FUTURE TOOLS FOR BIOMEDICAL RESEARCH
IN VITRO, IN SILICO AND IN VIVO DISEASE MODELING

October, 1\textsuperscript{st}-2\textsuperscript{nd}, 2015
COSMOCAIXA BARCELONA, ISAAC NEWTON, 26, BARCELONA
B·Debate
International Center for Scientific Debate

BARCELONA

“B·Debate strives to help position Barcelona as a benchmark in generating knowledge and Catalonia as a country of scientific excellence”

B·Debate is an initiative of Biocat with support from “la Caixa” Foundation which aims to drive top-notch international scientific events to foster debate, collaboration and open exchange of knowledge among experts of renowned national and international prestige. The debates are focused on the integration of diverse disciplines of science in order to tackle major scientific and societal challenges.
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01 WELCOME

02 PROGRAM

03 ORGANIZING COMMITTEE

04 INVITED SPEAKERS

05 PRACTICAL INFORMATION

06 ADDITIONAL INFORMATION

07 ORGANIZERS AND COLLABORATORS

08 NOTES
FUTURE TOOLS FOR BIOMEDICAL RESEARCH 
IN VITRO, IN SILICO AND IN VIVO DISEASE MODELING 

October, 1st and 2nd, 2015

WELCOME

Dear Guests and Participants,

It is our pleasure to welcome you on the meeting “Future Tools for Biomedical Research: in Vitro, in Silico and in Vivo Disease Modeling”, co-organized by B-DEBATE (an initiative of Biocat and “la Caixa” Foundation) and the Institute for Bioengineering of Catalonia (IBEC).

The increasing costs of biomedical research and drug discovery and the continually rising numbers of compound failures provoke an urgent need for novel tools for basic research and preclinical testing of drugs. The cross-breeding of nanotechnologies, life and computational sciences is harnessing enabling technologies for drug discovery, development, toxicity testing and disease modeling. These advances can move in vitro cell and tissue cultures beyond the current stages, which poorly reflect patient physiology, and create “in vitro human-like” platforms that allow cheaper and efficient drug and toxicity assays. At the same time, important efforts are being made to create improved animal and computational models to better mimic human physiology in health and disease.

Initiatives as the precision medicine, launched by President Obama in USA last January, that takes into account individual differences in people’s genes, environments, and lifestyles for disease prevention, diagnosis and treatment requires new technological advances in disease modelling

Most medical treatments have been designed for the “average patient.” As a result of this “one-size-fits-all-approach,” treatments can be very successful for some patients but not for others. This is changing with the emergence of precision medicine, an innovative approach to disease prevention and treatment that takes into account individual differences in people’s genes, environments, and lifestyles. Precision medicine gives clinicians tools to better understand the complex mechanisms underlying a patient’s health, disease, or condition, and to better predict which treatments will be most effective.

Under this frame, this meeting is an opportunity to debate with experts and professionals of the field to review experiences and best practices and to identify and address barriers in the development and adoption of advanced methods for disease modeling, with a potential to revolutionize preclinical research in particular, and the validation and commercialization of new therapies and diagnostics at large

We thank you in advance for your input and participation in the discussion. We hope to build a stimulating forum, where debate results in new perspectives and, if possible, a certain consensus on the road to follow.

Josep Samitier (IBEC) and B-DEBATE (Biocat and “la Caixa” Foundation)
PROGRAM
Thursday, October, 1st, 2015

9:15 Welcome
Ignasi López, Deputy Director of the Science and the Environment Area, “la Caixa” Foundation
Llara Arnal, Head of Research and Scientific Debate, Biocat
Josep Samitier, Director of Institute for Bioengineering of Catalonia
Didac Ramírez, Rector of the University of Barcelona
Antoni Castellà, Secretary for Universities and Research of the Government of Catalonia
Carmen Vela, Secretary of State for Research, Development and Innovation in the Spanish Ministry of Economy and Competitiveness

9:30 Animal Research and Possible Alternatives in Biomedicine: Overview
Elisabet Berggren, JRC-Institute for Health and Consumer Protection, EVCAM Unit, Italy

10:30 Coffee Break

11:00 SESSION 1: BEYOND CELL CULTURE SYSTEMS
Chair: Xavier Trepat, IBEC/ICREA/UB, Barcelona, Spain

11:05 Cellular Crosstalk in Vitro and its Use in Regenerative Medicine
James Kirkpatrick, Johannes Gutenberg University, Mainz, Germany

11:30 Engineering Microenvironments with Growth Factors – Looks Matters
Manuel Salmerón, University of Glasgow, UK

12:00 SESSION 2: IPS-BASED APPROACHES
Chair: Angel Raya, CMRB/ICREA/IBEC, Barcelona, Spain

12:05 Defining the Origins of Variation in Human Pluripotent Stem Cells
Ron McKay, Lieber Institute, Baltimore, USA

12:30 Establishing Standardised Access to Human Induced Pluripotent Stem Cell Line Acquisition via the European Bank for Induced Stem Cells
Paul de Sousa, School of Clinical Sciences, University of Edinburgh, UK

12:55 Making Medicines more Precise: the Role of iPSCs and EBiSC
Timothy Allsopp, Pfizer Ltd, Cambridge, UK

13:20 Open Debate

13:45 Lunch

14:45 SESSION 3: ORGAN-ON-A-CHIP
Chair: Josep Samitier, IBEC, Barcelona, Spain

14:50 Emergence of Organ-on-a-Chip Technologies: The Hype and the Reality
Roger Kamm, Massachusetts Institute of Technology, USA

15:20 Use of iPSC Progeny to Model Disease and Drug Toxicity
Catherine Verfaillie, KU Leuven, Belgium

15:45 Coffee Break

16:15 SESSION 4: IN SILICO MODELS AND SYSTEMS BIOLOGY
Chair: Roger Guimerà, URV/ICREA, Spain

16:20 Systems biology: Metabolic plasticity in chronic degenerative diseases
Pablo Miguel García Roves, University of Barcelona, Barcelona, Spain

16:45 The Virtual Physiological Human Initiative: Applications in Bone Regeneration
Liesbet Geir, University of Liege, Belgium

17:15 Open Debate
### PROGRAM

**Friday, October, 2nd, 2015**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session Title</th>
<th>Presenter/Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00</td>
<td><strong>SESSION 5: VALIDATING NEW ANIMAL MODELS</strong></td>
<td>Chair: Fàtima Bosch, CBATEG, Universitat Autònoma de Barcelona, Spain</td>
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<tr>
<td>10:05</td>
<td>The International Mouse Phenotyping Consortium: New Insights into the Genetic and Molecular Bases of Disease</td>
<td>Steve Brown, MRC Harwell, Didcot, UK</td>
</tr>
<tr>
<td>10:30</td>
<td>Deciphering Genetic and Epigenetic Function in Diabetes</td>
<td>Martin M. Hrabe de Angelis, Helmholtz Zentrum München, Munich, Germany</td>
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<tr>
<td>11:00</td>
<td>Coffee Break</td>
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</tr>
<tr>
<td>11:30</td>
<td><strong>SESSION 6: PLAYING SAFE, PLAYING FAIR</strong></td>
<td>Chair: Miquel Borràs, CERETOX, Universitat de Barcelona, Spain</td>
</tr>
<tr>
<td>12:00</td>
<td>Use of Alternative Methods in Drug Safety Assessment</td>
<td>Antonio Guzmán, Lab. Esteve, Barcelona, Spain</td>
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<tr>
<td>12:30</td>
<td>EVCAM and SEURAT-1 Experiences Looking Towards a More Efficient Safety Assessment</td>
<td>Elisabet Berggren, JRC-Institute for Health and Consumer Protection, EVCAM UNIT, Italy</td>
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<tr>
<td>12:55</td>
<td>Open Debate</td>
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<tr>
<td>13:15</td>
<td>Closing Remarks</td>
<td></td>
</tr>
</tbody>
</table>
SCIENTIFIC COMMITTEE

Josep Samitier, Director of the Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

Full Professor of Electronics and Biomedical Engineering, Electronics Department, Faculty of Physics, University of Barcelona (UB). Background in Physics (M.S. Degree in Physics, University of Barcelona and Ph.D. in Physics, University of Barcelona). Group leader of the Nanobioengineering Group at IBEC. EIT Health Supervisory Board member. Coordinator of the Spanish Nanomedicine Platform (NanomedSpain). President of the Catalan Association of Research Centres (Associació Catalana d’Entitats de Recerca - ACER). His main research areas are Biosensors, Microfluidics and Organ-on-chip. In 2003, he was awarded the City of Barcelona prize in the Technological Innovation category.

Roger Guimerà, ICREA Research Professor at the Department of Chemical Engineering, Universitat Rovira i Virgili, Tarragona, Spain

Roger Guimerà is an ICREA Research Professor at the Department of Chemical Engineering, Universitat Rovira i Virgili, Tarragona, where he co-directs the Science and Engineering of Emerging Systems Lab. He graduated in Physics at Universitat de Barcelona in 1998, and obtained a PhD in Chemical Engineering from Universitat Rovira i Virgili in 2003. He then moved to Northwestern University where he worked as a postdoctoral fellow, as a Fulbright Scholar, and as a Research Assistant Professor. In 2010, he accepted his current position as an ICREA Research Professor. Roger's research is devoted to the study of complex systems (from cells to ecosystems and societies) and, particularly, of the structure of complex networks and the interplay between network structure and dynamics. During his career, he has: (i) made methodological contributions to the study of complex networks, and (ii) used complex network analysis to gain understanding on a number of systems. His research has won him the Premi Nacional de Recerca al Talent Jove from the Catalan Government (2010), and the Erdos-Renyi Prize in Network Science from the Network Science Society (2012), and the Yong Scientist Award in Socio- and Econophysics from the German Physical Society (2014).

Fátima Bosch, Director of the Centre of Animal Biotechnology and Gene Therapy (CBATEG) and Professor at Universitat Autònoma de Barcelona, Cerdanyola del Vallès, Spain

Fatima Bosch is a Pharmacist (1980) and PhD in Biochemistry (1985) by the University of Barcelona. She conducted post-doctoral studies at Vanderbilt University (1985), Case Western Reserve University (1988-1990), and NCI-Frederick Cancer Research and Development Center (1991). She is currently Full Professor of Biochemistry and Molecular Biology (1999) and Director of the Center of Animal Biotechnology and Gene Therapy (2003) at the Universitat Autònoma Barcelona. She has been granted the Rey Juan Carlos I (1985), Francisco Grande Covión (1998), Narcís Monturiol (2002), Sant Jordi Cross (2005), Alberto Sols (2006) and ICREA Academia (2013) awards. She has been Founding member of the European Society of Gene and Cell Therapy (1992), President of the Spanish Society of Gene and Cell Therapy (2007-2009), Vice-President of the European Association for the Study of Diabetes (2009-2012) and member of the Gene Doping Expert Group of the World Anti-Doping Agency (2013-present). Her research focuses on studying the pathophysiological causes of diabetes mellitus using transgenic animal models and developing gene therapy approaches to this disease by in vivo genetic manipulation of tissues using non-viral and viral vectors. Recently, she has applied her know-how on gene transfer technologies to the development of gene therapies for inherited metabolic disorders such as Mucopolysaccharidosis.

Ángel Raya, ICREA Research Professor and Director at Center of Regenerative Medicine in Barcelona (CMRB), Barcelona, Spain

Ángel Raya holds an MD and a PhD from the University of Valencia. He pursued postdoctoral training at the Instituto de Investigaciones Citológicas (currently, Centro de Investigación Príncipe Felipe) in Valencia, from 1995 to 2000. He then was a Research Associate (2000-2004) and a Senior Research Associate (2004-2006) in the Gene Expression Laboratory of the Salk Institute for Biological Studies, La Jolla, CA (USA). He returned to Spain in 2006 as an ICREA Research Professor. He was Scientific Coordinator at the Center of Regenerative Medicine in Barcelona (CMRB) until 2009, when he joined the Institute for Bioengineering of Catalonia (IBEC) as group leader of the Control of Stem Cell Potency Group. In 2014 he was appointed Director at CMRB.
**Miquel Borràs**, Associate Professor of Toxicology, Department of Pharmacology and Therapeutical Chemistry, **University of Barcelona**, Barcelona, Spain

Miquel Borràs has 20 years experience as a toxicologist in the pharmaceutical industry (including 14 as Head of the Department of Toxicology), and then another 12 years of research in environmental toxicology, as a member of the Consolidated Group of Vertebrate Biology, University Barcelona. Currently, a member of the Toxicology Research Group (Consolidated Research Group). He is also Technical Auditor (ISO 17025) and GLP inspector for the Spanish Agency of Accreditation (ENAC). Head of the Unit for Experimental Toxicology and Ecotoxicology (Barcelona Science Park), 2002-2015. Director of Toxicology Research Centre (CERETOX), a center for technology transfer belonging to the TECNIO Network of the Generalitat de Catalunya, 2008-2015. Member of the Ethical Committee for Animal Research of the University of Barcelona (5 years) and President of the same Committee at Parc Científic de Barcelona, 2008-2015. Principal investigator or collaborator in many European and Spanish projects. Member of more than 10 Scientific Societies. Director or coordinator of more than 10 seminars and/or courses. Invited lecturer in more than 80 occasions. Has published over 50 scientific papers or book chapters related to experimental toxicology and ecotoxicology.

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**Xavier Trepat**, ICREA Research Professor and Group Leader at the **Institute for Bioengineering of Catalonia** Barcelona, Spain

Xavier Trepat is an ICREA Research Professor and Group Leader at the Institute for Bioengineering of Catalonia. Trepat’s research aims to understand how cells and tissues grow, move, invade and regenerate in a variety of processes in health and disease. To achieve this, he has developed and patented different technologies to measure cellular properties at the micro- and nanoscales. His multidisciplinary background, which combines an education in physics (2000) and electronic engineering (2001), followed by a PhD from Barcelona’s Medical School (2004) and postdoctoral work at Harvard University (2004-2008), has led to his focus today on understanding the physical mechanisms in biology via basic research and translating the results to the clinic, the market and society. Since his return to Barcelona from the USA in 2008, his research at the intersection between Life and Physical sciences has attracted ample support from the most prestigious Funding Agencies including the European Research Council (ERC), which awarded him one Starting Grant, one Consolidator Grant, and one Proof of Concept Grant. He has published research articles in the most prestigious scientific journals including Nature, Nature Physics, Nature Materials, Nature Methods, and Nature Cell Biology and has obtained more than 3000 citations.
INVITED SPEAKERS

Thursday, October, 1st, 2015

Elisabet Berggren, Deputy Head of Unit of Systems Toxicology and EURL ECVAM, Institute for Health and Consumer Protection, Joint Research Centre, European Commission, Ispra, Italy

Elisabet Berggren is Deputy Head of Unit at the Systems Toxicology Unit (STU) and the European Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM). The STU assists in the development of a new and more efficient safety assessment of chemicals based on in vitro, in silico and in chemico methods. The aim is to develop new predictive methodologies more relevant to human health, encouraging innovation and avoiding animal testing. Berggren is also contributing to the coordination of SEURAT-1, the largest EU initiative ever on alternative testing, focussing on toxicity testing for repeated dose toxicity and funded by European Commission (FP7) and Cosmetics Europe. Berggren started to work for the European Commission in 1996, and she was responsible for the Technical Committee of Classification and Labelling of Dangerous Chemicals at the European Chemicals Bureau during many years. She made her PhD in physical chemistry at Stockholm’s University in 1991. In her academic career she primarily focussed on the development of theoretical dynamic models for liquid crystals and biological relevant systems.

Animal Research and Possible Alternatives in Biomedicine: Overview

There is currently several international initiatives, such as USEPA Tox21 (http://www.epa.gov/nct/Tox21/) and SEURAT-1 (http://www.seurat-1.eu/) supporting a new vision to fundamentally change the way we assess the safety of chemicals and pharmaceuticals, by superseding traditional animal experiments with a predictive toxicology that is based on a comprehensive understanding of how chemicals can cause adverse effects in humans. The strategy is to adopt a toxicological mode-of-action framework to describe how any substance may adversely affect human health, and to use this knowledge to develop complementary theoretical, computational and experimental (in vitro) models that predict quantitative points of departure needed for safety assessment. We develop a theoretical Adverse Outcome Pathway (AOP) describing the key events of the biological process initiated by a chemical stressor, and we then develop a testing strategy for toxicity prediction, based on AOP knowledge relevant to the toxicity to be predicted. Typically a combination of in vitro, in silico and in chemico data is needed to trigger selected key events. Finally the results of testing strategies in combination with already existing data (physical chemical information, animal or human in vivo data or other) and biokinetic modelling, should provide sufficient evidence to support safety assessment more time- and cost-efficiently compared to traditional methods.

Xavier Trepat, ICREA Research Professor and Group Leader at the Institute for Bioengineering of Catalonia, Barcelona, Spain

Chair of the SESSION 1: BEYOND CELL CULTURE SYSTEMS

See his CV at the Scientific Committee Section

James Kirkpatrick, Emeritus Professor of Pathology, the Johannes Gutenberg University Mainz, Mainz, Germany

C. James Kirkpatrick has a triple doctorate in science and medicine (MD, PhD, DSc) from the Queen’s University of Belfast (N. Ireland) and is Emeritus Professor at the Johannes Gutenberg University (JGU) in Mainz, Germany, having directed the Institute of Pathology from 1993-2015. He has a special interest in human cell culture techniques to study cell-biomaterial interactions, and has pioneered complex co-culture systems in three-dimensions. His “REPAIR-lab”, is a member of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine. He is a former President of both the German and the European Society for Biomaterials and was the latter's recipient of the George Winter Award in 2008. In 2010 he was awarded the Chapman Medal from the Institute of Materials, Minerals & Mining, London, UK for “distinguished research in the field of biomedical materials”. Since 2013 he is an Honorary Member of the German Society for Biomaterials, and in 2014 he received the TERMIS-EU Career Achievement Award.
Cellular Crosstalk in Vitro and its Use in Regenerative Medicine

In Nature there is no more sophisticated delivery system for biological signals than the cell. This being the case, the question arises how this can be integrated into our strategies for tissue and organ regeneration. The most obvious translation is the adoption of cell-based therapies, a prime example being the use of mesenchymal stem cells (MSC) as immunomodulators. However, exposing naked cells to different compartments of the body is generally unphysiological - hence the need for a cell delivery system in the form of a biomaterial. Co-culture systems represent a complex in vitro technology, with which heterotypic cellular crosstalk, either through direct contact or as a close paracrine mechanism, can be studied in the context of biomaterials, and the knowledge gained used in developing strategies for regenerative medicine. This presentation will illustrate how co-culture systems with human cells can be developed to model regenerative niches, such as in bone and the upper respiratory tract. In addition, barrier systems, such as the alveolocapillary barrier in the lung or the blood-brain barrier can also be established to study strategies for nanomedicine, including the optimization of nanoparticle targeting.

Manuel Salmerón, Professor of Biomedical Engineering, Head of Division of Biomedical Engineering, School of Engineering, University of Glasgow, Glasgow, UK

Head of Biomedical Engineering Research Division in the School of Engineering at the University of Glasgow. He is the holder of an ERC Consolidator grant (2013-2018) and leads a multidisciplinary group working at the cell/material interface (www.mimeresearch.com). He received his PhD from the Technical University of Valencia (2002) and has held postdoctoral positions at Charles University in Prague (2003) and the Katholieke Universiteit in Leuven (2004, 2006). He was Associate Professor (2008) and then Professor (2010) at the Technical University of Valencia and Visiting Professor at the Georgia Institute of Technology (2010). In 2012 he was appointed to set-up the materials research division in Abengoa (international company with 20000+ employees). His group has played a pioneering role in the development of material surfaces to trigger the self-assembly of proteins. He authored 100+ articles in major international journals. And sits in the editorial board of Scientific Reports (Nature group). He is an active reviewer for a high number of journals and has acted as an expert for research agencies in different countries.

Engineering Microenvironments with Growth Factors – Looks Matters

Growth factors are ubiquitous molecules in tissue development and homeostasis, and are key components in regenerative medicine strategies. In vivo, growth factors are bound to the extracellular matrix, a fibrillar mesh of proteins that provides mechanical support and cell function, including adhesion, migration and differentiation. Most cells assemble rich protein matrices via an integrin-dependent mechanism that incorporates protein molecules (e.g. fibronectin, FN) into matrix fibrils. The process involves integrin binding and activation of cell contractility to extend FN and expose cryptic domains that promote protein-protein interactions. We have shown that this process can occur by simple adsorption of individual protein molecules onto particular surface chemistries – in absence of cells. Protein – material interactions would induce changes in protein conformation to expose of self-assembly sites and drive protein assembly into nanonetworks at the material interface, a process that we have named material-driven fibrillogenesis. The resulting material-driven matrix assembled at the material interface consists of a protein network with enhanced biological activity: it supports cell adhesion, matrix remodelling, and trigger cell differentiation. Moreover, it provides a robust platform to engineer advanced microenvironments in combination with growth factors to tune stem cell differentiation, enhance vascularisation and promote tissue healing.

Ángel Raya, ICREA Research Professor and Director at Center of Regenerative Medicine in Barcelona (CMRB), Barcelona, Spain

Chair of the SESSION 2: IPS-BASED APPROACHES

See his CV at the Scientific Committee Section

Ron McKay, Director of Basic Sciences, Lieber Institute for Brain Development, Baltimore, USA

Ron McKay, Ph.D. is the Lieber Institute of Brain Development Director of Basic Sciences. Before joining the Lieber Institute, Dr. McKay was Chief of the Laboratory of Cellular Neurobiology of the National Institute of Neurological Disorders and Stroke (NINDS). Dr. McKay received a B.Sc. in 1971 and a Ph.D. in 1974 from the University of Edinburgh. His postdoctoral training was at the University of Oxford. In Edinburgh and Oxford, he contributed to the earliest work showing that the tools of molecular biology would make a major contribution to human genetics. In 1978, he moved to Cold Spring Harbor Laboratory. At Cold Spring Harbor, he was the first to show that specific DNA-protein complexes could be analyzed with antibodies, and pioneered the field of molecular neuroscience. Joining the MIT faculty in 1984, Dr. McKay identified neural stem cells as a tool to study brain development and function. In 1993, he joined the NIH as Chief of the Laboratory of Molecular Biology at NINDS. His laboratory at the Lieber Institute studies pluripotent and somatic stem cells with a particular interest in the development of the nervous system. His research is focused on using the biology of stem cells to understand the genetic basis of human disease and to regenerate injured tissue. He is a founding board member of the International Society of Stem Cell Research.
Defining the Origins of Variation in Human Pluripotent Stem Cells

Pluripotent stem cells and their lineage-committed derivatives are poised to revolutionize biomedicine. Efforts to characterize these cells have shown that their differentiation potential can vary widely. The sources of this variability across human stem cell lines have been elusive without tools to control the early transitions that lay out the body plan of a new individual. We report a system where human stem cells spontaneously self-organize to form an epithelium with developmentally distinct zones primed to generate anterior or posterior fates along the primary embryonic axis. This system defined stable differences between cell lines in the earliest patterning events and in transcriptional signatures specific to individual humans. Reconstructing the earliest stages of development in the laboratory opens a systematic strategy to map the origins of variation in human development.

Paul de Sousa, Reader, Centre for Clinical Brain Sciences, University of Edinburgh, Chief Scientific Officer, Roslin Cells Ltd, UK

Following graduate and postdoctoral training in Canada and the US as a developmental biologist, Dr De Sousa joined the Roslin Institute in 1998 as a group leader in embryo biotechnology focused on development of animal cloning and transgenesis by somatic cell nuclear transfer and associated technologies such as egg and embryo culture, parthenogenesis and pregnancy maintenance across diverse species including mouse, pig, cow, sheep and human. In 2001 he shifted and narrowed his focus to human embryo stem cells, specifically development of culture environments to support their isolation and growth for human clinical applications. Dr De Sousa joined the University of Edinburgh in 2005, at which time he also co-founded Roslin Cells Ltd, a not-for-profit company serving to translate stem cell research into quality assured Good Manufacturing Practice (GMP) for advanced cellular therapies. His academic research concerns advancing knowledge and tools to enable the isolation, growth, and qualification of induced and embryo derived pluripotent stem cells for their safe and efficacious use in therapy and discovery, notably for the treatment of neurodegenerative diseases. Dr De Sousa currently serves as an Executive Director and Chief Scientist for Roslin Cells Ltd, and leads work-packages to establish foundational collections for the EU Innovative Medicines Initiative European Bank for Induced Stem Cells, GMP translation of a human pluripotent stem cell based therapy for Huntington’s Disease (EUP77 Repair HD) and automated developmental toxicity screening (EUP77 Dropect). He is also an executive director of Roslin Cellab Ltd, and on the scientific advisory board of the UK government Department of Health Advisory Committee for Safety of Blood Tissues and Organs.

Establishing Standardised Access to Human Induced Pluripotent Stem Cell Line Acquisition via the European Bank for Induced Stem Cells

Under joint Innovative Medicines Initiative (IMI) funding from the European Commission and a consortium of European Federation of Pharmaceutical Industries and Associations (EFPIA) members (AstraZeneca AB, H Lundbeck A/S, Janssen Pharmaceutica AB, Novonordisk A/S, Pfizer Ltd, UCB Biopharma SPRL), the European Bank for Induced Stem Cells (www.ebisc.org) has been established to provide standardised access to disease representative human induced pluripotent stem cells for discovery to benefit both industry and the broader community. This includes detailed scrutiny of ethical provenance, safety screening, scientific characteristics and intellectual property issues. EBISC has established acceptability criteria and a management process to evaluate and approve new lines, and assure consistency of stem cell lines at an early phase of accession. These procedures are captured in a Quality Manual designed to assure consistent delivery of high quality cell lines to users. To launch the bank a fast track “Hot Start” process was implemented with EBISC project partners at the Universities of Bonn, Cologne, Huberecht, Newcastle, Instituto de Salud Carlos III, Bioneer and Roslin Cells, to provide early release of established iPS/C lines. Data characterising these lines supplied by the depositors directly will be available via the hESCre database (www.hescreg.eu/). Cell lines will be stored at central and mirror banking facilities at Roslin Cells in Edinburgh and Babraham UK, and Fraunhofer IBMT, in Sulzbach Germany and Babraham, UK, and distributed via the European Collection of Cell Cultures, Public Health England, UK with certificates of analysis for each lot of cells. Here we present the experience of the bank to date and discuss scientific and technological challenges for the field in the procurement, processing and use of this resource in discovery.

Timothy Allsopp, Co-ordinator IMI project EBISC, Neuroscience & Pain Research unit, Pfizer Ltd, Cambridge, UK

Tim is a biology graduate from University of London & has published in the field of stem cells, regenerative medicine (Reading JL et al, J. Immunol. 2013; Hook L et al Neurochem Int. 2011; Allsopp T et al Med. Chem. Comm 2010). He has 15 years industrial experience in the translation of stem cell science, the development of regenerative cell therapies and product development. Before joining Pfizer he was CSO of a stem cell biotech company. He is considered a subject matter specialist in stem cells, reviewing and evaluating technology for internationally funded, public sector and charity supported regenerative medicine programmes. He is co-chair of the ISSCR Industry Committee, and Director on the ISSCR Board, an industry representative, advisory group member for the Commercialization Committee of the ISCT. He teaches and mentors students and tenure track investigators in a number of academic programmes & holds a Programme Associate position at the Cambridge university MBE course in biotechnology.
Making Medicines more Precise: the Role of iPSC and EBISC

If rapid advancements in genome sequencing have provided access to the code of disease development, then iPSC technology is the blueprint with which to functionally translate this code into new treatments and on a patient by patient basis. Induced pluripotent stem cells derived from diagnosed patients, standardized according to how they are made and behave, offer huge potential. It is an enabling technology that could refine original clinical diagnosis into one based on disease stratification and thereby offer prospects for the design of more precise experiments to discover novel pathogenic pathways, drug targets and new medicines. Drugs fail in development due to lack of efficacy, even when they have been demonstrated to be safe and human iPSC technology provides a prospect to more accurately predict efficacy of new medicines, during preclinical development. But what is the ‘real world’ pharmaceutical company experience of using the technology? What to date has been the impact to the pharma process and more importantly new medicines development pipelines? One key challenge in striving to realize the translational potential of iPSC has been the inconsistency of quality attributes and cell line performance, due to lack of a standardized production. This is a key area addressed by the EBISC project and more details on progress made by this significant EU-funded initiative will be described.

Josep Samitier Marti, Director of the Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

Chair of the SESSION 3: ORGAN-ON-A-CHIP

See his CV at the Scientific Committee Section

Roger Kamm, Cecil and Ida Green Distinguished Professor of Biological and Mechanical Engineering, Massachusetts Institute of Technology, Baltimore, USA

Roger D. Kamm is the Cecil and Ida Green Distinguished Professor of Biological and Mechanical Engineering at MIT. He is the recipient of numerous awards including the ASME Lissner Award and the Eunopean Society of Biomechanics Huiskes Medal. He was elected to be a member of the National Academy of Medicine in 2010. A primary objective of Kamm’s research group is the application of fundamental concepts in fluid and solid mechanics to better understand essential biological and physiological phenomena. His lab focuses on the molecular mechanisms of cellular force sensation, and the development of new microfluidic technologies for vascularized engineered tissues and models of metastatic cancer.

Emergence of Organ-on-a-Chip Technologies: The Hype and the Reality

The use of microfluidic technologies to create three-dimensional organ models with multiple organ-specific or even patient-specific cell types has experienced tremendous growth since the early microfluidic cell culture systems of about ten years ago. Today, such systems are increasingly capable of recapitulating certain aspects of in vivo biology, with potential applications in drug screening or in the creation of models of human physiology or pathology. In this presentation, I will discuss the range of organs-on-a-chip technologies that is currently available, the limited success of these to date, and the prospects for future applications. Some examples from our lab will be discussed including models of microvascular networks, neuromuscular junctions, and the blood brain barrier.

Catherine Verfaillie, Director Interdepartmental Stem Cell Institute, Leuven; Professor department Development and Regeneration, head Cluster Embryology and Stem Cell Biology, KU Leuven, Belgium

Catherine Verfaillie received her Medical degree from the KULeuven in 1982. She then trained as an internist/hematologist at the KULeuven between 1982 and 1987. She went to the U. of Minnesota in 1987 for a postdoctoral fellowship. After completing her post-doctoral fellowship, she was appointed consecutively as Instructor, assistant professor, associate professor and full professor of Medicine in 1998. In 2001, she became the Director of the U of Minnesota’s Stem Cell Institute. In 2006, she accepted to become the director of the Interdepartmental Stem Cell Institute Leuven (SCI; http://www.kuleuven.be/samenwerking/scil/) at KU Leuven. She has a longstanding career in stem cell biology, initially focusing on normal hematopoietic stem cells and leukemic stem cells, and the role played by the microenvironment in regulating their self-renewal and differentiation ability. Since 1997 she has also focused extensively on more pluripotent stem cells. Her group described in 2002 a novel cell population culture from rodent and human bone marrow samples with greater expansion and differentiation potency, named multipotent adult progenitor cells or MAPC. The current research of the Verfaillie lab is focused on understanding what regulates selfrenewal and (de)differentiation of adult as well as embryonic pluripotent stem cells using gene editing strategies based on insights gained from multi-omics, as well as organoid culture systems. Areas of interest are hematopoiesis, development of human iPSC-derived models for neurodegeneration and hiPSC derived models of liver metabolism and toxicity.
Use of iPSC Progeny to Model Disease and Drug Toxicity

With the discovery that somatic cells can be reprogrammed to cells with many features of embryonic stem cells by Yamanaka and colleagues, it has now become possible to generate cells with pluripotent characteristics of any individual. The ability to create “mature” cells of many tissues from these induced pluripotent stem cells (iPSCs) opens the possibility to use such cells in drug discovery and regenerative medicine. However, many hurdles will still need to be overcome to make suitable fully mature. Thanks to the very fast progress made in material sciences, allowing the creation of stem cell and mature cell niche equivalents, as well as methods for genome editing, use of patient derived iPSCs as well as isogenic genetically corrected cells to model disease, or develop high throughput cell models for drug toxicity and metabolisation studies, is being pursued by many academic teams as well as the pharmaceutical industry. A few examples of these approaches will be discussed.

Roger Guimerà, ICREA Research Professor at the Department of Chemical Engineering, Universitat Rovira i Virgili, Tarragona, Spain
Chair of the SESSION 4: IN SILICO MODELS AND SYSTEMS BIOLOGY
See his CV at the Scientific Committee Section

Pablo Miguel Garcia-Roves, Associate professor, Department of Physiological Sciences II, University of Barcelona, Barcelona, Spain
For more than a decade my research is focusing in the elucidation of the mechanisms that control energy metabolism in skeletal muscle and more recently as an integrative approach to whole body energy metabolism. During my PhD and post-doctoral periods I have been trained in Nutrition, Energy Metabolism and Integrative Physiology research areas. I have experience participating in human studies, mainly during my years as a PhD student. Most of my work has been conducted using animal models, both rats and mice. In these studies we have used gene therapy approaches, dietary and pharmacological interventions and exercise protocols. Biochemical, molecular biology, genetics and in vivo analysis are regularly used. My current research focused on a systemic perspective of the etiology and potential treatments of metabolic diseases (system biology approach). For this purpose functional parameters, metabolism, genetics, epigenetics and proteomics platforms should be used and a wide range of bioinformatics tools should be implemented for the mapping, combination and integration of datasets.

Systems Biology: Metabolic Plasticity in Chronic Degenerative Diseases

One of the major concerns in health care is the growing prevalence of metabolic disorders. Therefore, major research efforts are focused on the identification of potential targets for new drug development and/or treatment strategies (nutritional interventions and physical activity programs) that help to combat the growing incidence of metabolic diseases such as obesity-related type 2 diabetes. Obesity-related type 2 diabetes is a multi-organic disease by means that many tissues play an important role in the early development of insulin resistance and the later onset of the disease. In this context our work ambition to develop broad, systems-biology approaches devoted to integrate information from different areas of investigation (phenotype data, functional data, signalling and –omics) to supply new insights and a better understanding of the integrated mechanisms that regulate whole body energy metabolism during physiological and pathophysiological states.

Liesbet Geris, Professor in Biomechanics and Computational Tissue Engineering at the Universities of Liège and Leuven, Belgium

Liesbet Geris is professor in Biomechanics and Computational Tissue Engineering at the universities of Liège and Leuven (Belgium). Her research interests encompass the mathematical multi-scale modeling of bone regeneration in tissue engineering applications. She works in close collaboration with experimental and clinical researchers of the university hospitals of Leuven and Liège focusing on the development of mathematical models of impaired healing situations and the in silico design of novel treatment strategies. In 2011 she received an ERC starting grant. She has received a number of young investigator and early career awards. She is chair of the policy affairs work group of the Virtual Physiological Human Institute, member of the Young Academy of Europe and co-chair of the Young Academy of Belgium (Flanders).

The Virtual Physiological Human Initiative: Applications in Bone Regeneration

For many years now, researchers have created computational models of biological processes to complement and interpret in vitro and in vivo experiments. The Virtual Physiological Human (VPH) initiative is a worldwide effort to develop computer technologies that will enhance these early models and will allow to integrate all information available for each patient. The generated computer models will then be capable of predicting how the health of that patient will evolve under certain conditions or treatment. The applications of these models will depend on the user: patients (personal health forecasting), clinicians (digital patients), researchers (virtual guinea pigs) or industry (in silico clinical trials). In this talk the general concept of the VPH will be explained.
Fátima Bosch, Director of the Centre of Animal Biotechnology and Gene Therapy (CBATEG) and Professor at Universitat Autònoma de Barcelona, Cerdanyola del Vallès, Spain

Chair of the Session: VALIDATING NEW ANIMAL MODELS

See her CV at the Scientific Committee Section

Steve Brown, Director of the Medical Research Council’s Mammalian Genetics Unit at MRC Harwell, Oxford, UK

Steve Brown research interests cover mouse functional genomics, including the use of mouse mutagenesis and phenotyping approaches to study the genetic basis of disease and to develop pre-clinical disease models. A particular focus has been the use of mouse models to study the molecular basis of genetic deafness. He has initiated a substantial research effort in the genetics of otitis media or glue ear, a common cause of hearing loss in children, employing mouse models to elaborate the key genetic pathways involved and develop novel therapeutic strategies. He is currently Chair of the international steering committee for the International Mouse Phenotyping Consortium (IMPC) that is establishing a comprehensive catalogue of mammalian gene function by the generation and phenotyping of a mutant for every gene in the mouse genome. He is a Fellow of the Royal Society, a Fellow of the Academy of Medical Sciences and a member of EMBO.

The International Mouse Phenotyping Consortium: New Insights into the Genetic and Molecular Bases of Disease

A major challenge facing mammalian genetics over the next decade is the systematic and comprehensive annotation of mammalian gene function. As part of the International Knockout Mouse Consortium, several programmes are ongoing to generate conditional mutants for all mouse genes. An even greater challenge will be the determination of phenotypic outcomes for each mutation and the identification of disease models. The International Mouse Phenotyping Consortium (IMPC, www.impc.org) will undertake the development of a comprehensive Catalogue of Mammalian Gene Function and proposes to build on the several pilot programmes that have explored the feasibility of large-scale mouse phenotyping, such as the EUMODIC programme. The IMPC incorporates 18 major mouse centres around the world that will undertake mouse production and phenotyping. The IMPC envisages two phases to its programme: Phase 1, 2011-2016, is already well underway and is carrying out the phenotyping of around 5000 mouse lines; and Phase 2 from 2016-2021 which will undertake the analysis of the remaining genome. IMPC centres operate a core, standardised, broad-based adult phenotyping pipeline encompassing the major biological and disease systems, including gross pathology and tissue collection as a mandatory requirement. Many centres have also begun to employ a standardised embryonic phenotyping pipeline to analyse the many homozygous lethals, incorporating an assessment of time of lethality and morphological defects. In addition, lacZ expression data is being collected for adult organs and E12.5 embryos. All data from each production and phenotyping centre is uploaded to a central Data Coordination Centre (DCC), and following QC and analysis is archived and disseminated to the wider biomedical sciences community along with appropriate annotation tools. In the first 4 years of the programme, nearly 8000 ES cell lines have been injected, over 4500 mouse mutant lines generated and phenotype data from nearly 2500 mutants collected at the DCC. We will describe many new insights into the genetic and molecular bases of disease, report the generation of numerous novel disease models, and elaborate a fundamental appraisal of the pleiotropic landscape of mammalian gene function.
**Martin M. Hrabe de Angelis**, Director Institute for Experimental Genetics (IEG), Helmholtz Zentrum München, Germany

Professor Hrabe de Angelis studied biology at Philipps Universität in Marburg and completed his PhD on the influence of growth factors on early embryonic development in 1994. During his time as a postdoctoral researcher (1994 – 1997) at Jackson Laboratory in Bar Harbor (USA) he examined the Delta/Notch signaling pathway and mouse models in somitogenesis. Since 2000 Professor Hrabe de Angelis has directed the Institute for Experimental Genetics at Helmholtz Zentrum München (German Research Centre for Environmental Health). In 2001 he founded the German Mouse Clinic (GMC) for the systemic analysis of mouse models for human diseases. In 2003 he was appointed to the Chair of Experimental Genetics at TUM. Prof. Hrabe is also the director of the European Mouse Mutant Archive (EMMA), cofounder of INGENIUM Pharmaceuticals AG (1998), NanoRepro AG (2006) and cofounder and director of INFRAFRONTIER GmbH (2013). He has published over 350 original works and is an author of many textbooks. He directs international research projects and is a founder as well as member of the board of directors of the German Center for Diabetes Research (DZD), which was set up in 2009.

**Deciphering Genetic and Epigenetic Function in Diabetes**

The GMC (German Mouse Clinic) was originally founded as the world first open access mouse clinic for systemic phenotyping in order to characterize pleiotropic gene functions and to identify affected organs in mutant mouse lines. GMC has been instrumental for the elucidation of undiscovered gene functions and the development of new pre-clinical models for human diseases. With its comprehensive phenotyping data, GMC I contributes to the worldwide initiative to fully annotate the first mammalian genome with at least one function for every coding gene (IMPC). For secondary analysis we have set a focus on genes relevant for metabolism and diabetes. Strategy and first results will be presented. Besides the importance of genetic elements for metabolism and diabetes epigenetic factors seem to play an important role. We focus on trans-generational epigenetic factors for acquired diabetes. Evidence will be presented for both germ lines that trans-generational epigenetic events exist and play an important role with respect to susceptibility to body weight gain and insulin resistance.

**Miquel Borràs**, Associate Professor of Toxicology, Department of Pharmacology and Therapeutical Chemistry, University of Barcelona, Barcelona, Spain

Chair of the SESSION 6: PLAYING SAFE, PLAYING FAIR

See his CV at the Scientific Committee Section

**Antonio Guzmán**, Head of Toxicology Department, ESTEVE. Barcelona Science Park, Barcelona, Spain

Graduate in Biological Sciences and Ph.D. in Genetics from the Autonomous University of Barcelona. University Expert in Toxicology (Seville University) and EUROTOX registered Toxicologist. He is responsible for all non-clinical safety assessment conducted from early candidate selection to regulatory toxicology testing and post-approval activities. As non-clinical toxicity expert he is involved in preparing technical reports and regulatory documents to support safety aspects of ESTEVE’s R&D projects (NCEs and ATMPs) and marketed products, and interacting with regulatory agencies. Author of several publications on non-clinical safety assessment of drug candidates in peer reviewed journals, reviewer in several scientific journals and invited lecturer in several Scientific Society Meetings and University Master Degrees. He is member of several scientific societies: the Spanish Environmental Mutagenesis Society (SEMA), the Spanish Laboratory Animal Science Society (SECAL) and the Spanish Toxicology Society (AETOX).

**Use of Alternative Methods in Drug Safety Assessment**

Drug discovery and development is a complex and time consuming process in which non-clinical toxicity testing is a pivotal component. During the early candidate selection phases the conducted toxicology screening studies allow selecting those compounds showing the most favourable safety profile. In vitro screening studies are consequently designed to assess an extensive number of molecules within a short time period and with a limited use of compound. To support clinical development, regulatory toxicology studies are conducted both in advance and in parallel to clinical studies, aiming to characterize the toxicological profile of the drug candidate and identifying potential risk for human toxicities and parameters for clinical monitoring. While far from optimal, animal models still play a pivotal role in regulatory toxicity testing. However, in the last decades there has been an ever growing role for the use of alternative models (in vitro and in silico) as part of the safety assessment required by regulatory authorities.
Elisabet Berggren, Deputy Head of Unit of Systems Toxicology and EURL ECVAM, Institute for Health and Consumer Protection, Joint Research Centre, European Commission, Ispra, Italy

ECVAM and SEURAT-1 Experiences Looking Towards a More Efficient Safety Assessment

EURL ECVAM (https://eurl-ecvam.jrc.ec.europa.eu/) is through their development, evaluation and validation of non-animal methods striving to contribute to a more relevant and efficient safety assessment of chemicals, including e.g. pharmaceutical or cosmetic ingredients. SEURAT-1 (http://www.seurat-1.eu/) was the largest EU research initiative ever on alternative methods, but also here the focus was supporting a new vision to fundamentally change the way we assess the safety of chemicals and pharmaceuticals and improve predictions compared to traditional animal models. The idea here is to provide examples on currently available tools and methods, how to combine them in safety assessment strategies and which will be the next problems that need to be tackled.
PRACTICAL INFORMATION

Venue

CosmoCaixa Barcelona
Sala Agora
C/ Isaac Newton, 26  08022 Barcelona, Spain
obrasocial.lacaixa.es/laCaixaFoundation/home_en.html

CosmoCaixa offers interactive, enjoyable science and an open door for anyone who is eager to learn and understand and who never stops wondering why things are the way they are. CosmoCaixa Barcelona boasts the Geological Wall and the Amazon Flooded Forest, which features more than 100 plant and animal species that convince visitors they have been transported from the Mediterranean to the very heart of the tropical jungle. In addition to its permanent facilities and its open areas, CosmoCaixa offers a scientific and educational programme that includes exhibitions, workshops, conferences, courses and debates involving experts from all over the world.

More info: obrasocial.lacaixa.es

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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 “FUTURE TOOLS FOR BIOMEDICAL RESEARCH. IN VITRO, IN SILICO AND IN VIVO DISEASE MODELING”

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ORGANIZERS

B-Debate International Center for Scientific Debate Barcelona is a Biocat initiative with support from “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.

B-Debate sees debate as a powerful, effective way to generate new knowledge. 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 organized more than 50 activities, invited about 1,200 recognized speakers and over 7,000 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 Institute for Bioengineering of Catalonia is a research centre whose purpose is to carry out interdisciplinary research at the highest international quality level which, by creating knowledge, helps to improve health and quality of life and generate wealth.

IBEC research is structured in three broad avenues of knowledge: nanomedicine, cell engineering and ICT for health. These are placed at the service of science and society to progress in three major application areas, namely Future Medicine, Regenerative Therapies and Healthy Ageing.

More info: www.ibecbarcelona.eu
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