UNSOLVED PROBLEMS IN HEART REPAIR

November, 28th, 29th and 30th, 2012
COSMOCAIXA. C/ ISAAC NEWTON, 26. BARCELONA

www.bdebate.org
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.
UNSOLVED PROBLEMS IN HEART REPAIR

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Dear Invited Speakers and Participants,

It is our great pleasure to welcome you to the meeting “Unsolved Problems in Heart Repair”, co-organized by B-Debate International Center for Scientific Debate Barcelona, an initiative of Biocat with support of “la Caixa” Foundation, and the Vall d’Hebron Research Institute (VHIR).

Over the past few years, cell therapy for these cardiac diseases and those of other organs has moved to the forefront of several medical fields. Many of these therapies are now in the initial or mid-stage clinical trials. Although the available results are encouraging it is becoming increasingly clear that is and will remain very difficult, if not impossible, to compare the results obtained by different investigators using similar therapies and also to compare the effect of different therapies. This problem is likely to slow down the broad clinical application of these therapeutic approaches at a time where effective methods to prevent and treat heart failure is becoming an urgent necessity, particularly in the developed world. Unfortunately, a heart transplant is available to only a very small number of patients and even if the scarcity of the donor were not the limiting step, the high cost and live-long sequel of the transplant would bankrupt the national health care system of all develop countries.

Cell therapy, using different types of cells, either stem cells from the heart itself or proliferative cells from other tissues have shown that, either directly or indirectly, they can stimulate the regenerative capacity of the heart muscle itself and improve the function of the damaged heart and also prevent or at least diminish the appearance of heart failure. Thus, the potential of these therapies seems very significant and for this reason it is important to accelerate the rate of progress toward their clinical application. In order to apply these therapies to the human with a minimal risk and obtain the optimal benefit, it is a requirement to first demonstrate their efficacy and tolerance in animal models such that the results obtained can be extrapolated with a degree of confidence to the human. Unfortunately, there is no consensus about critical issues among different investigator groups and also among the regulatory agencies in charge of protecting the safety of the experimental subjects.

The goal of the meeting is to bring together many of the expert of these therapies from around the world and have an open a free discussion about these topics in an attempt to reach a consensus about the protocols which should be followed and the information which should be collected in laboratory and animal experiments before a given cell treatment is tested in humans.

On behalf of B-Debate and the Vall d’Hebron Research Institute, we thank you for joining this event, an hope that you enjoy the meeting, and encourage you to participate actively in the discussions and debates.

Sincerely,

B-Debate, Manuel Galiñanes, Bernardo Nadal-Ginard and Jordi Barquinero
UNSOLVED PROBLEMS IN HEART REPAIR

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GENERAL CONSIDERATIONS

It is expected that the meeting will produce guidelines and recommendations on the following areas of research:

1. Most appropriate animal and experimental models for the study of cell therapy
2. The ideal experimental tools to identify the progeny of newly formed cardiac tissue
3. Necessary requirements for the performance of meaningful preclinical studies
4. Conditions in which the use of allogeneic material is safe and desirable
5. When clinical studies should be performed? What kind of end points should be used?
6. Definition of the ethical frame in which clinical studies can be carried out safely but without unnecessary constraints or limitations that could slow and delay a wide and quick clinical application of therapies much needed in the clinical arena.

To facilitate the discussion and concentrate on the important issues, the B-Debate meeting has been organized without podium presentations but as a set of question to be discussed and agreed upon. Each question has been assigned a “leader” but over 90% of the time will be dedicated to discussion among the participants. The end result will be a summary of the questions and the consensus response of the participants when one has been reached.

If no consensus arises for some of the questions, the different alternatives proposed will be listed in an effort to help this very young field of medicine to move forward in a more expeditious manner while increasing the safety of the patients who are the first recipients of these therapies.
PROGRAM

Wednesday, November, 28th, 2012

8:45 Registration

9:00 Welcome

9:10 BASIC SCIENCE

In light of the present knowledge, which stem cell type(s) is/are likely the most useful for an effective repair of the damaged myocardium? Advantages and drawbacks for each cell type (autologous, allogeneic, embryonic, IPS). Chair: Andre Terzic

Is it scientifically proven that allogeneic cells transplanted by whatever means into the myocardium (with or without spilling to other tissues) are eliminated in a short time by the host immune system? If so, does this affect the characterization requirements for these cells vs autologous. Chair: Dominique Charron

What are the essential parameters for the in vitro characterization of cell type(s)? Chair: Massimiliano Gnecci

What should be the goal of the cell therapy? Myocyte regeneration? Neo-vascularization? Prevention or amelioration of remodeling? Or a combination of both? Are these goals dependent on the cell type used? Should the goal determine the time of administration? Chair: Marc Penn

10:30 Coffee break

11:00 The term “stem cells” has been used very loosely in the field of myocardial cell therapy. Should the established criteria of stem cell therapy be limited to the therapeutic uses of bona fide stem cells or stem-progenitor cells, followed by the tissue of origin of the stem cells used? Chair: Daniele Torella

What is the intended mechanism of action of the therapeutic cells? Paracrine effect over cells at risk? Stimulation of the endogenous cardiac stem cells? Replenishment of the endogenous cardiac stem cell cohort? Direct contribution of the therapeutic cells to the regenerated/repaired myocardium? Chair: Bernardo Nadal-Ginard

What is the optimal time for the application of the therapeutic cells in the AMI animal model? In the acute phase before the development of the inflammatory reaction? In the post-acute phase when the inflammatory reaction has subsided? Is the time of intervention dependent on the type of cell used? Chair: Stefan Janssens

Tracking of the transplanted cells either autologous or allogeneic in experimental animals. How? When? In the case of allogeneic cells what is an accepted proof that ALL transplanted cells have been eliminated from the host? Chair: Bernardo Nadal-Ginard

13:30 Lunch

15:00 Dose and composition of the autologous and allogeneic cell therapy product. How to design tests which allow for a valid comparison of results among different animals and/or batches of cells? What is best, a pure or an heterogenous cell population? Chair: Felipe Prosper

Are the cells and the methodology used for AMI the same or different for the therapies intended for the treatment of heart failure? Chair: Maria José Goumans

How and when can tissue engineering help cell therapy? Chair: Wolfram Zimmermann
PROGRAM

Wednesday, November, 28th, 2012

15:00 Objective criteria for the evaluation of myocardial regeneration in animal models. Chair: Georgia Ellison

Should myocardial cell therapy be a one time event or should it be repeatable upon interval(s). What are these intervals? Should we use different routes of administration at the different intervals? Different criteria for AMI and HF? Chair: Andreas Zeiher

What preclinical data should be necessary to obtain prior to the initiation of clinical studies? Should the required preclinical information be the same for cell-based therapies than for cell-free therapies? Chair: Nabil Dib

What safety data is required for hES or iPS technologies? Chair: Andrew Baker

Logistics of iPS-derived cardiomyocytes: a) Can a line realistically be made for each patient? b) What is the likelihood of this overcoming immune rejection? c) Will each line need individual regulatory validation? Chair: Angel Raya

16:30 Coffee Break

17:00 Should it be a requisite for the initiation of clinical trials to have an understanding of the mechanism of action of the experimental therapy? Chair: Asterios Tsiftsoglou

What are the most appropriate experimental models (amphibians, rodents, bigger animals) for the study of cell therapy, its mechanisms and efficacy? Should clinical trials be started based solely on data obtained in rodent animal models? Chair: Keiichi Fukuda

What is the most appropriate large animal model in which to test myocardial regenerative therapies? What kind of parameters should be obtained to assess treatment efficacy? Chair: Gustav Steinhoff

What kind of immunological investigations and in which model should be performed before clinical application? Chair: Jordi Barquinero

Is there any useful information gained in the test of the therapeutic cells for tissue distribution and onco/teratogenesis in immunodeficient mice models? Should the criteria be the same for the autologous and allogeneic therapies? Chair: Felipe Prosper

Should the preclinical data on tissue distribution, oncogenic potential, etc. be the same for autologous and allogeneic cell therapy? Chair: Dominique Charron

18:30 Visit to the 3D Planetarium and CosmoCaixa

19:45 Dinner at CosmoCaixa

21:15 Transportation to the Hotel
PROGRAM

Thursday, November, 29th, 2012

9:00  CLINICAL STUDIES

What is the minimal and optimal set of preclinical information required before the start of clinical trials? Chair: Anthony Mathur

How to evaluate the results of clinical trials when the composition and dose of therapeutic agent is different for each patient? Chair: Andreas Zeiher

From a regulatory standpoint, what are the criteria the establish therapeutic equivalence of different cell populations and or different mixtures? Chair: Bernardo Nadal-Ginard

Criteria for patient selection. Does it depends on the cells used and/or the mode of administration? Chair: Nabil Dib

10:30  Coffee break

11:00  What should be the sequence and the protocol of the first-in-man trails? Dosis escaclation? Follow-up for how long? Chair: Asterios Tsiftsoglou

What type of primary end-points clinical studies should have? Chair: Stefan Janssens

What markers can be used ethically and practically to track cells implanted clinically? Chair: Sian Harding

Is it safe and desirable to undertake clinical studies without the demonstration of the mechanism involved? Chair: Manuel Galifianes

Should the end-points for AMI and HF be the same? Should the end-points be the same independently of the mode of administration of the cells: intracoronary, intramyocardial by catheter or by surgery? Chair: David García-Dorado

13:30  Lunch

15:00  What is the minimal follow-up time required to ascertain clinical effectiveness and evaluation of side effects of the therapy? Chair: Antoni Bayés Genis

Immunological implications of all regenerative therapies: a) Feasibility and safety of the use of allogeneic cells. b) What are the immunological consequences of applying allogeneic material? c) Are allogeneic cells, genetically modified or not, immunologically neutral? Chair: Dominique Charron

Use of MSC primarily to modulate immune and inflammatory responses: a) Is this a valid target per se? b) Could/should these cells be used in conjunction with others to dampen immune responses? Chairs: Marc Penn and Dominique Charron

Which is the best route of administration? Does it depend on the clinical condition to treat? Chair: Marc Penn
# PROGRAM

## Thursday, November, 29\textsuperscript{th}, 2012

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<th>Time</th>
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<tr>
<td>16:30</td>
<td>Coffee Break</td>
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<td>17:00</td>
<td>Should it always be randomised and blind to the patients? Chair: Andreas Zeiher</td>
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<td>Should an international register for cell therapy patients be established? If so, by whom? Chair: Daniele Torella</td>
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<td>What system(s) should be put in place to make comparable the results obtained by different groups using the same type of therapy and among the different types of cell therapy? Chair: Keichi Fukuda</td>
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<td>If these therapies become routine for millions of people, what will be the rate-limiting step for each strategy? Chair: Sian Harding</td>
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<td>Transportation to the Hotel</td>
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## Friday, November, 30\textsuperscript{th}, 2012

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<th>Time</th>
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<tr>
<td>9:00</td>
<td>ETHICS AND REGULATORY BODIES</td>
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<td>What are the ethical implications of cell therapy? a) for the donor; b) for the recipient; c) the same for autologous and allogeneic therapies? Chair: Asterios Tsiftsoglou</td>
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<td>What kind of information from animal models is required before seeking approval for clinical trials? Is it the same for autologous and allogeneic cell therapies? Chairs: Sol Ruiz and Sanne Jansen of Lorkees</td>
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<td>10:30</td>
<td>Coffee Break</td>
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<tr>
<td>11:00</td>
<td>Should a standarized protocol be agreed upon by the regulatory agencies for the design of phase I/IIa clinical trial for new cell types and/or novel protocols? Chair: Andreas Zeiher</td>
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<td>Role of EMA vs. National Agencies Chairs: Sol Ruiz and Asterios Tsiftsoglou</td>
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<td>13:00</td>
<td>Conclusions and closing remarks</td>
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<td>13:15</td>
<td>Lunch</td>
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**SCIENTIFIC ORGANIZERS**

**Manuel Galiñanes,** Head of the Department of Cardiac Surgery at the University Hospital Vall d’Hebron (HUVH) and Group Leader of Reparative Therapy of the Heart at the Vall d’Hebron Research Institute (VHIR), Barcelona, Spain

Graduated in Medicine (University of Salamanca, 1976) and in Cardiovascular Surgery (Universidad Complutense of Madrid, 1982), he got a PhD in Physiology and Biochemistry at the University of London (UK, 1992). He was postdoctoral clinical fellow at the St Thomas’ and Guys Hospitals (London, UK, 1993-6), become Reader (1996-2000) and then Professor of Cardiac Surgery (2000-2010) at the University of Leicester. He is co-founder and active member of the task force of the European Society of Cardiology for Cell Therapy. His research has focused primarily on understanding the mechanisms of ischaemic injury and its prevention and also in the repair of the damaged heart by stem cells. He has co-authored over 140 publications in scientific journals and book chapters and is a reviewer for several specialized scientific journals.

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**Bernardo Nadal-Ginard,** Professor in the Department of Sport Sciences and Medicine at John Moores Liverpool University, Liverpool, U.K.

In addition to his academic appointment, Dr Nadal-Ginard is Co-Founder Coretherapix, S.L. a biotechnology company focused on the development of cardiac regenerative therapies. Earlier in his career, Dr Nadal-Ginard held appointments at Harvard Medical School, where he was named Alexander S. Nadas Professor of Pediatrics and was Professor of Cellular and Molecular Physiology as well as Director of the Harvard-MIT MD-Ph.D. Program. He was also a Professor at New York Medical College, N.Y. and at Mount Sinai Medical School, N.Y. Dr Nadal-Ginard completed his medical studies at the University of Barcelona in Spain. While at the University of Barcelona, Dr Nadal-Ginard also completed his internship and residency at the university's School of Cardiology. He then pursued his residency at the National Heart Institute in Mexico, where he was later named Chief of Residents. Following these accomplishments, Dr Nadal-Ginard, went on to earn his doctorate at Yale University, Department of Biology and was later named NIG Fogarty International Fellow, J. March Foundation Fellow, and Population Council Fellow. Dr. Nadal-Ginard obtained his Ph.D. in Developmental Biology from the Department of Biology at Yale University in 1975. He was further awarded for his research accomplishments and received the John Spangler Nicholas Award for Outstanding Thesis Research, followed by the Sinheimer Faculty Award. He then assumed the role of Assistant Clinical Professor, Department of Pediatrics at Yale University School of Medicine before moving on to Albert Einstein College of Medicine in New York, where he served as Assistant and Associate Professor in the Department of Cell Biology until 1982 when he moved to Harvard Medical School. Dr Nadal-Ginard is active with several worldwide scientific advisory committees surrounding his research interests, and has contributed extensively to numerous scientific meetings and journals throughout his career, including 50 named lectures, 335 invited lectures and visiting professorships, and 35 keynote addresses. In addition to these contributions, his scientific meeting reports and over 260 full-length papers have been published in numerous worldwide journals. His main scientific interests have been focused on the biology of the cardiovascular system using the techniques of molecular and cellular biology. In particular, he made contributions to the role of alternative splicing in the generation of protein diversity and its role in development and cell differentiation. Early in this century, he and his group identified and characterized the adult cardiac stem cells and described their role in the maintenance of normal cardiac cellular homeostasis and repair. At present his main interest is the development of cardiac regenerative therapies by manipulating the growth and differentiation of the cardiac stem cells resident in the adult myocardium. Throughout his career, Dr Nadal-Ginard has received different honors and awards for his accomplishments and global contributions to cardiovascular research. Most recently, he was awarded the Prize Ramon Llull for Science and the Prize Joan D’ Alos. Hospital Sant Jordi by the Autonomous Government of Balearic Islands in Spain. Other notable honors include the Basic Research Prize, awarded by the American Heart Association, the Robert J. and Claire Pasarow Foundation Award for Cardiovascular Research, and an award for outstanding research by the International Society for Heart Research. He is Doctor Honoris Causa for the Universitat de les Illes Balears. He was awarded the title of “Cavaliere della Repubblica” by the President of Italy.
**Jordi Barquinero.** Group leader of the Gene and Cell Therapy Laboratory at the Vall d’Hebron Research Institute (VHIR), Barcelona, Spain

Graduated in Medicine (UAB, 1982), he finished his residency in Internal Medicine (1989) and he was a pre-doctoral fellow at the University of Louisville (USA, 1990). In 1992 he got his Ph.D. with Honors (UAB). He was postdoctoral fellow at the Fred Hutchinson Cancer Research Center (Seattle, USA, 1992-4). He collaborated in the magazine of Science and Medicine in the newspaper La Vanguardia (1988-96). In 1995, together with Dr. Antonio Salgado, he received the Boehringer Ingelheim Award for the best article on Biotechnology in Medicine. In 2004 he was President of the Organizing Committee of the 2nd Meeting of the Spanish Society of Gene Therapy (currently SETGYC), of which he is a founder member. His research has focused primarily on autoimmunity and preclinical gene therapy based on hematopoietic stem cells, and he has participated in several national and European projects related to these fields and has co-authored over 60 publications in scientific journals as well as several popular science or scientific books and book chapters. He is a reviewer for several specialized scientific journals. He is now coordinating a European project on the use of induced pluripotent stem cells to model pathogenic and therapeutic aspects of hemophilia A. Since 2009 he is vicepresident of the Societat Catalana de Biologia.
INVITED SPEAKERS

Wednesday, November, 28th, 2012

Andre Terzic, Professor of Medicine and Pharmacology and Director of the Center for Regenerative Medicine, Mayo Clinic, Rochester, USA

Dr. Andre Terzic studied at the University of Paris School of Medicine, Paris, France, and the University of Belgrade, Belgrade, Yugoslavia. Fellowship at Clinical Pharmacology, Thomas Jefferson Medical College, Philadelphia, PA, and Internal Medicine, University of Belgrade, Belgrade, Yugoslavia. Ph.D. – Department of Pharmacology, University of Illinois. Research interest:Cardioprotective and cardioregenerative medicine; Genetics of cardiac disease and stress tolerance; Bioenergetic signaling, nucleocytoplasmic communication and ion channel biology.

Dominique Charron, Professor and Head of the Dep of Hematology, Immunology and Therapeutic Target and CIB, Institut Universitaire d’Hematologie, Hospital Saint Louis, Paris, France

MD Medicine, Paris University and PhD Immunology, Stanford University (USA) Post Doctoral Immunology. Professor of Medicine - Immunology, University of Paris, France, Chairman-Department of Immunology/Histocompatibility - Saint Louis Hospital AP-HP Paris, Head of translational research in Hematology, Oncology, Transplantation CIB-HOG, Director of Research INSERM 662 “Immune responses : regulation and development” IUH, President Fonder HLA and Medicine, President: European Foundation of Immunogenetics (efiweb.org), President: Scientific Advisory Board BiobancInternational. Expert : European Community (EC) programmes FP4,5,6, European Science Foundation (ESF); NSF (Washington DC) SMM (Unesco) beyond others.

Massimiliano Gnecchi, Department of Cardiology, University of Pavia & IRCCS Policlinico San Matteo, Pavia, Italy

After completing his training in Cardiology at the University of Pavia in Italy, Dr. Gnecchi moved to USA where he worked for four years. First, he was at the Brigham and Women’s Hospital (Harvard Medical School, Boston, MA), then at the Duke University Medical Center (Durham, NC). During those years, he pioneered the "paracrine hypothesis" to explain how adult stem cells repair infarcted hearts. Since 2006, Dr. Gnecchi works as Assistant Professor at the University of Pavia. Dr. Gnecchi is also consultant in Cardiology and Head of the "Laboratory of Experimental Cardiology for Cell and Molecular Therapy" at the San Matteo Hospital. In the last years, Dr. Gnecchi has won several prestigious national and international research awards. His current research interests are mainly three: stem cell paracrine mechanisms, adult stem cell differentiation and diagnostic platforms based on patient specific iPS-derived cardiomyocytes.

Marc Penn, Professor of medicine and integrated medical sciences at Northeast Ohio Medical University, and director of research at the Summa Cardiovascular Institute in Akron, USA

M.D., School of Medicine, and Ph.D., Biomedical Engineering. Case Western Reserve University, Cleveland, Ohio. Dr. Marc Penn was Director of the Center for Cardiovascular Cell Therapy, Cleveland Clinic, Cleveland, Ohio from 2008 to 2011. Before he was the Director, of the Bakken Heart-Brain Institute, and Medical Director of the Cardiac Intensive Care Unit, Department of Cardiovascular Medicine, Cleveland Clinic Foundation, Cleveland.
Daniele Torella, Assistant Professor of Cardiology, Magna Graecia University, Catanzaro, Italy.

Prof. Daniele Torella is Associate Professor in Cardiovascular Diseases at the University of Catanzaro Magna Graecia. He graduated in Medicine and Surgery at the Second Universita degli Studi di Napoli. That same year he became qualified to practice medicine. He specialized in Cardiovascular Diseases at the School of Specialization in Cardiovascular Diseases, University Federico II of Naples, directed by Prof. M. Chiarlello. He worked in the laboratory of Experimental Cardiology at the Department of Cardiology, University Federico II of Naples, directed by Prof. M. Chiarlello. He received the title of Doctor of Philosophy in the PhD course "Clinical Physiopathology and Cardiovascular Sciences and Immunological" at the University Federico II of Naples. Post-doctoral fellow in the laboratory of Dr. Bernardo Nadal-Ginard at the Cardiovascular Research Institute at New York Medical College, Valhalla, NY, USA. Instructor of Medicine, Department of Medicine, New York Medical College, NY. He worked actively as a Visiting Professor with the laboratory of dr. Bernardo Nadal-Ginard at Mount Sinai School of Medicine, New York, NY. Currently, he collaborates with the research center Corterapix directed by dr. Bernardo Nadal-Ginard at the technology park of Madrid, Madrid, Spain. Author of important studies on coronary stenting on restenosis on drug eluting stents and stem cells cardiaiche adults and their use in the field of regenerative medicine.

Stefan Janssens, Professor of Medicine and Pediatrics, University of Leuven, Leuven, Belgium

MD: Univ. of Leuven, Leuven, Belgium, 1984. PhD: Univ. of Leuven, Leuven, Belgium, 1992. Research Fellow at MGH, Harvard Univ., Boston, USA, 1989-92. VIB Group leader until 31/12/2010. Research interests: Both acute and chronic rodent models of pulmonary hypertension have been used to test the efficacy of aerosol gene transfer with genes encoding vasodilatory, antithrombotic and antiproliferative gene products. Different NO-synthase isoforms were overexpressed in the lungs to inhibit hypoxic pulmonary hypertension, as well as pulmonary vascular remodeling associated with chronic hypoxia. He will next investigate whether gene transfer strategies are able to reverse established pulmonary hypertension (deremodeling studies). Recently, he has also explored the role of cytochrome P450 epoxygenase, which mediates production of arachidonic acid metabolites with NO-independent vasoconstrictor effects via hyperpolarization of smooth muscle cells. In the years to come, he will investigate the potential of endothelial progenitor cells (EPCs) and of multipotent adult progenitor cells (MAPCs) to home in on hypertensive and remodeled pulmonary vessels to alter the imbalance between vasodilatory and vasoconstrictor mediator release. To this end, he is characterizing new rodent models of monocrotaline pyrrole-induced pulmonary hypertension.

Felipe Prosper, Director of Cell Therapy and co-director of the Hematology Department of the University Hospital of Navarra, Pamplona, Spain

Bachelor and Ph.D. in Medicine from the University of Navarra. He completed his training with a fellowship in Hematology and Oncology at the University of Minnesota. Assistant Professor at the University of Navarra. His research is focused on two main areas: the epigenetic regulation of malignancies (leukemias and myeloma) and cell therapy with adult stem cells and its application to human diseases such as cardiovascular and autoimmune diseases. In the field of cell therapy clinical trials noncommercial directed in different pathologies such as myocardial infarction, arthritis, diabetes, and vitiligo or Crohn's disease using adult stem cells, being the major focus of his laboratory translational research in this field.

Marie-Josè Goumans, Professor at the Leids Universitair Medisch Centrum, Leiden, The Netherlands

While studying biology at the University of Utrecht, she became enthusiastic about the fields of cardiovascular development and stem cell biology. After graduating, she continued her research investigating the role of TGFbeta in cardiovascular development at the Hubrecht Laboratory under the supervision of Christine Mummery. She received her PhD in 1999 from the same university with a thesis entitled: Functional analysis of TGFbeta signalling in early mouse development. She started her post-doctoral training with Prof. Peter ten Dijke at the Ludwig Institute for Cancer research in Uppsala, Sweden on a project studying the role of ALK-1 in TGFbeta signalling. When the lab of ten Dijke moved to the
Netherlands in 2000, she continued her training at the Netherlands Cancer Institute in Amsterdam where she made important contributions on how TGFβ affects endothelial cell behaviour. In 2003 she moved to the department of cardiology at the university medical center in Utrecht, where she became an assistant professor and initiate studies on cardiac progenitor cells. She was awarded a VIDI grant from NWO to study the role of cardiac progenitor cells in myocardial regeneration. In 2008, Dr Goumans became an Associate Professor at the Dept of Molecular Cell Biology at the Leiden University Medical Center. Her current research interests include cardiac commitment and differentiation of cardiac progenitor cells as well as TGFβ signalling in cardiovascular development and disease. In 2009, she became a member of the Young Academy of the KNAW, the Royal Dutch Academy of Science.

**Wolfram Zimmermann**, Professor and Director of Department of Pharmacology at Georg-August University Göttingen, Germany

Dr. Zimmermann studied at the University Medical Center Hamburg-Eppendorf, University Hamburg Duke University Medical School in Durham, North Carolina, USA, the Harvard Medical School in Boston, Massachusetts, USA and Groote Schuur Hospital, University of Cape Town, South Africa. Obtained his PhD at the Institute of Experimental and Clinical Pharmacology, University Medical Center Hamburg-Eppendorf, University Hamburg. Member of the Executive board of the German Society of Cardiology. Speaker at the Commission of Experimental Cardiology at the German Society of Cardiology. His research interest are Cell based cardiac regeneration, Cardiac tissue engineering, Stem cells, Genetic engineering of stem cells and somatic cells, Mechanisms of cardiac hypertrophy, Paracrine factors in cardiac homoeostasis, Physiological and pathological calcium handling in the heart, Genetically engineered mouse models, Skeletal muscle tissue engineering, Substance screening and target validation.

**Georgina Ellison**, Professor, Liverpool John Moores University, Liverpool, UK

After completing her PhD in Sept 2004, Geena left for the USA to undertake her post-doctoral training in the laboratory of Dr. Nadal-Ginard at New York Medical College, Valhalla and then in May 2005 they moved to the Mount Sinai Hospital, New York City. She first visited New York in Nov 2003 after becoming interested in the work being carried out on stem cell therapy and heart regeneration. Geena was particularly interested in the pioneering research being undertaken by Dr. Nadal-Ginard on resident adult Cardiac Stem Cells. She was awarded a scholarship for academic excellence in June 2003 from the British Federation of Women Graduates which allowed her to make a 6 month visit to New York to learn techniques related to isolating and characterizing cardiac stem cells from the mammalian heart. During her post-doc training in the laboratory of Dr. Nadal-Ginard she acquired ‘state of the art’ techniques for isolating and studying stem cell biology and their potential in repairing and regenerating the damaged heart. She was integrated back to the UK from the USA through the award of a Marie Curie International Re-integration grant and she has now developed and established the Stem Cell and Regenerative Biology Unit (BIOSTEM), within the Research Institute for Sport and Exercise Sciences. Geena’s main focus of research is in Skeletal Muscle and Cardiac Stem Cell biology and the mechanisms that govern stem cell fate. She also investigates homoeostasis and the response of the muscle following stress or injury. Personally, she hopes to drive the field of stem cell biology and regenerative medicine into the Sport and Exercise Science arena.

**Andreas Zeiher**, Professor and Head of the Division of Cardiology, University of Frankfurt, Germany

Dr. Zeiher received his MD from the University of Freiburg, Germany, in 1981. He was an intern and resident from 1981 - 2/1986 at the Albert-Ludwigs-University in Freiburg. From 3/1986 - 12/1987 he was a clinical research fellow at Cedars Sinai Medical Center, Los Angeles, CA, supported by a research grant from the German Research Foundation. From 1988 – 1989 he completed his fellowship in cardiology at the Albert-Ludwigs-University of Freiburg. Dr Zeiher is a fellow of the European Society of Cardiology and is past-chairman of the Working Group on Interventional Cardiology of the European Society of Cardiology. He has served on the editorial boards of several journals, including Circulation, Circulation Research, European Heart Journal and others. Dr Zeiher is currently the Co-Chairman of the Excellence Cluster Cardio-Pulmonary System (ECCPS) of the German Research Foundation (DFG). His research interests include basic and clinical aspects of endothelial cell function and atherosclerosis, the role of stem and progenitor cells for endogenous cardiovascular repair as well as their therapeutic application for regenerating cardiovascular function, and the use of biomarkers for risk prediction and therapeutic stratification of patients with acute coronary syndromes.
**Nabil Dib.** Director of Cardiovascular Research at **Mercy Gilbert & Chandler Regional Medical Centers, USA**

Dr. Nabil Dib completed his Interventional Cardiology Fellowship Program at Harvard Medical School, Beth-Isreal-Deaconess Medical Center in Boston. Dr. Dib also completed an additional year in Investigational Devices at Harvard Medical School. Additionally, he continued his education at Harvard School of Public Health, where he obtained a degree in Master of Science in Epidemiology and Research, concentrated on a clinical trial designed and effectiveness. Dr. Dib completed three years of General Cardiology at the University of Wisconsin, Milwaukee Clinical Campus at Sinai Samaritan Medical Center. His residency was in Internal Medicine at Tufts University School of Medicine and his internship at Boston University. Dr. Dib received his Medical Degree from Damascus University School of Medicine in Damascus, Syria. Currently, he is Director of Cardiovascular Research at Mercy Gilbert & Chandler Regional Medical Centers, members of Catholic Healthcare West (CHW). He is also an Associate Professor of Medicine and Director of Clinical Cardiovascular Cell Therapy, University of California San Diego, Director of Cardiovascular and Stem Cell Consultants (CSCC) and Heart Sciences Center, President and Founder of the International Society for Cardiovascular Translational Research (ISCTR) and Founder and Editor in Chief of the Journal of Cardiovascular Translational Research (JCTR).

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**Andrew Baker.** Professor of Molecular Medicine, Institute of Cardiovascular and Medical Sciences, **University of Glasgow, UK**

Dr. Andrew Baker graduated from the University of London in 1990 with a First Class BSc (Joint Honours) in pharmacology and toxicology and then studied for his PhD with the Leukaemia Research Fund at the University of Wales College of Medicine, graduating in 1994. He then joined the group led by Professor Andrew Newby for his post-doctoral work in Cardiff and developed adenoviral vectors for gene delivery studies in the cardiovascular system. This was at the very early stages of gene therapy. Dr Baker then transferred to a lectureship at the University of Bristol (Bristol Heart Institute) to continue studies on adenovirus-mediated gene transfer to assess vascular function in different model systems. At the same time he initiated his independent research programmes focusing on how to engineer delivery systems for optimal use in vivo in gene therapy applications. In 1999, Dr Baker joined Professor Anna Dominiczak’s group at the University of Glasgow as a Senior Lecturer in Molecular Medicine, then as Reader and now as Professor of Molecular Medicine. He is based at the British Heart Foundation Glasgow Cardiovascular Research Centre (BHF GCR), which is a translational centre of excellence with a focus on primary and secondary prevention at cardiovascular disease. Gene therapy aims to harness the power of the genome in a clinical relevant setting, with a focus on diseases with unmet clinical need. For his work on cardiovascular disease, this initially included the generation of replication-defective adenovirus vectors that mediated overexpression of a variety of genes including metalloproteinase inhibitors (TIMPs), inhibitors of matrix degradation in pathological conditions. These vectors were used successfully to inhibit vein graft neointimal thickening in human and pig models. He is currently engaged in research to further develop gene therapy aimed at different aspects of vein graft biology, as well as development of vectors that mediate sustained gene overexpression in vivo.

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**Ángel Raya.** ICREA Research Professor at the **Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain**

He obtained an MD in 1990 from the University of Valencia, Spain and a PhD degree from the same university in 1995 for studies carried out at the Department of Physiology and at the Department of Neurology, Mayo Clinic, Rochester, MN. He pursued postdoctoral training at the Instituto de Investigaciones Citológicas (currently, Centro de Investigación Príncipe Felipe) in Valencia, from 1995-2000. 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. He returned to Spain in 2006 and was the Scientific Coordinator at the Center for Regenerative Medicine in Barcelona until 2009, when he joined the IBEC as Group Leader of the Control of Stem Cell Potency group. His research interest are to understand the tissue, cellular and molecular mechanisms that determine the regenerative response in certain species of vertebrates, as well as the genetic and epigenetic mechanisms that control cellular reprogramming. This phenomenon provides a link between the traditional study of epimorphic regeneration and the induced pluripotency strategies of regenerative medicine.
**Asterios Tsiftsoglou**, Professor of Pharmacology and Head, Department of Pharmacy, Aristotle University of Thessaloniki, and Chairman of Biotechnology Group in the Greek National Medicine Agency, Greece


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**Keiichi Fukuda**, Professor, Department of Regenerative Medicine and Advanced Cardiac Therapeutics, Graduate School of Medicine, Keio University, Japan

Dr. Fukuda treats patients with myocardial infarction, valvular heart disease, arrhythmia and heart failure applying the latest technology as well as uncovers the cause of these diseases at the molecular level. 23 graduate school students are enrolled. About 28 years ago when he became a doctor, the heart as a function of a pump was understood, but the reason of heart disease was still uncovered and elucidating the cause of heart disease at the molecular level was not possible. However, an outstanding progress has been made in the last 20 years, and today, many of the unexplained diseases are now uncovered, and clues to start treatment are now being found. It was his childhood dream to become a scientist, and after joining the School of Medicine, he has always aimed to uncover the cause of a disease and to come up with a new treatment method. The research to regenerate muscles of the heart that he started 16 years ago hoping to save lives of patients with heart failure was just like a fantasy in those days. He started regenerating heart muscles using stem cells obtained from bone marrow, but the development of human embryonic stem cells and discovery of iPS cells have accelerated research towards clinical application. And today, this has developed to become the world's trend. Also, his research on how valvular heart disease is caused and how it develops and findings that during heart failure, the cardiac sympathetic nervous system transdifferentiates into the parasympathetic nervous system have developed to research that surprised the world's cardiologists and researchers. Today, many young people who empathize with his efforts have gathered in his laboratory, and almost 80 people including doctors, graduate students, international students, research assistants and clinical research coordinators work together.

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**Gustav Steinhoff**, Professor and Director of the Department of Cardiac Surgery and Head of the Reference and Translation Center Cardiac Stem Cell Therapy (RTC) at the University of Rostock, Germany

After his medical studies at the Erasmus University Rotterdam and the Baylor College Houston, Texas, he received his MD in 1986. Steinhoff then specialised in general surgery at the Medical School, Hannover, where he also received his habilitation in general surgery in 1993. After that he worked for three years as Staff Surgeon at the Cardiothoracic and Vascular Surgery at the University of Kiel, before he changed to the Medical School of Hannover where he was engaged as Staff Surgeon and Associate Professor of Cardiothoracic Surgery. Since 2000, Steinhoff holds the position as Professor and Director of the Department of Cardiac Surgery at the University of Rostock. In 2003, Steinhoff founded the Institute of Regenerative Medicine and Stem Cell Therapy (IRMED) in the Biomedical Research Center Rostock and since 2008, he is head of the German Reference and Translation Center of Cardiac Stem Cell Therapy (RTC). Additionally, he is a foundation member of the Leibniz Research Laboratories for Biotechnology and Artificial Organs (LEBAO) and, since 2005, is a member of the German Central Ethics Commission (ZES) for stem cell research.
INVITED SPEAKERS

Thursday, November, 29th, 2012

Anthony Mathur, Professor of Cardiology & Lead for Clinical Cardiology, Center for Clinical Pharmacology, Barts and the London, London, UK

He works as an academic at Queen Mary's and an Honorary Consultant Cardiologist at Bart and the London NHS Trust. He divides his time equally between clinical work and basic science with the aim of conducting translational research. His basic science interests have evolved from his PhD undertaken at UCL, where he gained an understanding of platelet and stem cell biology as well as cellular bioenergetics. These interests are now consolidated in his work looking at the mechanisms by which stem cells may improve cardiac function. His clinical work is directed at interventional cardiology and the management of patients with heart failure and angina who have failed conventional therapy. He is Secretary of the ESC Task force on Stem cells in cardiovascular disease and also Chair the clinical group of the British Cardiac stem cells collaborative set up by Professor John Martin. These roles have enabled him to design a series of clinical trials that will address some of the outstanding issues surrounding the use of stem cells to treat cardiovascular disease. I also have a major interest in the use of advanced cardiac imaging for translational research and have the role of Lead Clinician for Advanced Cardiac Imaging. His current basic science interests are directed at understanding the role of cell therapy in the treatment of cardiovascular disease. This covers a broad spectrum of research ranging from the study of the mechanism by which cell therapy may improve cardiac function to optimization of cell therapies to ultimately produce cardiac regeneration. My clinical research is directed at new treatments for the 'no-option' patient - that is people who have cardiac disease and no further conventional treatments available to treat ongoing symptoms. I am the chief investigator of one of the largest clinical trials to date looking at the role of stem cells in cardiac repair for patients with heart failure.

Sian Harding, Professor of Cardiac Pharmacology at the National Heart and Lung Institute, Imperial College, UK

Sian Harding obtained her Ph.D. in Pharmacology from King's College, London in 1981, and since then the primary focus of her work has been cardiomyocyte function in the failing heart. This has extended to gene therapy to modulate cardiomyocyte function, and she is Scientific PI for the UK’s first clinical trial on myocardial gene therapy. More recently the scope has extended to the characterisation of cardiomyocytes derived from embryonic stem cells, and their use in cardiac repair, tissue engineering and drug discovery. Professor Harding is Past-President of the European Section of the International Society for Heart Research and Fellow of the AHA, ESC and ISHR. She sits on the Nuffield Council on Bioethics and the Scientific Advisory Board of the PPP "Stem Cells for Safer Medicines".

David García-Dorado, Head of the Laboratory of Experimental Cardiology and Cardiovascular Research Program, Research Institute - Hospital Universitari Vall d'Hebron (VHIR), Barcelona, Spain

M.D. degree (Universidad Complutense de Madrid, 1977), Residency in Cardiology (Hospital General Universitario Gregorio Marañón (Madrid), 1980). PhD degree (Universidad Complutense de Madrid, 1985). Spanish State Board of Cardiology (Hospital General Universitario Gregorio Marañón (Madrid), 1981-1990). Spanish State Board of Cardiology (Hospital Universitari Vall d'Hebron, 1990–). Head of the Laboratory of Experimental Cardiology and Cardiovascular Research Program (Research Institute - Hospital Universitari Vall d'Hebron, 1990–). Director of the Heart Division (Hospital Universitari Vall d’Hebron, 2007). Associated Professor of Medicine (Universidad Complutense de Madrid, 1987-1990). Associated Professor of Medicine (Universidad Autónoma de Barcelona, 1999–). Co-Editor of the official basic research journal of the European Society of Cardiology Cardiovascular Research (2002–). Member of the Council of the European Section of the International Society for Heart Research (2004–). Current research interests: Pathophysiology of acute coronary syndrome; Cell death during myocardial ischemia and reperfusion; Reperfusion injury, Cardioprotection; Connexins and Gap Junctions during ischemia-reperfusion; Involvement of Mitochondria in ischemia-reperfusion-injury and cardioprotection; Systems biology, NMR-based metabolomics.
Antoni Bayés-Genís. Head of the Cardiology Service at Hospital Universitari Germans Trias i Pujol (Badalona) and Full Professor at Universitat Autònoma de Barcelona (UAB), Barcelona, Spain

He is the head of the research group IREC, with ample experience in the investigation of progenitor cells, tissular engineering, and the pathophysiology of atherosclerosis and coronary restenosis. He has published over 150 SCI papers with more than 2641 citations. He has contributed to over 100 national and international conferences in oral format. He is inventor of 6 international patents and has established several collaboration agreements with biotechnological companies.

The research group IREC (Insuficiència Cardíaca i Regeneració Cardíaca), directed by Dr Antoni Bayés-Genís, belongs to the IGTP Foundation since 2010, and works in translational research on myocardial function. The group has taken an active part in pioneering experiments on chimerism and microchimerism in the human heart and is experienced in culturing circulating endothelial progenitor cells and mesenchymal stem cells. The IREC group is also involved in tissue engineering projects on biocompatible polymers to develop bioactive structures with biomedical applications.

Sol Ruiz, Head of Sector, Biotechnology and Advanced Therapies, Spanish Medicines Agency (AEMPS), Spain

She got a PhD in Biology (Immunology) from UCM (Universidad Complutense de Madrid) in 1997 although most of the research work was done at the University of California Irvine (UCI) from 1994 till 1997. She is the vicechair and Spanish representative in the BWP (Biologics Working Party), member of the CAT (Committee for Advanced Therapies) and a co-opted member of the CHMP (Committee for Human Medicinal Products) at the EMA (European Medicines Agency). She also participates in several working groups related to biotechnological products and advanced therapies both at the EMA and at the European Pharmacopoeia.

Sanne Jansen of Lorkeers, PhD Candidate in Cardiology at the University Medical Center Utrecht, The Netherlands

Her research comprises the pre-clinical challenges in cardiac stem cell therapy for ischaemic heart disease. Another main topic is the translation of results from pre-clinical studies towards clinical application. The research is led by Prof P.A.F. Döevendans MD, and S.A.J. Chamuleau MD, PhD. Sanne received her Bachelor degree in Biomedical Sciences in 2007 and became a MD and MSc in 2012 (University Medical Center Utrecht). As a member of the CAMARADES, she aims for improving the design, analysis and reporting of pre-clinical studies by performing meta-analysis. Her former research has been presented at several international congresses.
PRACTICAL INFORMATION

Debates venue and Dinner (November 28th)

CosmoCaixa Barcelona
3D Planetarium
C/ Isaac Newton, 26 08022 Barcelona, Spain
http://obrasocial.lacaixa.es/laCaixaFoundation/home_en.html

Speakers’ hotel

Hotel The Mirror
Carrer Corséu, 255
08036 Barcelona, Spain
Phone: +34 93 202 8685
http://www.themirrorbarcelona.com/

Contact person during the event

Laia Arnal
Project Director
larnal@biocat.cat | Phone: +34 662 315 529 | +34 93 310 33 30

B·Debate
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.

More information: www.bdebate.org

Vall d’Hebron Institute of Research (VHIR) is a public sector institution that promotes and develops innovative biomedical research at Vall d’Hebron University Hospital. VHIR is oriented towards finding solutions to the health problems of population and has the will to contribute to the scientific, educational, social and economic development within its area of competence. We want our research and innovation, carried out by the individuals who make up the institution, to expand the frontiers of knowledge and become a real and important reference for our society and our health system, attracting talent and ensuring that our business in terms of excellence, quality and translation, corresponds to the leading position that the hospital must have.

More information: www.vhir.org
COLLABORATORS

As a family-owned group of companies, staying true to our values is particularly important. One of the features that stands out when analyzing the Palex Group's evolution over three generations since its formation in 1955 is the support it has consistently provided to health professionals, its dedication to the quest for innovation in products, machines and systems, and its perseverance in maintaining a high level of quality in all areas of its business activity. Fruit of this business policy, the company has continuously brought Advanced Hospital Solutions to the Spanish and Portuguese health markets, with ground-breaking products and systems for use in medicine and surgery. The Palex Group introduced the first "Shiley" pivoting disc heart valve in 1969. It was also during this year that it decisively contributed to the development of hemodialysis with its products and services. In 1988, it started to market the "Jarvik" artificial heart. It also pioneered the implementation of minimally invasive heart surgery. In 1999, it formed the Key Accounts Division with the--at that time--innovative goal of concluding one-stop service agreements with leading hospitals, offering Advanced Hospital Solutions managed by a team of specialists. At present, Palex is making significant contributions to the fields of telemmedicine, remote presence and robotization of surgery and oncology.

But the best recognition for our corporate culture are the fruitful and lasting relationships we have with the companies we represent, our customers and our suppliers.

More information: www.palexmedical.com

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More information: www.biomenco.com
OUTCOMES

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, presentations, 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 “UNSOLVED PROBLEMS IN HEART REPAIR”:

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