

# SYNTHETIC BIOLOGY: ENGINEERING LIFE FOR THE MEDICINE OF THE FUTURE

## 01

WELCOME

Page 3

---

## 02

PROGRAM

Page 4

---

## 03

SCIENTIFIC COMMITTEE

Page 7

---

## 04

DETAILED PROGRAM

Page 8

---

## 05

PRACTICAL INFORMATION

Page 21

---

## 06

SUGGESTED READING

Page 22

---

## 07

OUTCOMES

Page 24

---

## 08

ORGANIZERS, COLLABORATORS AND SPONSORS

Page 25

---

## 09

NOTES

Page 27

---



# SYNTHETIC BIOLOGY: ENGINEERING LIFE FOR THE MEDICINE OF THE FUTURE

June 13th and 14th, 2019

## WELCOME

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Dear Speakers and Participants,

It is our pleasure to welcome you for the meeting "The Barcelona Debates on the Engineering life on the medicine of the future". This event is possible thanks to the great support of B-DEBATE, an initiative of Biocat and Obra Social "la Caixa", and the will of 2 research institutions, the Centre for Genomic Regulation (CRG) and the Pompeu Fabra University (UPF)

Synthetic Biology is defined as the rational engineering of biological systems to develop applications. Engineering life is revolutionizing medicine with thousands of clinical trials in gene therapy on-going, and the development of advanced new therapies. Novel therapies include the therapeutic modification of human genomes, genetically modified bacteria with enhanced properties or engineered animals for xenotransplantation. Synthetic biology is having impact beyond therapy and wellbeing. Together with AI, biotechnology is driven to become a fundamental component of the 4<sup>th</sup> industrial revolution. It drives to a new era in a wide variety of fields, including sustainable energy, industrial and food production, or bioremediation.

The different sessions of this B-DEBATE are composed by top experts from various scientific disciplines: technology development in gene editing, microbiome engineering, microbial applications, gene therapy/clinical deployment, and bioethics. The meeting will engage also with sessions focused on technology transfer and translation, and about societal impact of engineering life for therapeutic purposes.

The conference will be focused on medical applications of engineering life. A forum will be created to foster discussion between top scientists, to engage industry and society and to promote scientific advancement and its sustainable translation into economic and health benefits. The debate will highlight new tools development for genome engineering and new applications to diverse problems in biotechnology. It will focus in life science and medicine, also facing the ethical and philosophical concerns raised since its appearance, including in the conversation not only researchers but also the general public.

We encourage you to actively participate in the discussions and wish you a fruitful meeting over the next two days.  
Yours sincerely,

Luis Serrano, Marc Güell, Maria Lluç-Senar and B-DEBATE

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# PROGRAM

Thursday, July 13, 2019

|       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 9:30  | <b>Registration &amp; welcome coffee</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| 10:00 | <b>Welcome</b><br><b>Maria Lluch-Senar</b> , Centre for Genomic Regulation (CRG)<br><b>Montserrat Capdevila</b> , "la Caixa" Banking Foundation<br><b>Jordi Naval</b> , Biocat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 10:15 | <b>SESSION 1. Basic tool development</b><br>Chair: <b>Marc Güell</b> , Pompeu Fabra University (UPF), Barcelona<br><br><b>The human microbiome: from metagenomes to therapeutics</b><br><b>Julia Oh</b> , The Jackson Laboratory, USA<br><br><b>Predicting communication efficiency in synthetic microbial consortia</b><br><b>Jordi García-Ojalvo</b> , Pompeu Fabra University, Barcelona                                                                                                                                                                                                                                                                                                                                                                          |
| 11:25 | <b>Coffee break and networking</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 12:00 | <b>Pioneering live biotherapeutics in the respiratory tract</b><br><b>Maria Lluch-Senar</b> , Centre for Genomic Regulation, Barcelona<br><br><b>Therapeutic strategies via genome and transcriptome engineering</b><br><b>Prashant Mali</b> , UC San Diego, US                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 13:10 | <b>SESSION 2. Synthetic biology of microbial systems</b><br>Chair: <b>Maria Lluch-Senar</b> , Centre for Genomic Regulation (CRG), Barcelona<br><br><b>Good news and bad news: The microbes rule the Earth (including ourselves)</b><br><b>Victor de Lorenzo</b> , Spanish National Centre for Biotechnology, Madrid, Spain                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 13:45 | <b>Lunch</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| 14:45 | <b>HiBIT: bringing the power of bioluminescence to protein detection at endogenous levels</b><br><b>María Jurado</b> , Promega, Madrid, Spain<br><br><b>Terraforming the planet: Using synthetic biology to avoid ecological tipping points</b><br><b>Ricard Solé</b> , Pompeu Fabra University, Barcelona<br><br><b>Synthetic biology approaches applied to genetically intractable organisms: From the identification of virulence factor to the construction of new vaccinal strains</b><br><b>Carole Lartigue</b> , French National Institute for Agricultural Research, Bordeaux, France<br><br><b>Direct modulation of the skin microbiome as potential therapy for Acne vulgaris: a pilot study</b><br><b>Bernhard Paetzold</b> , S-Biomedic, Beerse, Belgium |

**Short presentations:**

- **Evolving new antimicrobials**  
**Daniela A. Garcia-Soriano**, Pompeu Fabra University, Barcelona
- **PepID technology combines multi-genome wide surface protein analyses with peptide high density arrays and mapping of expressed epitopes for vaccine development**  
**Josef Maier**, ATG:biosynthetics GmbH, Merzhausen, Germany

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17:30    **End of the session**

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## Friday, July 14, 2019

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9:30    **Registration & welcome coffee**

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9:45

**SESSION 3. Synthetic biology for human therapy**

Chair: **Francesc Posas**, Pompeu Fabra University, Barcelona

**Genome Editing for Human Therapeutics**

**Matthew Porteus**, Stanford Medicine, US

**Lentiviral Gene Therapy and Genome editing for the treatment of a Rare Hemolytic Disease, Pyruvate Kinase Deficiency**

**José Carlos Segovia**, Centre for Energy, Environment and Technology Research, Madrid, Spain

**Synthetic biology for human therapy: CAR T-cells against tumors**

**Manel Juan Otero**, Hospital Clínic de Barcelona, Barcelona

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11:30    **Coffee break and networking**

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12:00

**Implementing Biological computation with Distributed Multicellular Consortia**

**Francesc Posas**, Pompeu Fabra University, Barcelona

**Engineering E. coli bacteria for the injection of proteins into tumor cells**

**Luis Ángel Fernández**, Spanish National Centre for Biotechnology, Madrid, Spain

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13:15    **Lunch**

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14:15

**SESSION 4 (round table). Translational directions of Synthetic biology**

Chair: **Luis Serrano**, Centre for Genomic Regulation (CRG), Spain

**Laia Crespo**, Sanofi Ventures, France

**Sylvain Sachot**, Asabys Partners, Barcelona

**Lluís Pareras**, Invivo Capital and Healthequity, Barcelona

**John L. Collins**, SynbiCITE, UK

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15.45

**Coffe break and networking**

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**16:00    SESSION 5. Ethics, Philosophy and Scientific responsibility. Video projection and Open Discussion.**

Chair: **Pere Estupinyà**

**Lluís Montoliu**, Spanish National Centre for Biotechnology, Madrid, Spain

**Sonja Erikainen**, The University of Edinburgh, UK

**Marc Güell**, Pompeu Fabra University, Barcelona

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**17:30    Closing remarks and farewell**

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# SCIENTIFIC COMMITTEE



**Luis Serrano**, Director of Centre for Genomic Regulation (CRG), Barcelona, Spain

Luis Serrano did his PhD at the CBM (Madrid, Spain) on Cell Biology. Then he spent 4 years in the laboratory of Prof. A.R. Fehrst (MRC, UK) working in protein folding. In 1993, he became Group Leader at the EMBL (Heidelberg, Germany) working in Protein Folding and design. Ten years later, he was appointed head of the Structural & Computational Biology programme at the EMBL and he started to work on Systems Biology. By the end of 2006 he moved back to Spain to lead a programme working on Systems Biology, where he was appointed vice-director before finally becoming the CRG director on July 2011.

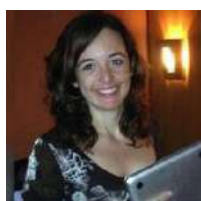
He is a member of the Spanish Society for Biochemistry and Molecular Biology (SEBBM), member of the European Molecular Biology Organization (EMBO), and member of the Royal Spanish Academy of Sciences (Spain). In 2003 he received the Marie Curie Excellence Award, in 2009 he was awarded the City of Barcelona prize (science category), an annual award organized by Barcelona City Council and in 2018 the Francisco Cobos award (<http://fundacionfranciscocobos.org/>).

In recent years he has won four prestigious grants from the European Research Council, two ERC Advanced Grants and two ERC Proof of Concept grants. He is Professor of ICREA and has directed 18 PhD thesis. He has published more than 360 papers in international journals. He was involved in the creation of one of the first Spanish Biotech Companies (Diverdrugs) in 1999. And co-founder of Cellzome, EnVivo and TRISKEL companies. He has been Director and Founder of the association of European Institutes of Excellence EU-LIFE, as well as of the equivalent association at Spanish level, SOMMA.



**Marc Güell**, Tenure-Track professor and Principal Investigator at Translational Synthetic Biology, Pompeu Fabra University, Barcelona, Spain

My research interests are focused on technology development in Synthetic Biology. My laboratory is currently centered on applied mammalian gene editing for therapeutic purposes and skin microbiome engineering. I'm principal investigator and Assistant Professor at Pompeu Fabra University, founding scientist at Egenesis Biosciences (xenotransplantation, [egenesisbio.com](http://egenesisbio.com)), and cofounder of Sbiomedic (skin microbiome thx, [sbiomedic.com](http://sbiomedic.com)).



**Maria Lluch-Senar**, Staff scientist and associate researcher at Centre for Genomic Regulation (CRG), Barcelona, Spain

Dr. Maria Lluch-Senar did her PhD in the Institute of Biotechnology and Biomedicine. During her thesis, she started to work with Mycoplasmas, developing genetic tools and studying cell division and virulence. In 2010, she started as postdoc in the group of Professor Luis Serrano, studying *Mycoplasma pneumoniae* by Systems Biology approaches. In 2013 she was promoted to staff scientist (associate researcher). She co-coordinates part of the group of Design of Biological Systems, working in Synthetic biology approaches to engineer *M. pneumoniae* for human therapeutic use. She was involved in the identification of signals to expose and secrete therapeutic proteins by MycoChassis and, in the design and characterization of the two first products that the intended spin-off "Pulmobiotics" aims to develop as proof of concept. She has long-standing experience in systems and synthetic biology. She published 20 articles, of which 15 in the last 6 years, in international peer-reviewed scientific journals (h-index 11; mostly in journals belonging to Q1, and >50% to D1, of their respective fields). In recognition to her scientific trajectory she received two international awards (Luis Denis Award (2012) and the Derrick Edward Award (2016)). In addition, she was recognized as an independent researcher by getting the Miguel Servet grant (ISCIII, 2016) and she is co-coordinator of a H2020 grant (MycoSynVac) and partner in a CSA H2020 grant (BioRobost) and supervisor of EraSynBio (MiniCell).

# DETAILED PROGRAM AND INVITED SPEAKERS

Thursday, July 13, 2019

## Session 1: Basic tool development

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**Marc Güell**, Tenure-Track professor and Principal Investigator at Translational Synthetic Biology, **Pompeu Fabra University**, Barcelona, Spain

**Chair of session 1.**  
Read bio in page 7.

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**Julia Oh**, Assistant Professor at **The Jackson Laboratory**, Farmington, USA

Julia Oh received her B.A. from Harvard University and her Ph.D. in genetics from Stanford University. As a graduate student, she developed technologies for high-throughput gene annotation and drug-target discovery in pathogenic fungi. As a postdoctoral fellow at the National Institutes of Health, she studied the human skin microbiome, focusing on microbiome-host interactions and how changes in the microbiome can result in skin disease. In 2015, she joined The Jackson Laboratory as an assistant professor. The goal of her laboratory is to combine high-resolution computational reconstructions of the microbiome with synthetic biology to devise innovative approaches to create novel therapeutic interventions and investigate the underlying ecology of microbial communities.

### The human microbiome: from metagenomes to therapeutics

The human skin harbors an abundant microbial ecosystem with bidirectional metabolic exchanges supporting symbiotic and commensal functions. Sequence-based analysis of microbial community structure and organization of the human microbiome has yielded valuable insight into the microbial diversity and function of its different body niches. Metagenomic analyses of the diverse skin sites in healthy humans demonstrate that contrasting forces of the skin's biogeography and individual characteristics shape the skin microbiome and the dynamics of its bacteria, fungi, and viruses. However, shifts in the ecological properties of the skin microbiome are significantly associated with skin disease, disease severity, and other physiologic host factors such as age or primary immunodeficiency. Understanding the function, structure, and dynamics of the microbiome is important to design therapeutics that precisely target the pathogen of interest, yet spare the surrounding beneficial microbiota.

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**Jordi Garcia-Ojalvo**, Professor at the **Pompeu Fabra University**, Barcelona, Spain

Jordi Garcia-Ojalvo obtained his PhD in statistical physics at the University of Barcelona in 1995. He did postdoctoral work at the Georgia Institute of Technology in Atlanta in 1996, working on laser dynamics, and at the Humboldt University of Berlin in 1998 as an Alexander von Humboldt Fellow, studying noise effects in excitable media and neuronal systems. In 2003 he was IGERT Visiting Professor at Cornell University in Ithaca, New York, at which time he began working in the field of systems biology. In 2008 he became Full Professor at the Polytechnic University of Catalonia, where he had been teaching applied physics since 1991. He is Visiting Research Associate in Biology at the California Institute of Technology since 2006, and joined the Pompeu Fabra University as Full Professor in October 2012, where he leads the laboratory of Dynamical Systems Biology. His laboratory studies the dynamics of living systems, from unicellular organisms to human beings. He uses a variety of experimental biochemical and electrophysiological data to constrain computational models of living systems, and thereby unravel the underlying mechanisms of physiological processes in both natural and synthetic systems.



## Predicting communication efficiency in synthetic microbial consortia

The microbiome is quickly becoming an important target for clinical applications, in particular within the context of synthetic biology approaches. An important feature of the microbial communities inhabiting our bodies is their ecological diversity. Indeed, our microbiota consists of a large variety of bacterial species that live together and interact closely, influencing each other by sharing resources and exchanging molecular signals. It is thus natural to contemplate synthetic cell-cell communication among bacterial species as a potentially useful medical strategy in the midterm. But building synthetic intercellular communication systems is non-trivial. This approach would therefore benefit from being able to anticipate the degree of successful communication as a function of the relative abundances of the different bacterial species forming the synthetic community. Here we present a theoretical framework to address this issue, and describe our ongoing experimental efforts to validate it.



**Maria Lluch-Senar**, Staff scientist and associate researcher at Centre for Genomic Regulation (CRG), Barcelona, Spain

Read bio in page 7.

## Pioneering live biotherapeutics in the respiratory tract

Engineering bacteria to deliver locally therapeutics to treat diseases is an emerging area of research with great clinical potential. Working with the human lung bacterium *M. pneumoniae*, we developed proprietary methods and tools to engineer it to treat severe lung diseases such as ventilator associated pneumonia (VAP). VAP is a disease with significant unmet need that in many cases does not respond to antibiotics and can lead to death. During one decade, we have collected essential know-how to engineer *M. pneumoniae*:

- i) Virulence factors and signals promoting optimal secretion and exposure of proteins were identified;
  - ii) Novel genetic tools were implemented to obtain an attenuated (non-pathogenic) chassis ("MycoChassis") and further engineer it;
  - iii) Safety of MycoChassis has been validated in vivo in mice;
  - iv) Delivery of several therapeutic agents by the MycoChassis has been achieved;
  - v) We have obtained two first products (VAP\_PB1 and VAP\_PB2) to treat biofilms of *S. aureus* and *P. aeruginosa*, respectively;
  - vi) Shown that VAP\_PB1 can dissolve *S. aureus* biofilms formed in vivo in a mice catheter model;
  - vii) Shown that VAP\_PB2 can dissolve *P. aeruginosa* biofilms in vitro more effectively than conventional antibiotics;
  - viii) We have developed an animal component-free medium that will facilitate production as GMP for clinical applications.
- At present, we are evaluating safety it in healthy pigs, and the efficacy on acute in vivo mice models of *P. aeruginosa* infection.



**Prashant Mali**, Assistant Professor at University of California San Diego, San Diego, USA

Prashant Mali received a bachelor's and master's in Electrical Engineering from the Indian Institute of Technology Bombay, with a research focus on solid-state biosensors; and a doctorate in Biomedical Engineering at the Johns Hopkins University, with a research focus on human pluripotent stem cell engineering. During his postdoctoral fellowship in the Department of Genetics at the Harvard Medical School, he pioneered the development of the CRISPR-Cas systems for eukaryotic genome engineering. For his graduate work he received the Siebel Scholar Award in 2011, and in 2014 he received the Burroughs Wellcome Career Award at the Scientific Interface. Mali joined the University of California, San Diego faculty in Fall 2014 as an assistant professor in the Department of Bioengineering. In 2016 he received the March of Dimes Basil O'Connor Scholar Award, the Kimmel Scholar Award, and was named a Kavli Frontiers of Science Fellow. In 2017 he received the Young Alumnus Achiever Award from the Indian Institute of Technology Bombay India. Research in his laboratory lies at the interface of basic science and technology development, with a core thrust in developing tools for engineering biology towards enabling gene and cell based human therapeutics.

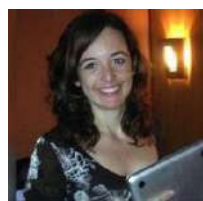
## Therapeutic strategies via genome and transcriptome engineering

The recent advent of RNA-guided effectors derived from clustered regularly interspaced short palindromic repeats (CRISPR)-CRISPR-associated (Cas) systems have dramatically transformed our ability to engineer the genomes of diverse organisms. As unique factors capable of co-localizing RNA, DNA, and protein, tools and techniques based on these are paving the way for unprecedented control over cellular organization, regulation, and behavior. These are also poised to hugely impact our ability to enable in situ human gene therapeutics. However efficaciously achieving some of these objectives will entail research and development of aspects including and beyond the CRISPR-Cas systems. In this regard, I will describe here some of our ongoing efforts towards engineering corresponding toolsets.

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## Session 2. Synthetic biology of microbial systems

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**Maria Lluch-Senar**, Staff scientist and associate researcher at Centre for Genomic Regulation (CRG), Barcelona, Spain

**Chair of session 2.**

Read bio in page 7.

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**Víctor de Lorenzo**, Professor of Research at Spanish National Research Council (CSIC), Madrid, Spain

Víctor de Lorenzo (Madrid, 1957) is a Chemist by training and he holds a position of Research Professor in the Spanish National Research Council (CSIC), where he currently heads the Laboratory of Environmental Molecular Microbiology at the National Center for Biotechnology. After his PhD at the CSIC Institute of Enzymology (1983), he worked at the Pasteur Institute (1984), the University of California at Berkeley (1985-1987), the University of Geneva (1988) and the Federal Center for Biotechnology in Braunschweig until 1991, the year in which he joined the CSIC in Madrid. He specializes in Molecular Biology and Biotechnology of soil bacteria (particularly *Pseudomonas putida*) as agents for the decontamination of sites damaged by industrial waste. In 2001 this work received the National Award Rey Jaime I for Environmental Protection.

In June 2008 he was honored with the GSK International Award of the American Society for Microbiology, and in October of the same year he was granted a Grand Prix of the French Academy of Sciences. He is a member of the EMBO (European Molecular Biology Organization) and the American Academy of Microbiology, and he has co-chaired with Drew Endy the EC-US Working Group on Synthetic Biology. He has published well over 300 articles in scientific journals and specialized books (<https://goo.gl/M4sA5N>) and he has served as advisor of numerous international panels. At present, his work explores the interface between Synthetic Biology and Environmental Biotechnology, supported inter alia by an Advanced Grant of the European Research Council.

### Good news and bad news: The microbes rule the Earth (including ourselves)

Microorganisms were on planet Earth much before we arrived and they will survive much after we become extinct. The role on bacteria in running the bio-geological cycles of the Biosphere, their being causal agents of infectious diseases (and the associated problem of antibiotic resistance) and their domestication for biotechnological purposes -whether industrial, agricultural or environmental has been both in the textbooks and in the popular culture for quite a few decades. But the development of massive DNA sequencing and the onset of extreme genetic engineering (e.g. Synthetic Biology) is exposing a degree of dependence on extant and new-to-nature microbial activities which was by no means suspected just a few years ago. The pillars of this new scenario include [i] the access to the composition and activities encoded in environmental DNA, from open settings (e.g. soil, water, Oceans etc) to animal-associated microbiomes [ii] the dissection of the molecular interplay between the human body and the whole of bacteria which colonize each of our bodily niches. This relationship goes much beyond a mere metabolic interchange and occasional episodes of disease. It involves also a suite of bioactive molecules that mediate both individual well-being (e.g. neuroactive agents) and inter-human interactions, [iii] the deep

engineering of microorganisms as live chassis for engineering of intricate traits e.g. cell factories for production of complex molecules, live therapeutic agents and multi-scale environmental interventions for pollution prevention/remediation (including climatic change) and [iv] the refactoring and repurposing of genetic devices found in the bacterial world, for example the CRISP/Cas9 system for genome engineering. Unlike traditional views, microorganisms are not just our foes to combat for overcoming infectious diseases -but our only allies for facing phenomenal challenges where our fate is at stake.

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**María Jurado**, Technical Service and Application Support Manager at **Promega**, Madrid, Spain

Degree in Biology (UCM) and Biochemistry (UAM). PhD in Molecular Biology in 2010 (UAM). PhD and post-doc (one year) at Severo Ochoa Molecular Biology Center (Madrid). Stays in Molecular Biology Institute (Copenhaguen) and Neuroscience Research Center-Merck Sharepoint and Dohme (Harlow, UK). Joined the Technical Service Department at Promega Biotech Ibérica in 2011. Head of the Technical Services Department since 2012. Application Support Scientist Manager since 2017. Course in Leadership and Team Management by ESADE in 2018. Promega is a multinational biotechnology company (headquarters in Madison, WI) with branches all around the world. Our branch covers Spain and Portugal. My team offers technical and scientific support to customers and also to our sales team and distributors, covering our whole portfolio (around 4000 references): PCR products, cloning, nucleic acid purification, cell health assays, other cell-based assays, gene expression, STRs genetic identification, proteomics, nucleic acid extractors, luminometers, etc. We also help customers adopting our technologies for new applications, and support or prepare webinars/seminars covering new technologies that our R&D department develop, among other functions.

### **HiBiT: bringing the power of bioluminescence to protein detection at endogenous levels**

HiBiT technology simplifies protein tagging in live cells, providing a streamlined, antibody-free protocol for detecting tagged proteins that requires only a luminometer for detection. With the dynamic range to detect proteins in live cells without overexpression, and the convenience of a single-reagent-addition method, HiBiT technology opens up a universe of possibilities for researchers studying protein biology. HiBiT technology makes CRISPR-mediated tag knock-ins accessible by eliminating the need for molecular cloning prior to insertion. HiBiT technology has been used in receptor internalization studies or studies on protein abundance, quantifying proteins down to endogenous levels, even those maintained at low expression levels. Different PROTACs have been evaluated using this technology.

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**Ricard Solé**, ICREA research professor and head of the Complex Systems Lab at **Pompeu Fabra University**, Barcelona, Spain.

Ricard Solé is ICREA research professor (the Catalan Institute for research and Advanced Studies) currently working at the Pompeu Fabra University, where he is the head of the Complex Systems Lab located at the PRBB. He teaches undergraduate courses on Biomathematics, principles of biological design and cell-tissue engineering.

He completed degrees in both Physics and Biology at the University of Barcelona and received my PhD in Physics at the Polytechnic University of Catalonia. He is also External Professor of the Santa Fe Institute (New Mexico, USA). His main goal is understanding the evolutionary origins of complexity and innovation.

His current research includes synthetic evolutionary transitions, unstable evolution, liquid brains and network theory.

### **Terraforming the planet: Using synthetic biology to avoid ecological tipping points**

As the perception of climate emergency becomes widespread, our planet faces potential tipping points that threaten the social, economic and ecological stability. Temperature increases beyond the 2°C limit might trigger a runaway effect toward aridity will cause transitions from vegetated to desert states in semiarid habitats, where a third of the current human population lives. Plastics are becoming a major concern to public health. Can interventions based on the engineering and deployment of synthetic microorganisms help avoiding major shifts? Such possibility should be considered as part of the agenda and future plans targeting the origins and consequences of the Anthropocene.

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**Carole Lartigue**, Principal Scientist at French National Institute for Agricultural Research, France, Bordeaux, France

Her scientific path has started in a context where genetic tools were lacking for the functional genomics of mollicutes while genome sequences were getting available for several species. During her PhD studies in A. Blanchard lab's, most of her work has been dedicated to the development of replicative plasmids and transformation methods that could take advantage of all the knowledge from the genome sequence to investigate cell physiology and host-pathogen interactions. Then, she joined

Dr. J. Glass' group as a post-doctoral fellow to work on the emerging so-called synthetic biology (SB) project developed at the J. Craig Venter Institute. There, she was one of the main actors who accomplished the complete chemical synthesis of a mycoplasma genome, its assembly into yeast and its transplantation into a phylogenetically related recipient cell. This work opened the way to many developments for the study and the manipulation of mollicutes and, hopefully in the future, many other micro-organisms. Now, she's working as a principal scientist in A. Blanchard lab's, and her team is at the front line of the major developments in synthetic biology field.

### **Synthetic biology approaches applied to genetically intractable organisms: From the identification of virulence factor to the construction of new vaccinal strains**

During the past decade, synthetic biology (SB) methods have emerged as powerful approaches for accelerating the engineering of microorganisms with a growing impact on fundamental questions as the molecular organization of living systems and on a wide range of applications from human health to industrial biotechnology.

One of the most remarkable milestones was obtained by the J. C. Venter Institute with the cloning of a mycoplasma genome in yeast, its engineering using efficient genetic tools and its back transplantation into a suitable recipient cell. First developed with *Mycoplasma mycoides* subsp. *capri* (Mmc) as donor genome and *Mycoplasma capricolum* subsp. *capricolum* (Mcap) as recipient cell, SB methods are currently being improved and extended to other bacterial species. Even though the mechanisms and genetic determinants required for successful genome transplantation are still largely unknown, our results show that the phylogenetic distance between the donor cell and the recipient cell is a key parameter for transplantation. This finding is in agreement with the requirement for the host machinery to be able to read the genetic information carried by the incoming genome, to direct protein synthesis and to replicate this genome.

As in-yeast genome engineering and subsequent back transplantation has been now achieved for a number of pathogenic strains of ruminant mycoplasmas, new ways to develop attenuated strains and potential tailor-made vaccine strains have emerged. This strategy is currently being used to develop new vaccines against mycoplasma diseases of utmost importance. Main steps include: cloning a mycoplasma genome into yeast, deletion of virulence genes to get a non-pathogenic chassis, expression of selected antigens at the surface and back transplantation to get a living bacteria which can then be evaluated as a candidate vaccine. A better knowledge of the *Mycoplasma* virulence traits and proteins that induce efficient immune responses would also be of great benefit for the development of rationale vaccines and the improvement of livestock protection.



**Bernhard Paetzold**, CSO at S-Biomedic, Beerse, Belgium

Bernhard completed his PhD in synthetic biology, working together in collaboration with the pharmaceutical industry to engineer bacteria as a living pill. He is a scientific co-founder of S-Biomedic, and is leading the research and product development. S-Biomedic is engineering the skin microbiome by adding certain strains or establishing new communities. His passion is understanding the complex interplay of the bacterial communities that live within and on us. He is fascinated by the untouched potential of active compounds that are naturally produced every day right on our own skin.

### **Direct modulation of the skin microbiome as potential therapy for *Acne vulgaris*: a pilot study**

**Background and objectives:** An imbalance in the skin microflora and strains of *Cutibacterium acnes* (previously *Propionibacteria acnes*), may explain the cause of acne. This leads to the hypothesis that by application of the beneficial,

non-acne causing strains of *C. acnes* on the skin, a shift in the microbiome of the skin, leading to acne reduction may be possible. The current pilot study aims to assess safety and efficacy of such microbiome modulation on acne-prone skin.

**Methods:** This single-blind study had an active induction phase (5% benzoyl peroxide gel for 7 days) and an interventional treatment phase (5 weeks). Patients were randomized to one of the two topical skin formulations A2 (2 strains of *C. acnes* Single Locus Sequence Typing [SLST] type C3 and K8, 50% each) or B4 (4 strains of *C. acnes* SLST type C3 [55%], K8 [5%], A5 [30%] and F4 [10%]). Safety was assessed by experienced dermatologists and efficacy evaluated based on lesion count, skin pH and sebumeter measurements.

**Results:** Fourteen patients were included (A2=8/14, B4=6/14). The skin microbiome composition shifted towards the composition of the two formulations. No untoward tolerability issues, visible irritation, or significant flare-up were observed. Non-inflamed lesions and skin pH were reduced. High background counts impeded measurement of sebum production.

**Conclusion:** Clinical improvements were observed in all patients without any further deterioration of acne. Further studies are required to validate the stability, efficacy and safety of the two formulations in acne patients. (German Clinical Trials Registry number: DRKS00015717)

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## Short presentations:

**Daniela A. Garcia-Soriano**, Pompeu Fabra University, Barcelona.

### Evolving new antimicrobials

In our current society, we require eco-friendly and efficient ways of production. Nature has always offered us an immense array of compounds with different chemical properties and applications. An important type of this natural products includes polyketides (PKs) produced by polyketide synthases (PKSs). Normally PKs have been produced using native organisms, but given the hurdle to maintain them in the lab, the production was changed to model organisms such as *Escherichia coli*. Our main goal is to develop a platform for the development of new antimicrobials. We will first generate PKs and glycosylation libraries using multiplexed genome engineering (MAGE) as a genome editing technology and later, we will use those libraries to produce bioactive molecules. Given the interchangeability of PKs modules, some of them might be novel molecules for the market. We aim to synthesise them in vivo as well as in vitro harvesting the power of cell as miniaturise factories to produce molecules of interest.

**Josef Maier**, ATG:biosynthetics GmbH, Germany.

### PepID technology combines multi-genome wide surface protein analyses with peptide high density arrays and mapping of expressed epitopes for vaccine development

Infectious diseases resulting from the increasing prevalence of antibiotics resistance phenomena in pathogenic bacteria are also caused by Mycoplasma species in atypical pneumonia. Emerging viruses like the West Nile, Zika or Chikungunya virus conquering new geographic areas are threats which need to be tackled on different independent levels in order to assure the health of human populations and its domestic animals. Besides the screening for new antibiotics, complementary approaches selectively programming the immune system with artificially designed stimuli are promising improvement of protection against infectious diseases. For this purpose ATG:biosynthetics is presently developing an efficient new workflow which improves the discovery of new diagnostic and therapeutic epitopes. Starting with available genomic data, we integrate molecular biodiversity of all relevant strains to increase the scope of protection. Simultaneously we minimize molecular complexity by removing redundancy as well as by considering structure and function of the antigens to be analyzed. As a result, PepID's computational algorithms allow us to generate rationally designed, deterministic DNA-encoded peptide libraries. Such libraries will be expressed and submit to antibody recognition either by colony immunoblotting or by cell surface display technology. Our objectives are to increase the specificity of the diagnostic repertoire, to improve the experimental significance and to maximize the efficacy of multi-epitope vaccines. In addition, our efforts are aiming to increase the successful outputs in terms of neutralizing activity. We will present different levels of bioinformatics approaches we are following as well as a demonstration of the proof of concept of the PepID-technology and

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## Friday, July 14, 2019

### Session 3. Synthetic biology for human therapy

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**Francesc Posas**, Director of Institute for Research in Biomedicine (IRB) Barcelona and Professor of Biochemistry and Molecular Biology at **Pompeu Fabra University**, Barcelona, Spain

**Chair of session 3.**

Francesc Posas is Full Professor at the Universitat Pompeu Fabra (UPF) and the Director of IRB Barcelona (Institute for Research in Biomedicine (2018-)). After obtaining his doctorate in Biochemistry and Molecular Biology at the Universitat Autònoma de Barcelona (1995), he made a postdoctoral stay at Harvard University (Boston, USA). From 1999 co-leads the Cell Signaling Research Group (<https://www.irbbarcelona.org/en/research/cell-signaling>). He was the chair of the Department of Health and Experimental Sciences at the UPF (2007-2013), Vice-rector for Science Policy at the UPF (2013-2017) and Commissioner for UPF scientific strategy (2017-2018). Dr. Posas received the award to Young Investigators from the Catalan Government (2001), EMBO Young Investigator Program (2000), EURYI to young investigators (ESF) (2004), EMBO member (2006), awarded with an ICREA Academia (2009-2014) and the "Carmen and Severo Ochoa" Award (2011). Co-Recipient of an ERC Advanced Grant (2012).

Dr. Posas' and de Nadal's group aim to unravel how cells detect and respond to environmental changes, focusing on the characterisation of stress signal transduction pathways, especially those regulated by MAP kinases of the Hog1/p38 family, also known as the stress-activated MAP kinases (SAPKs). Proper adaptation to stress involves the modulation of several basic aspects of cell biology, among them the cell cycle and gene expression. Using *S. cerevisiae* budding yeast as a model organism, as well as higher eukaryotic cells, the group dissects the molecular mechanisms underlying cell response to changes in the extracellular environment and characterising the adaptive responses required for cell survival. Based on the knowledge of signal transduction and using synthetic biology, they also seek to modify cell behaviour to reprogram cell response to specific inputs/stimuli.



**Matthew Porteus**, Professor of Paediatrics at **Stanford Medicine**, Stanford, USA

Matthew Porteus MD, PhD is a Professor in the Department of Paediatrics and Institute of Stem Cell Biology and Regenerative Medicine and Child Health Research Institute at Stanford. His primary research focus is on developing genome editing as an approach to cure disease, particularly those of the blood but also of other organ systems as well. His research program has made important discoveries in advancing the field of genome editing including the first use of genome editing using engineered nucleases in human cells and optimizing the use of the CRISPR/Cas9 system in primary human stem cells. He also works as an attending physician on the Paediatric Hematopoietic Stem Cell Transplant service at Lucile Packard Children's Hospital where he cares for children under going bone marrow transplantation for both malignant and non-malignant diseases. His goal is to combine his research and clinical interests to bring innovative curative therapies to patients. He served on the National Academy Study Committee of Human Genome Editing and as a History and Science major at Harvard he wrote his undergraduate thesis on the social interpretation of the recombinant DNA controversy in the early 1970s.

#### **Genome Editing for Human Therapeutics**

Genome editing provides a method to change the DNA sequence of a cell with single nucleotide precision. The most efficient approach to genome editing is to induce a site-specific DNA double-strand break and the CRISPR/Cas9 system has made

genome editing broadly accessible to the scientific community because of its ease of design, high activity and excellent specificity. We have developed a genome editing system using the *S. pyogenes* Cas9 system combined with AAV6 delivery of a donor molecule to achieve high frequencies of genome editing in primary therapeutically relevant human cells. This system is efficient to permit multiplexed targeted knock-ins. I will discuss our progress towards applying the system to develop genetically engineered cell based drugs for human disease. I will also briefly review the stringent criteria that the National Academy Study Committee on Human Genome Editing proposed should be adopted before germline editing might be attempted. These strict criteria, while not a direct call for a moratorium, would, if adopted, provide a functional moratorium to its use in humans.



**José Carlos Segovia Sanz**, Head of Division at Center for Energy, Environment and Technology Research, Madrid, Spain

Dr. José Carlos Segovia has focused his research on the study of hematopoietic stem cells (HSC), their interaction with viral pathogens, their ex vivo purification and manipulation and, on gene transfer of Hematopoietic Stem Cells, with the aim of developing gene therapy protocols for the treatment of genetic diseases with hematopoietic pathology. He is currently the Head of the Cellular Technology Division at the Center for Energy, Environmental and Technological Research (CIEMAT). He has published more than 100 scientific articles in journals of high impact in the areas of Gene Therapy and Cell Therapy, has participated in more than 45 projects, being a Principal Investigator of more than 10 and has obtained 7 patents, one of them already licensed. During the last years he has focused his research on the development of gene therapy protocols for Pyruvate Kinase Deficiency (PKD). He has achieved the Orphan Drug Designation by the European Agency and the American Agency for Medicines (EMA and FDA, respectively) for an addition gene therapy drug, which will be used in the first-in-human gene therapy clinical trial for PKD. He has coordinated meetings with PKD affected patients in Spain and Europe, to report on the progress being made with this new therapy. Recently, he has applied the new technologies of gene editing to the treatment of PKD. As a result of these studies, he has published 3 scientific papers and presented a patent that is in the process of being approved. He has directed three workshops of gene editing during the last years. Dr. Segovia is also a collaborator in master's degrees in biotechnology and biomedicine taught at various public and private universities and is the assistant coordinator of the Genetic Engineering module at the Biotechnology Master's Degree at the Francisco de Vitoria University. Finally he has been vocal and secretary of the Spanish Society of Gene and Cell Therapy and currently vice president of the Iberian Cytometry Society.

### **Lentiviral Gene Therapy and Genome editing for the treatment of a Rare Hemolytic Disease, Pyruvate Kinase Deficiency**

The modification of the genome is increasingly becoming recognized as a safe and effective strategy to treat genetic diseases, many of which are life-threatening or associated with extensive morbidity. Some therapies have been already approved by the regulatory agencies, such as Strimvelis™, approved by the European Medical Agency (EMA) for the treatment of Adenosine Deaminase (ADA) inherited immunodeficiency. With the improvement of gene editing tools that allow precise integration of desired genetic sequences, the possibility of making this technology a clinical option is becoming a reality. We are working to develop all the aforementioned modalities for the treatment of Pyruvate Kinase Deficiency, a genetic hemolytic anemia with extensive morbidity and likely diminished life-expectancy.

Pyruvate kinase deficiency (PKD) is an autosomal recessive disorder caused by mutations in the PKLR gene leading to a reduction of the activity of erythroid pyruvate kinase (RPK) protein. This disease is associated with reticulocytosis, splenomegaly and iron overload, and may be life-threatening in severely affected patients. Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) has been shown to correct the disorder; however this is associated with extensive toxicity. Autologous HSCT of genetically corrected cells is intended to provide a durable and curative therapeutic option. Preclinical gene therapy studies conducted in pyruvate kinase deficient mice have shown safety and efficacy of a new PGK-coRPK-Wpre therapeutic lentiviral vector that has been granted orphan drug designation by the European Medicine Agency (EU/3/14/1330) and the US Food and Drug Administration (FDA#DRU-2016-5168).

A first-in-human PKD gene therapy clinical trial has been recently presented to the FDA and the Spanish Medical Agency and the trial is anticipated to start during the following months. Over the last years, gene editing has emerged as a promising gene therapy approach for blood cell disorders. To correct PKD in human HSPCs, we set up a knock-in gene editing strategy at the genomic starting site of the PKLR gene by combining RNP electroporation and adeno-associated viral vector (AAV6) carrying donor sequences. Specific gRNAs generating up to 60% indels at the RPK starting site in human Cord Blood CD34+ (CB-CD34+) were designed. Two different AAV6 constructions were produced to deliver a TurboGFP expression cassette or a promotor-less therapeutic codon optimized RPK cDNA (coRPK), flanked by specific homologous arms. Up to 40%

specific integration and stable expression of both donors was detected in colony forming units generated from gene edited CB-CD34+ cells, without evident toxicity related to the procedure. Moreover, these edited CB-CD34+ cells engrafted efficiently in both primary and secondary NSG mice, demonstrating the gene editing of HSCs. Overall, gene therapy for PKD is approaching clinical-stage and may offer a potentially curative alternative for PKD patients.

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**Manel Juan Otero**, Head of Immunotherapy Section at Hospital Clínic, Barcelona, Spain

Degree and Doctorate: Medicine and Surgery (1988 and 1994). Clinical specialty: Immunology (1994). **CLINICAL WORK:** Head of immunotherapy Section; Immunology Service (2007 -). Direct Responsibilities; - Cell immunotherapy + Cytometry coordination + 2 main approaches: DCs + CART. **TEACHING:** Assistant Professor (2015 -). Department of Medicine. Medical School, Universitat de Barcelona (UB). Assistant Professor of Immunology (1997- 2007). A3.3 level. Medical School.

UAB. Coordinator in master of autoimmune diseases (UB); 9 directed doctoral theses (5 co-directed). **RESEARCH (SUMMARY):** 80 articles in journals with IF (3 national and 71 international); 105 papers in total. Total IF: 497.321. Publications in last 5 years: 16. Summatory impact factor: 152.952. Communications: 75 National + 87 International Congresses. 2 active projects + 10 previous projects as Principal Investigator + 16 projects as a research collaborator. 3 licenced patents (3 PCT).

### **Synthetic biology for human therapy: CAR T-cells against tumors**

T-cells transduced with a Chimeric Antigen Receptor (CAR) is already one of the available treatments against CD19+ B-cell leukemias and lymphomas, but hundreds of clinical trials with other CARs are locating this immunotherapy as one of the most promising proposals. CART combines gene therapy tools (mainly lenti and retrovirus) in T-cells, with cell therapy processes to obtain by ex-vivo manipulation a cell product to be reinfused into the patient. Although in general CART is defined as an autologous drug, donor-obtained product (allogeneic drug) are also done with the aim to have an "off-the-shelf" drugs. In any case there are still a lot of work to improve constructs, introduce gene editing for transduction, increasing efficacy of the current proposals, reducing adverse effects ... In fact, CRS and Neurotoxicity are severe adverse effects that should be improved.

It is quite clear that if we want to go one step forward, the improvement of CART antitumoral proposal should continue and probably only collaboration between pharma and academic proposals can assure this strong and continuous development. Our experience in Hospital Clínic of Barcelona with CART19-BE-001 CT is our first model for developing an Academic Clinical Trial in Spain, although we have additional proposals for the most near-future pipeline.

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**Francesc Posas**, Director of Institute for Research in Biomedicine (IRB) Barcelona and Professor of Biochemistry and Molecular Biology at Pompeu Fabra University, Barcelona, Spain

Read bio in page 14.

### **Implementing Biological computation with Distributed Multicellular Consortia**

Engineering approaches to synthetic biology have shown that there are a number of strategies allowing to build complex functional constructs with computational abilities. There are a number of efforts towards building artificial computational devices that could be used for a wide range of applications, including bioremediation, food production or biomedicine. Using yeast as a model organism we have been able to implement complex circuits by distributing computation within cellular consortia. This approach to biological computation has opened the possibility to develop a novel method of properly design general purpose which can be combined in multiple ways to create complex computational circuits. The potential use of this approach is demonstrated by implementation of complex logical functions responding to up to six inputs, the building of a synthetic biological memory switch or a circuit with an incoherent feed-forward loop architecture (FFL) to generate single pulse responses or implementing reprogrammable biological devices. Our results might serve as a blueprint for future development of biocomputing cellular devices.

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**Luis Ángel Fernández**, Principal Investigator at **Spanish National Center for Biotechnology (CNB-CSIC)**, Madrid, Spain

Luis Ángel Fernández obtained his PhD in 1995 in the Department of Molecular Biology, Universidad Autónoma de Madrid, and was a postdoctoral fellow in the Department of Microbiology and Immunology, School of Medicine, University California, San Francisco. Later, a postdoctoral fellow and Ramón y Cajal investigator of the Department of Microbial Biotechnology of CNB-CSIC. Since 2005 he leads a research group in this department aimed to study protein secretion systems from pathogenic bacteria and to exploit their biotechnological potential. His current work focuses on engineering *E. coli* bacteria for biomedical applications, including the design of *E. coli* strains for cancer therapy using synthetic biology.

### **Engineering *E. coli* bacteria for the injection of proteins into tumor cells**

This presentation summarizes research work in my laboratory aimed to engineer *E. coli* bacteria for the controlled and specific delivery of therapeutic proteins into the cytosol of tumor cells, using a type III secretion system (T3SS). We engineered the expression of functional filamentous injectisomes from enteropathogenic *E. coli* (EPEC) in the non-pathogenic commensal *E. coli* K-12 strain, by reformatting the EPEC operons encoding T3SS structural proteins and chaperones. The resulting strain, named Synthetic Injector *E. coli* (SIEC), was shown to translocate a natural EPEC effector called Tir (for translocated intimin receptor) into HeLa cells (Ruano-Gallego et al., 2015). Recent work has demonstrated that other effector proteins can be efficiently delivered by SIEC into mammalian cells. In addition, we have shown that SIEC can translocate a number of heterologous proteins (e.g. antibody fragments) into human and mouse cell lines. In order to provide cell specificity for protein injection, we have investigated the expression of synthetic adhesins (SAs) in SIEC bacteria. SAs are protein fusions developed in our laboratory displaying single-domain antibody fragments (nanobodies) on the bacterial surface. SAs can mediate the efficient attachment of *E. coli* bacteria to mammalian cells expressing a surface antigen recognized by the nanobody domain (Piñero-Lambea et al., 2015). Our results indicate that SAs expressed in SIEC allow the targeted delivery of a protein payload into tumor cells.

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## **Session 4 (round table). Translational directions of Synthetic biology**

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**Luis Serrano**, Director of **Centre for Genomic Regulation (CRG)**, Barcelona, Spain

**Chairs of session 4.**  
Read bio in page 7.

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**Laia Crespo**, Head of Europe at **Sanofi Ventures**, Paris, France

Laia joined Sanofi Ventures in 2018 with a background in biotech. Prior to Sanofi, Laia was Investment Director for Ysios Capital, where she served on the Boards of OxThera, Minoryx Therapeutics, Inbiomotion and AM-Pharma. Earlier in her career, Laia was part of the European New Business Development team of Janssen-Cilag (Johnson & Johnson). Previously she worked as a researcher in the UK in companies such as Spirogen (now AstraZeneca), Medivir and UCB-Celltech.

Laia graduated in Chemistry from the University of Barcelona, where she also completed a PhD with honors. Laia holds an MBA from Cambridge Judge Business School, University of Cambridge.

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**Sylvain Sachot**, Investment Director at **Asabys Partners**, Barcelona, Spain

Sylvain Sachot is investment director at Asabys Partner. Sylvain joined Asabys in 2018 from Ysios Capital, where he was an associate responsible for sourcing and diligence of investment opportunities in the fields of biopharmaceuticals and medtech. He was particularly involved in the investments in Corwave and Vivet Therapeutics in France, Anaconda Biomed in Spain, Xeltis in Switzerland, Galecto and Oxthera in Sweden. Previously, Sylvain was a postdoctoral fellow in the department of Genetics and Genomic Sciences at the Mount Sinai School of Medicine in New York. He obtained his Ph.D. in Molecular Medicine from University of Nantes in 2009. Biotechnologist by training, Sylvain particularly focused during his (post)doctoral studies in the field of gene and cell therapy and lysosomal storage disorders. He has a broad understanding of the needs and the trends in the biopharma and medtech industries.

Sylvain obtained his master's degree in biotechnology with honors from University Paris XII. He also completed an MBA at Esade Business School in Barcelona in 2014. Sylvain has full professional proficiency in French, English and Spanish.

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**Lluís Pareras**, Founding Partner at **Invivo Capital**, Barcelona, Spain

Degree and PhD in Medicine, specialist in Neurosurgery, and Global Executive MBA (IESE). He founded the "Innovation and entrepreneurship program" at the Barcelona Medical Association (CoMB), where he has been coaching entrepreneurs and he has founded and directed the Healthcare Investment Forums since 2009. He has been an entrepreneur himself in the healthcare space and raised capital from investors. Deeply involved in the innovation ecosystem, he is a member and advisor of many healthcare innovation organizations such as Biocat (Board of Trustees), CIMTI, BarcelonaActiva Mentoring Program, Generalitat de Catalunya-CASOST and HEALTHIO among others. Author of numerous books in the field of innovation, venture capital and healthcare, such as "Innovation and Entrepreneurship in Healthcare", published internationally. In the academic space, he has been a teacher in several business schools about healthcare innovation and venture capital.

He remains as the Director of Healthequity, SCR, a venture capital fund focused in early-stage companies in the healthcare sector, where he led the investment strategy and transaction processes of the different portfolio companies. Member of the Board of Directors of different life-sciences companies including Healthequity's investments: Versantis, n-life Therapeutics and Minoryx Therapeutics.

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**John L. Collins**, Operations & Commercial Director at **Imperial College London (SynbiCITE)**, London, UK

John is Operations & Commercial Director of the UK National Centre for commercialising Engineering Biology - SynbiCITE - at Imperial College London. SynbiCITE is growing industry based on using the engineering of biology to 'do useful things & make useful stuff to heal us, feed us, fuel us & sustain us'. John helps turn 'upstarts into start-ups and start-ups to become grown ups' through business incubation & acceleration programmes, such as the '4-Day MBA: More Business Acumen'® course that has been run all around the UK & has, so far, produced more than 360 new entrepreneurially-minded technologists ready to start a start-up & 24 start-ups! For several years since 2010 John ran the UK's 'Emerging Technologies and Industries' programme at InnovateUK and BEIS, tasked with taking new, disruptive technologies and promoting them to Government for support to become industries of tomorrow; several are now part of UK government's Industrial Strategy. The one John is most proud to have ensured funding is Synthetic Biology – the technology that will grow a new industry solving global challenges. Prior to this John has had a varied portfolio career including R&D, product development, technical sales, business development, international development for a trade association, innovation and digital creativity growth in educational services.

Throughout his careers John has run his own 'Disruptive Technologies and Innovations Management' consultancy – Innovation Foundry Ltd. – and continues to work with a diverse spread of technologies, services and creative industry. He sits on UK government Programme Expert Groups covering the National Measurement Service for digital, chemical, biological, advanced manufacturing, life sciences, and environmental metrology & standards. John is also Chair of the Real Time Club – the world's oldest technology networking club, running 52 years – working with leading philosophers, scientists & technologists promoting 'technology for good'.

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## Session 5. Ethics, Philosophy and Scientific responsibility. Video projection and Open Discussion.

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**Pere Estupinyà**, Science Communicator, Madrid, Spain

Pere Estupinyà is a biochemist, writer and science communicator. He is the author of the books “El ladrón de cerebros” (Debate, 2010), “S = EX2: La ciencia del sexo” (Debate, 2013) and “Comer cerezas con los ojos cerrados” (Debate, 2016). He currently co-presents the science section of the program “A Vivir” on Cadena Ser, writes in several media, and directs and presents the program “El Cazador de cerebros” on TVE. Before returning to Spain he lived eight years in the USA (2007-2015), where he was Knight Science Journalism Fellow at the Massachusetts Institute of Technology (MIT).

He also worked at the Media Branch of the National Institutes of Health (NIH), was a consultant for the Inter-American Development Bank (IDB), wrote the acclaimed blog “Apuntes Científicos desde el MIT” in El País, and began to travel throughout Latin America, giving lectures and consultancies to companies and organizations. He is considered one of the most original writers and thinkers in the field of the current scientific and technological revolution.

### Chair of session 5.

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**Lluís Montoliu**, CSIC Research Scientist at **National Center for Biotechnology (CNB-CSIC)**, Madrid, Spain

Lluís Montoliu (Barcelona, 1963) is a biologist (UB, 1986) and PhD in molecular genetics (CID-CSIC and UB, 1990) working as CSIC Research Scientist at the Spanish National Centre for Biotechnology (CNB) in Madrid, where he has been leading his laboratory since 1997, after two postdoctoral periods at the German Cancer Research Center (DKFZ, Heidelberg, 1991-95) and at UAB (Barcelona, 1995-96). He joined in 2007 the Biomedical Research Networking Center on Rare Diseases (CIBERER-ISCIII) as Group Leader, where he was appointed in 2016 coordinator of the CIBERER Neurosensory Disorders area and member of the CIBERER Steering committee. He is also Honorary Professor at the Autonomous University of Madrid since 1998, and Director of the European Mouse Mutant Archive (EMMA/INFRAFRONTIER) Spanish node since 2007. His lab is interested in understanding how genes are organized within mammalian genomes and has used different genetically-modified animals (mostly mice and zebrafish) to investigate the role of several non-coding DNA regulatory elements. He has been a leading contributor of the technology of artificial-chromosome-type transgenes. He has also generated numerous animal models of human rare diseases, such as albinism. Recently, he has pioneered the use of CRISPR-Cas9 tools in mice for the functional understanding of DNA regulatory elements and the production of new mouse models of different types of albinism. He is a member of the CSIC Ethics Committee since 2006 and of the ERC Ethics Panel since 2013. In 2006, he founded the International Society for Transgenic Technologies (ISTT) for which he has served as President from inception to 2014. He currently is President of the European Society for Pigment Cell Research (ESPCR) and serves at the board of additional scientific societies such as IMGS and IFPCS.



**Sonja Erikainen**, Research Fellow at **Centre for Health, Technologies and Social Practice (University of Leeds)** and **Centre for Biomedicine, Self and Society (University of Edinburgh)**, Edinburgh, UK

Sonja Erikainen is a research fellow at the University of Leeds Centre for Health, Technologies and Social Practice and a visiting fellow at the University of Edinburgh Centre for Biomedicine, Self and Society. Her research focuses on ethical, social and historical issues around biomedicine and biotechnology, with an emphasis on questions concerning equitable governance and social justice. Her work has covered areas including experimental therapy, systems medicine and digital health innovation, sport science and performance enhancement technologies. More recently, she has also been working on social and ethical approaches to participatory medicine, knowledge exchange and public engagement with science.

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**Marc Güell**, Tenure-Track professor and Principal Investigator at **Translational Synthetic Biology (Pompeu Fabra University)**, Barcelona, Spain

Read bio in page 7.

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# PRACTICAL INFORMATION

## Venue: CosmoCaixa Barcelona

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

**Conference room**  
Àgora (-2 floor)

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## Contact person during the event

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### **Marta Soler**

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[www.bdebate.org](http://www.bdebate.org) | [www.biocat.cat](http://www.biocat.cat)

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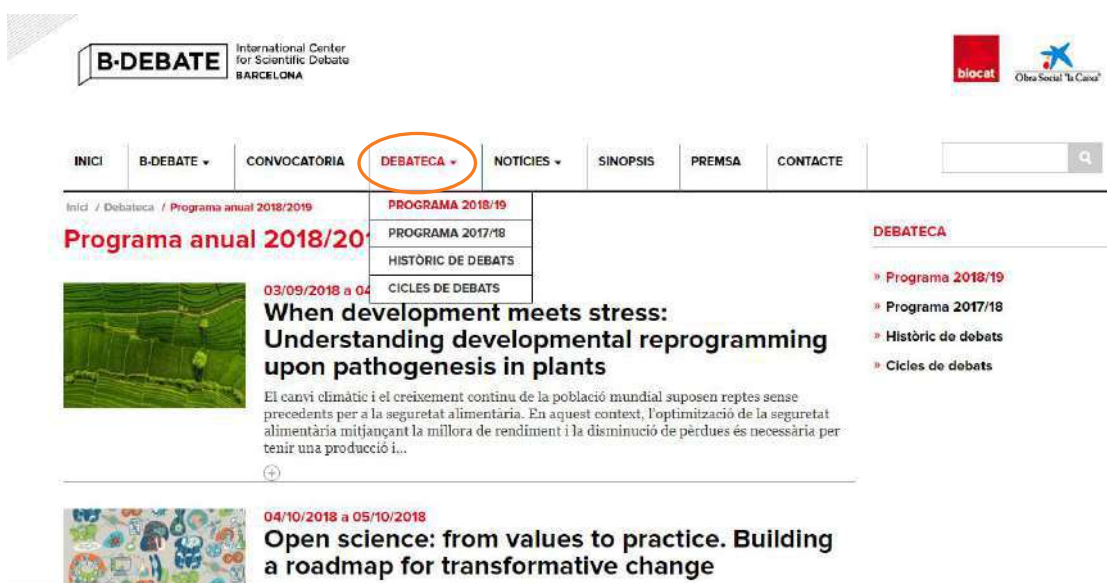


# OUTCOMES

## 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](http://www.bdebate.org)

Contents of the meeting: **"Synthetic biology. Engineering life for the medicine of the future"**



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# ORGANIZERS

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International Center  
for Scientific Debate  
BARCELONA



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

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

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

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The **Centre for Genomic Regulation (CRG)** is an international biomedical research institute of excellence, created in December 2000. It is a non-profit foundation funded by the Catalan Government through the Departments of Business & Knowledge, the Spanish Ministry of Science, Innovation & Universities, the "la Caixa" Banking Foundation, and includes the participation of Pompeu Fabra University.

The mission of the CRG is to discover and advance knowledge for the benefit of society, public health and economic prosperity. The CRG believes that the medicine of the future depends on the groundbreaking science of today. This requires an interdisciplinary scientific team focused on understanding the complexity of life from the genome to the cell to a whole organism and its interaction with the environment, offering an integrated view of genetic diseases.

The CRG is a unique centre in Spain, based in an innovative organization research model. Group leaders at the CRG are recruited internationally and receive support from the centre to set up and run their groups. An external Scientific Advisory Board, made up of 15 world leaders in the different areas, evaluates them. The result of evaluations conditions the future of the CRG scientists, no matter whether they have open-ended or time-limited contracts. This ensures the mobility and the renewal of the workforce.

More info: <http://www.crg.eu/>

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# COLLABORATORS

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Annually, infections caused by *Mycoplasma* bacteria in poultry, cows, and pigs result in multimillion Euro losses in the USA and Europe. An effective vaccine for livestock would increase animal welfare, decrease disease management expenses and reduce the environmental footprint of food production.

The coordinated EU-project MycoSynVac aims at using cutting-edge synthetic biology methods to engineer *Mycoplasma pneumoniae* as a universal chassis for vaccination. We (1) modify existing methods of genome transplantation used for *Mycoplasma* species, (2) develop serum-free medium for scale-up in bioreactors and (3) analyze how to bring the product to market after efficacy of the vaccine has been shown in animal studies, ultimately to fight *Mycoplasma* infections in farm animals.

More information: <https://www.mycosynvac.eu/>

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# SPONSORS

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Originally founded in 1978 in Madison, Wisconsin, USA, Promega has branches in 16 countries and more than 50 global distributors serving 100 countries.

With a portfolio of more than 4,000 products covering the fields of genomics, protein analysis and expression, cellular analysis, drug discovery and genetic identity, Promega is a global leader in providing innovative solutions and technical support to life scientists in academic, industrial and government settings.

Promega products are used by life scientists who are asking fundamental questions about biological processes as well as by scientists who are applying scientific knowledge to diagnose and treat diseases, discover new therapeutics, and use genetics and DNA testing for human identification.

More information: <https://www.promega.es>

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# NOTES

Handwriting practice lines consisting of 28 horizontal dotted lines.

