Chair of the Open Debate

Victoria Camps, Professor at Autonomous University of Barcelona, Sant Cugat del Vallès, Spain

Professor of Moral Philosophy at the Autonomous University of Barcelona, she is also President of the Víctor Grifols i Lucas Foundation and Chairperson of the Bioethics Committee of Spain. Her professional career has included a period as a member of the Audiovisual Council of Catalonia from 2002 to 2008, and she was chairperson of the Commission for Television Content from 1993 to 1996, a period during which she was an independent senator for the socialist party of Catalonia and Spain, the PSC-PSOE.

Victoria Camps has published several books on bioethics and philosophy, including: Una vida de calidad, La voluntad de vivir, Paradojas del individualismo or Virtudes públicas, for which she was awarded the Espasa Non-fiction Prize in 1990. Her most recent publications are: Creer en la educación, El decline de la ciudadanía, El gobierno de las emociones. Victoria Camps' professional achievements have been recognised by the Josep Mª Lladó Prize for Freedom of Expression, in 1999; the Prize for Achievement in Education, awarded by the Regional Government of Andalucia in 1999; and the Menéndez Pelayo International Prize, received in 2008.

Pere Estupinyà, Writer, Science Communicator and TV Host, Madrid, Spain

Pere Estupinyà is a biochemist, writer and science communicator. He is the author of the books “El ladrón de cerebros” (Debate, 2010), “S = EX2: La ciencia del sexo” (Debate, 2013) and “Comer cerezas con los ojos cerrados” (Debate, 2016). He currently co-presents the science section of the program “A Vivir” on Cadena Ser, writes in several media, and directs and presents the program “El Cazador de cerebros” on TVE. Before returning to Spain he lived eight years in the USA (2007-2015), where he was Knight Science Journalism Fellow at the Massachusetts Institute of Technology (MIT). He also worked at the Media Branch of the National Institutes of Health (NIH), was a consultant for the Inter-American Development Bank (IDB), wrote the acclaimed blog “Apuntes Científicos desde el MIT” in El País, and began to travel throughout Latin America, giving lectures and consultancies to companies and organizations. He is considered one of the most original writers and thinkers in the field of the current scientific and technological revolution.

Laura Sancho, Actress, Barcelona, Spain

**Clara Rosàs**, Manager at **Catalan Federation of Entities Against Cancer (FECEC)**, Barcelona, Spain

Bachelor in Business Sciences and Master in Businesses Direction and Management by ESADE. Her first years of profession were developed in different big companies in the area of marketing. In 2005 she joined the Third Social Sector, as Manager of the Catalan Federation of Entities Against Cancer (FECEC). In this position she has contributed to the growth and consolidation of this second level entity, whose mission is to be the platform for the unionization of the organizations that work to improve the quality of life of patients with cancer in Catalonia.

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**Rosa Gasa**, Associate investigator at **August Pi i Sunyer Biomedical Research Institute (IDIBAPS)**, Barcelona, Spain

Rosa Gasa is a Doctor of Biology from the University of Barcelona. In 2004, after completing two postdoctoral positions at the Universities of Texas (Dallas, US) and California (San Francisco, US), she joined the Laboratory of Diabetes and Obesity of the August Pi i Sunyer Biomedical Research Institute (IDIBAPS) in Barcelona as a researcher. Her current research aims at deepening the knowledge of the molecular mechanisms that regulate the formation and number of insulin-producing cells of the pancreas, with the objective of being able to design regenerative medicine strategies for the treatment of diabetes. Oncological patient, breast cancer 2016.

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**Joan Brunet**, Oncologist and genetic counselor at **Catalan Institute of Oncology (ICO)**, Barcelona, Spain

Joan Brunet is a medical oncologist with a conviction that genetics is the best way to prevent cancer. He got the Accreditation of Excellence in Hereditary Cancer of the Spanish Society of Medical Oncology. He has published more than 100 papers related to cancer genetics. He is currently the Head of the Medical Oncology Department at the Catalan Institute of Oncology (ICO) in Girona and the Corporate Director of Cancer Clinical Genetics. He shares his interest in cancer genetics with teaching as Assistant Professor of Bioethics and Critical Appraisal at the School of Medicine at the University of Girona. He pioneered the settlement of cancer genetic counselling units in Spain and founded the Hereditary Cancer Working Group of the Spanish Society of Medical Oncology. His research is focused on the clinical translation of multi-gene panel testing for hereditary cancer. He is also involved in many projects related to Hereditary Breast and Ovarian Cancer and Lynch syndrome, such as the role of microbiota and the development of a genetic screening test for gynaecological cancer. He is also promoting clinical trials on hereditary cancer prevention. He participates of international consortia and research groups and he is a member of the European Reference Networks (ERN) Genturis (Genetic Tumour Risk). He is very proud of being part of such an enthusiastic, multidisciplinary and highly competitive group that is the ICO Hereditary Cancer Program.

2. Álvaro Lahiguera, Diana Garzón, Agnès Figueras, Iain McNeish, José Carlos Perales and Francesc Viñals. Effect of TP53 and BRCA2 double deletion on oxidative metabolism of ovarian cancer cells.


5. Aleix Noguera-Castells, Leire Recalde-Percaz, Núria Moragas, Patricia Fernández-Noguera, Gemma Fuster, Paloma Bragado, Pere Gascon and Mario Mancino. STX1A signaling pathway characterization in different breast cancer subtypes.


10. Arantza Zubeldia-Plazaola, Leire Recalde-Percaz, Núria Moragas, Mario Mancino, Miquel Prats de Puig, Flavia Guzman, Paloma Bragado, Pedro Gascon and Gemma Fuster. Glucocorticoids mediate DCIS transition to IDC through myoepithelial cell apoptosis.


13. José F. Boán. Dedicated breast PET allows better identification of breathhigh gradelesions compared to whole body PET-CT.


17. Leire Recalde-Percaz, Aleix Noguera-Castells, Núria Moragas, Mario Mancino, Patricia Fernández-Nogueira, Gemma Fuster, Pere Gascon and Paloma Bragado. NRP2-SEMA3s-PLXNs axis regulates the dormancy state of disseminated tumour cells and metastasis progression in breast and head and neck cancer.


20. Marta Palafox, Maria-Teresa Herrera, Meritxell Bellet, Mafalda Oliveira, Aleixandra Bruna, Olga Rodríguez, Marta Guzmán, Judit Gruesa, Cristina Viana, Joaquín Arribas, Emmanuelle di Tomaso, Faye Su, Carlos Caldas, Nicholas C. Turner, Rodrigo Dienstmann, José Baselga, Maurizio Scaltriti, Javier Cortés, Cristina Saura and Violeta Serra. *Biomarkers of response to CDK4/6 inhibitor (CDK4/6i) in Hormone Receptor (HR) positive and HER2-positive Breast Cancer (BC) Patient-Derived Xenografts (PDX).*


PRACTICAL INFORMATION

Venue: CosmoCaixa Barcelona

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

Conferences Meeting
Auditorium (-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 occurred in the context of B·Debate.

Contact persons during the event

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SUGGESTED READING

- A comprehensive custom panel design for routine hereditary cancer testing: preserving control, improving diagnostics and revealing a complex variation landscape.
  PubMed PMID: 28051113; PubMed Central PMCID: PMC5209725.

- Benchmarking of Whole Exome Sequencing and Ad Hoc Designed Panels for Genetic Testing of Hereditary Cancer.
  PubMed PMID: 28050010; PubMed Central PMCID: PMC5209723.

- Associations Between Cancer Predisposition Testing Panel Genes and Breast Cancer.
  PubMed PMID: 28418444; PubMed Central PMCID: PMC5599323.

- Clinical Decision-Making in Patients with Variant of Uncertain Significance in BRCA1 or BRCA2 Genes.
  Welsh JL, Hoskin TL, Day CN, Thomas AS, Coghswell JA, Couch FJ, Boughey JC.
  PubMed PMID: 28766224.

- Prediction of Breast and Prostate Cancer Risks in Male BRCA1 and BRCA2 Mutation Carriers Using Polygenic Risk Scores.
  LeCarpentier J, et al.
  PubMed PMID: 28448241; PubMed Central PMCID: PMC5501359.

- Olaparib for Metastatic Germline BRCA-Mutated Breast Cancer.
  Narod S, Booth CM, Foulkes WD.
  PubMed PMID: 29094857.

- Evaluation of Polygenic Risk Scores for Breast and Ovarian Cancer Risk Prediction in BRCA1 and BRCA2 Mutation Carriers.
  PubMed PMID: 28376175; PubMed Central PMCID: PMC5408990.

- The contribution of pathogenic variants in breast cancer susceptibility genes to familial breast cancer risk.
  PubMed PMID: 28649662; PubMed Central PMCID: PMC5466608.
• Functionally Null RAD51D Missense Mutation Associates Strongly with Ovarian Carcinoma.
  PubMed PMID: 28646019.

• Risk of breast cancer after a diagnosis of ovarian cancer in BRCA mutation carriers: Is preventive mastectomy warranted?
  PubMed PMID: 28314588.

• Implementing rapid, robust, cost-effective, patient-centred, routine genetic testing in ovarian cancer patients.
  PubMed PMID: 27406733; PubMed Central PMCID: PMC4942815.

• BRCA1/2 testing in newly diagnosed breast and ovarian cancer patients without prior genetic counselling: the DNA-BONus study.
  PubMed PMID: 26350514; PubMed Central PMCID: PMC4867439.

• Developing and evaluating polygenic risk prediction models for stratified disease prevention.
  Chatterjee, N., Shi, J. and García-Closas, M.
  PMID: 27140283


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: “Women’s Cancer”

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ORGANIZERS

B-Debate International Center for Scientific Debate Barcelona is a joint initiative of Biocat and “la Caixa” Foundation. It drives first-rate international scientific debates, to foster dialogue, collaboration and open exchange of knowledge with prestigious national and international experts, to approach complex challenges of high social interest in life sciences. B-Debate sees debate as a powerful, effective way to generate knowledge and strives to help position Barcelona as a benchmark in generating knowledge and Catalonia as a country of scientific excellence.

The debates are top-notch international scientific meetings featuring a selection of experts of renowned international prestige and scientists who 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 Catalan Institute of Oncology (ICO) is a public health center working exclusively in the field of cancer. Its approach to the disease is comprehensive, combining care, prevention, research and specialized training in one organization. Through an extensive network of hospitals, the ICO constitutes the referral center for more than 50% of the adult population of Catalonia. Thus, ICO’s Mission is “to work to reduce the impact of cancer in Catalonia” and, based on benchmark scientific ranks, the ICO is at the forefront of biomedical research in Spain and placed 28th worldwide. The present year is the 20th anniversary of the ICO and it has launched a new “research program against cancer therapeutic resistance” (ProCURE). The Mission of ProCURE is to make a significant contribution to “reducing the impact of cancer” through a global, multidisciplinary approach to the questions of why resistance to current (and future) cancer treatments develops and how it can be impaired. Thus, nine research groups work coordinately with clinicians and additional ICO Programs to accomplish the Mission. Collectively, ProCURE is committed to foster improvement in precise and effective cancer therapy.


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 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: http://www.idibell.cat/
The Catalan Federation of Organisations Against Cancer (FECEC) is a second-level entity formed by 12 organisations working together to improve the life quality of cancer patients and their families. The Federation, created on 13 February 2001, aims to integrate efforts in the fight against cancer-related diseases in Catalonia. It provides census information and serves member organisations, while promoting volunteer actions in the oncology sector. It further develops programmes for spreading information and prevention strategies, and supports psychosocial research. Subject to Government of Catalonia regulations as a non-profit organisation, FECEC was declared a public service organisation by the Catalan Justice Department on 10 September 2008.

More info: http://www.juntscontraelcancer.cat/

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**AstraZeneca** is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three main therapy areas - Oncology, Cardiovascular & Metabolic Diseases and Respiratory. The Company also is selectively active in the areas of autoimmunity, neuroscience and infection. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.

More info: www.astrazeneca.es

**Oncovision** is a leading provider of innovative medical imaging devices for the diagnosis and treatment of cancer. Has grown into a dynamic brand in a technologically competitive, high-growth industry. We boast a clinical product line that includes market-leading Sentinella, a unique intra-operative Gamma Camera and the revolutionary Mammi PET, a breast cancer diagnostic device capable of visualizing lesions of less than 1.6mm and quantifying tumor activity. Completes its portfolio with Wprobe, the gold standard in radio guided surgery. Oncovision has distinguished itself through for developing and bring to the market innovative products to generate significant benefits on patients. Also, the company plans to bring forth technical and clinical solutions for an accurate diagnosis and treatment of cancer, providing the highest-quality, best-performing products.

More info: www.oncovision.com
**Amgen** is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on therapeutic areas with high-unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. Amgen has grown to be one of the world's leading independent biotechnology companies and has reached millions of patients around the world since 1980.


**NanoString® Technologies** provides life science tools for translational research and molecular diagnostic products. The Company's nCounter® Analysis System, which has been employed in basic and translational research, has also now been applied to diagnostic use as the nCounter DX Analysis System. The nCounter-based Prosigna™ Breast Cancer Prognostic Gene Signature Assay is both CE-marked and FDA 510(k) cleared for FFPE samples.

More info: [https://www.nanostring.com/](https://www.nanostring.com/)

**SOLTI** is a non-profit organization with more than 20 years of experience in conducting innovative clinical and translational research that aims to address unmet medical needs in breast cancer and answer questions of major scientific interest and relevance in the field of oncology. SOLTI has a network of more than 260 professionals, distributed in over 70 hospitals in Spain, Portugal, France and Italy.

More info: [www.gruposolti.org](http://www.gruposolti.org)

**Thermo Fisher Scientific**

The discovery of genetic biomarkers and their subsequent application in oncology research are paving the path toward a future in targeted therapy development, linking genes to disease states and prognosis and, ultimately, more effective treatments. Oncomine™ assays, developed by Thermo Fisher Scientific in partnership with leading cancer clinicians, are multi-biomarker targeted assays designed for cancer research and enable next-generation sequencing analysis of multiple biomarker types — fusions, insertion/deletions (indels), single nucleotide variants, and copy number variations — in a single assay. Oncomine™ assays are part of an end-to-end workflow that includes simple, scalable sequencing with Ion S5™ Series sequencers, and optimized bioinformatics and reporting with the Oncomine™ Knowledgebase Reporter.

More info: [http://www.thermofisher.com](http://www.thermofisher.com)
An innovative medical technology company primarily focused on improving women's health and well-being, Hologic enables healthier lives everywhere, every day, with clinical superiority that delivers life-changing diagnostic, detection, surgical and medical aesthetic products rooted in science and driven by technology. Hologic: The Science of Sure in action.

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More info: www.roche.com