REVERSING A DYSTOPIAN FUTURE
NEW STRATEGIES TO DISCOVER ANTIBACTERIAL AGENTS

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Dear Speakers and Participants,

It is our pleasure to welcome you for the meeting "Reversing a dystopian future. New strategies to discover antibacterial agents". This event is possible thanks to the great support of B-DEBATE, an initiative of Biocat and “la Caixa” Foundation, and the will of Barcelona Institute for Global Health (ISGlobal).

Bacterial resistance to antimicrobial drugs is a serious problem in many respects: it threatens our ability to treat infectious diseases, increases health costs, and poses a serious risk to the progress made in global health by individuals and communities in the past decades. Infections caused by multidrug resistant (MDR) bacteria are globally recognized as an emergent disease and antimicrobial resistance is a priority for global health action as declared by institutions such as the World Health Organization and the European Centre for Diseases Control. In order to fight antimicrobial resistance we need to promote innovation, research and the development of new tools.

This B-Debate offers a vision of the state-of-the-art of novel strategies that are currently being developed to fight against MDR bacteria, including the design, search and development of new antimicrobial agents, as well as policies and strategic interventions to tackle antimicrobial resistance. Moreover, there will be debates in order to explain and discuss in an open way the concerns and benefits of new research strategies in a controversial field such as health.

We encourage you to actively participate in the discussions and wish you a fruitful meeting over the next three days.

Yours sincerely,

Jordi Vila, Sara M. Soto, Clara Ballesté-Delpierre and B-DEBATE
PROGRAM

Tuesday, November 12, 2019

15:00   Registration & welcome coffee

15:15   Welcome
Antoni Plasència, Barcelona Institute for Global Health (ISGlobal)
Àngel Font, “la Caixa” Banking Foundation
Cristina Bescos, EIT Health Spain
Marta Soler, Biocat

15:30   DAY 1: STATE-OF-THE-ART OF ANTIMICROBIAL RESISTANCE
SESSION 1
Chair: Sara Soto, Barcelona Institute for Global Health (ISGlobal), Barcelona

Overview of the current situation of antimicrobial resistance
Jordi Vila, Barcelona Institute for Global Health (ISGlobal), Barcelona

The economic challenges of antimicrobial resistance
Laurence Roope, Health Economics Research Centre (HERC), Oxford, UK

Current pipeline of new antibiotics
Ursula Theuretzbacher, Centre of Anti-Infective Agents, Vienna, Austria

16:30   Coffee break and networking

17:00   SESSION 2
Chair: Jordi Vila, Barcelona Institute for Global Health (ISGlobal), Barcelona

Old drugs revisited
Jesús Rodríguez-Baño, Hospital Universitario Virgen Macarena, Seville, Spain

Antibiotic combination therapy
Javier Garau, Clínica Rotger Quirónsalud, Palma de Mallorca, Spain

Do we really need new antimicrobials?
Luis Martínez-Martínez, University Hospital Reina Sofia and University of Cordoba, Córdoba, Spain

18:00   Networking cocktail
Wednesday, November 13, 2019

9:00  Registration & welcome coffee

9:20  **DAY 2: NEW APPROACHES FOR THE DISCOVERY OF NEW ANTIMICROBIAL AGENTS**
**SESSION 3**
Chair: Clara Ballesté-Delpierre, Barcelona Institute for Global Health (ISGlobal), Barcelona

- **Secondary metabolites with antibacterial activity**
  Olga Genilloud, Fundación Medina (IIMENA), Granada, Spain

- **Oceans as natural source of antibiotics**
  Sara Soto, Barcelona Institute for Global Health (ISGlobal), Barcelona

- **Design of synthetic antibiotics**
  Domingo Gargallo-Viola, ABAC Therapeutics, Barcelona

10:20  Coffee break and networking

10:50  **SESSION 4**
Chair: Sara Soto, Barcelona Institute for Global Health (ISGlobal), Barcelona

- **Microbiota as a therapeutic approach**
  Àlex Soriano, Hospital Clínic, Barcelona

- **Novel mAbs Against Serious *Pseudomonas aeruginosa* infections: Are We Ready for a Paradigm Change?**
  Hasan Jafri, AstraZeneca, Gaithersburg, USA

- **New drug delivery systems to treat bacterial infections**
  Eduard Torrents, IBEC, Barcelona

- **Efficacy and tolerability of a cocktail of bacteriophages against *Pseudomonas aeruginosa* to treat infected burn wounds**
  Patrick Jault, Paris, France

- **Nano technology for AMR infections**
  Joan Gavaldà, VHIR, Barcelona

12:30  Lunch

13:30  **SESSION 5**
Chair: Jordi Vila and Climent Casals, Barcelona Institute for Global Health (ISGlobal), Barcelona

- **Antimicrobial cyclic peptides: the case of polymyxins**
  Francesc Rabanal, University of Barcelona, Barcelona

- **Harnessing the power of protein aggregation to develop new antibiotics**
  Els Beirnaert, Aelin Therapeutics, Leuven, Belgium

- **Reversing β-lactam resistance with new β-lactamase inhibitors**
  Jean-Denis Docquier, University of Siena, Siena, Italy

- **Antivirulence drugs**
  Younes Smani, Institute of Biomedicine of Seville, Seville, Spain
14:50  Coffee break and networking

15:10  **Novel antibiotics effective against gram-positive and -negative multi-resistant bacteria with limited resistance**  
_Brice Felden_, Rennes University, Rennes, France

15:30  **Discussion panel: Open discussion on new research strategies**  
Chair: _Javier Vega_, EIT Health Spain, Barcelona  
_Brice Felden_, Rennes University, Rennes, France  
_Domingo Gargallo-Viola_, ABAC Therapeutics, Barcelona  
_Eduard Torrents_, IBEC, Barcelona  
_Olga Genilloud_, Fundación Medina (IIMENA), Granada, Spain

16:00  Closing remarks and farewell

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_Thursday, November 14, 2019_

9:00  Registration & welcome coffee

9:20  **DAY 3: BEYOND THE DISCOVERY OF NEW ANTIMICROBIAL AGENTS**  
**SESSION 6**  
Chair: _Rafael Vilasanjuan and Jordi Vila_, Barcelona Institute for Global Health (ISGlobal), Barcelona

**Flash talks**  
Moderator: _Jordi Vila_, Barcelona Institute for Global Health (ISGlobal), Barcelona

Jury:  
_Domingo Gargallo-Viola_, ABAC Therapeutics, Barcelona  
_Núria Martí_, Biocat, Barcelona  
_Seamus O’Brien_, GARDP, Geneva, Switzerland

10:10  **How to stimulate innovation in the public and private sectors?**  
_Joan Bigorra_, Barcelona Institute for Global Health (ISGlobal), Barcelona

**Science and policy interface: JPIAMR**  
_Laura Marin_, JPI-AMR, Stockholm, Sweden

**Public-Private Partnership to address the public health challenge of antibiotic resistance**  
_Seamus O’Brien_, GARDP, Geneva, Switzerland

11:20  Coffee break and networking

11:50  **Wellcome Trust Initiatives to tackle antimicrobial resistance**  
_Gemma Buckland-Merrett_, Wellcome Trust, London, UK

**The role of Marie Sklodowska-Curie actions in the fight against Antimicrobial Resistance**  
_Gaetano Castaldo_, European Commission-Research Executive Agency, Brussels, Belgium
12:20  **Discussion panel: Open discussion on the discovery of new antimicrobial agents**
Chair: **Jordi Vila**, Barcelona Institute for Global Health (ISGlobal), Barcelona

  **Joan Bigorra**, Barcelona Institute for Global Health (ISGlobal), Barcelona
  **Laura Marin**, JPI-AMR, Stockholm, Sweden
  **Seamus O’Brien**, GARDP, Geneva, Switzerland
  **Gemma Buckland-Merrett**, Wellcome Trust, London, UK
  **Gaetano Castaldo**, European Commission-Research Executive Agency, Brussels, Belgium

12:50  **Closing remarks and farewell**
Jordi Vila, Head of the Department of Clinical Microbiology at Hospital Clinic and Research Professor, Director of the Antimicrobial Resistance Initiative and Head of the Viral and Bacterial Infections Programme at ISGlobal, Barcelona

Dr. Vila is the Head of the Department of Clinical Microbiology of the Hospital Clinic in Barcelona, Full Professor of the School of Medicine, University of Barcelona, and Research Professor in the Institute for Global Health (ISGlobal) of Barcelona, Spain. In this last institution, he is leading the initiative on “Antimicrobial Resistance”. His main fields of interest are the research on the molecular basis of antimicrobial resistance as well as development of new drugs against MDR bacteria and molecular tools for rapid diagnosis of infectious disease. Dr. Vila was the Programme Director of the Congress of ESCMID from 2009 to 2014, and member of the ICAAC from 2007 to 2010. He has received several awards, the last one being “Award of the National Plan against Antibiotic Resistance (PRAN) 2018 for the Micro-combat card game, presented by the Barcelona Global Health Institute Foundation (ISGlobal) in the category of better communication and public awareness initiative on the antibiotic resistance”. He is currently the president of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC). He has published 425 articles in peer-reviewed journals. He has patented two molecules.

Sara María Soto, Associate Research Professor at Barcelona Institute for Global Health (ISGlobal), Barcelona

She completed her Bachelor’s degree in Biology from the University of Oviedo. She obtained my PhD degree in 2002 at the University of Oviedo. In this initial period, she obtained a 4-year PhD Grant from the Spanish Ministry of Education being awarded with the “Extraordinary Doctorate Award”. She spent her postdoctoral period at the Federal Institute for Risk Assessment (BfR), Berlin (Germany) and at the IDIBAPS (Barcelona, Spain). In 2005, she obtained the Miguel Servet research contract from the Spanish Ministry of Health that allowed her to establish as independent researcher. Nowadays, she is Associate Research Professor at ISGlobal and Associate Professor at the University of Barcelona. She has published 60 international articles, eight invited reviews, four book chapters. She has directed two doctoral theses and three are in progress. She is Coordinator of a H2020 European Project “NOMORFILM” directed to search new antimicrobial agents from microalgae and PI of several projects directed to search new synthetic molecules with antibacterial activity.

Clara Ballesté-Delpierre, Coordinator of the Antimicrobial resistance Initiative at Barcelona Institute for Global Health (ISGlobal), Barcelona

Clara is a Doctor in Biology from the University of Barcelona. She has a degree in Human Biology from the Pompeu Fabra University where she also completed a Master in Pharmaceutical and Biotechnology Industry. Before starting the doctorate, she worked for two years as a researcher at the R&D center of the pharmaceutical laboratories Ferrer Internacional, S.A. in new antibacterial discovery projects. Subsequently, and in this same context, she worked on the search for new antituberculosis drugs at the Biosafety 3 facilities of the Animal Health Research Center (CreSA) in Bellaterra. In 2011 she began as a PhD student at ISGlobal in the research group “Molecular basis of antibiotic resistance” led by Dr. Jordi Vila. His research was focused on studying the relationship between resistance acquisition to the family of antibiotics called quinolones and their effect on virulence in Salmonella enterica.

She currently assumes the role of Coordinator of the Antibiotic Resistance Initiative and is Project Assistant of Dr. Vila’s research group.
Tuesday, November 12, 2019

**DAY 1: STATE-OF-THE-ART OF ANTIMICROBIAL RESISTANCE**

Session 1

**Sara María Soto**, Associate Research Professor at **Barcelona Institute for Global Health (ISGlobal)**, Barcelona

Chair of session 1.

Read bio in page 8.

**Jordi Vila**, Head of the Department of Clinical Microbiology at **Hospital Clinic** and Research Professor, Director of the Antimicrobial Resistance Initiative and Head of the Viral and Bacterial Infections Programme at **ISGlobal**, Barcelona

Read bio in page 8.

**Overview of the current situation of antimicrobial resistance**

From a holistic point of view, antimicrobial resistance (AMR) is a steadily increasing problem associated with multiple factors. Different scenarios can be envisaged among which the use of antibiotics contribute to the emergence of multidrug resistant bacteria. The WHO coined the term of “One health” to define the interaction between animals, humans and the environment when AMR is discussed. Therefore, the interventions to decrease the emergence and spread of multidrug resistant bacteria (MDRB) should be taken at different levels and in an integrated way. However, these measures that could be taken, will not generate zero resistance, therefore new antibiotics are need. In the last years the number of available antimicrobial agents active against resistant pathogens has decreased, reducing the therapeutic options to treat infections due to MDRB. Although MDR pathogens are mainly causing infections in the hospital, the figures regarding infections caused by MDR bacteria in the community are increasing. When resistance to first-line drugs increases, infections last longer and become more expensive to treat, with hospitalization required in many cases. This situation increases health costs and poses a serious risk to the progress made in global health by countries, communities and individuals in the past decades. In fact, a report published by Lord Jim O’Neill indicates that annually over 700,000 people die worldwide due to infections caused by MDR pathogens, and it is predicted that this number will achieve 10 million deaths by 2050 unless new policies and actions are implemented.

**Laurence Roope**, Senior Researcher at **Health Economics Research Centre, University of Oxford**, Oxford, United Kingdom

Dr Laurence Roope is a Senior Researcher at the Health Economics Research Centre, part of the Nuffield Department of Population Health at the University of Oxford. His research interests lie broadly within development economics and health economics. He has particular expertise in the economics of poverty and inequality, and in applying economic principles to tackle global challenges such as antimicrobial resistance and air pollution. His academic work has been published in a wide variety of academic journals, including the prestigious journal Science. His work on global inequality was featured in the United Nations Human
Development Report 2016. Laurence has worked as a consultant for the United Nations University World Institute for Development Economics Research (UNU-WIDER), and is an External Associate at the Global Development Institute (GDI, University of Manchester). Prior to working in academia Laurence was a professional econometrician in the private sector.

The economic challenges of antimicrobial resistance

As antibiotic consumption increases, bacteria are becoming increasingly resistant to treatment. Antibiotic resistance undermines much of modern healthcare, which relies on access to effective antibiotics to prevent and treat infections associated with routine medical procedures. The resulting challenges have much in common with those posed by climate change, which economists have responded to with significant research that has informed and shaped public policy. Drawing on economic concepts such as ‘externalities’ and the ‘principal-agent relationship’, this presentation will suggest how economics can help to solve the challenges arising from increasing resistance to antibiotics. It will discuss solutions to the key economic issues; from incentivizing the development of effective new antibiotics, to improving antibiotic stewardship through financial mechanisms and regulation.

Ursula Theuretzbacher, founder of Center of Anti-Infective Agents, Vienna, Austria

Ursula Theuretzbacher founded the Center of Anti-Infective Agents, Vienna, Austria in 1988. She is an independent expert for antibacterial drug Research and Development (R&D) strategies and policies based on clinical and public health needs. Her broad therapeutic area of expertise includes predicting medical needs and market potential, designing target product profiles, early integration of pharmacokinetic/pharmacodynamic concepts, optimisation of dosing and usage approaches, and public funding strategies for antibacterial R&D and initiatives to recover the global pipelines. Previously, she was work package leader or partner in several EU funded international collaborative projects focused on antibacterial drug R&D and reviving of old antibiotics. Additionally, she served as President of the International Society for Anti-Infective Pharmacology, Founding President of the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) PK/PD of Anti-Infectives Study Group, and as Executive Committee member of the International Society for Infectious Diseases (ISID). U. Theuretzbacher was member of the coordinating group of the WHO project Priority Pathogen List for R&D and is leading scientist for the Clinical and Preclinical Pipeline analysis, and development of Target Product Profiles at WHO. She is member of scientific advisory groups of national and international funding organisations such as REPAIR Impact Fund and CARB-X. She holds a PhD in Microbiology from the University of Vienna and the University of Innsbruck in Austria and lectured at the University of Vienna for 10 years.

Current pipeline of new antibiotics

The current global clinical pipeline is dominated by β-lactam based drugs, mostly in combination with a β-lactamase inhibitor. Other drugs in development are modified versions of well-known antibiotics of old classes. They usually provide improvements for selected class-specific resistance mechanisms and increase susceptibility rates in some pathogens but are still limited by cross-resistance to existing drugs. In contrast to the clinical pipeline the preclinical pipeline is much more diverse with scientifically interesting approaches. Less than half of all projects are direct-acting small molecules (“traditional antibiotics”) with a clear regulatory pathway. A strong trend towards non-traditional approaches, including diverse antivirulence approaches, microbiome-modifying strategies, and engineered phages and probiotics points to a high anticipated failure rate in clinical development as basic translational hurdles are not adequately addressed yet. The high number of pathogen-specific and adjunctive approaches is unprecedented in antibiotic history and will reveal major challenges in late clinical development.

Session 2

Jordi Vila, Head of the Department of Clinical Microbiology at Hospital Clinic and Research Professor, Director of the Antimicrobial Resistance Initiative and Head of the Viral and Bacterial Infections Programme at ISGlobal, Barcelona

Chair of session 2.
Read bio in page 8.
Old drugs revisited

The emergence and spread of multidrug-resistant bacteria has increased the interest towards some old drugs which are sometimes active against them. This includes fosfomycin, the aminoglycosides, trimethoprim-sulfamethoxazole, chloramphenicol or temocillin. For many of these drugs, some basic aspects were not adequately developed when discovered, such as the most adequate dosing, their toxicity and real efficacy in different types of infections. New academic studies are now providing relevant information that may allow a more optimized use of these antibiotics, which would allow to avoid the overuse of last resort or new drugs and contribute to improving the outcome of patients.

Dr. Javier Garau

Dr. Javier Garau is the former President of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID)(2010), Associate Professor of Medicine at the University of Barcelona and former Head of the Department of Medicine at Hospital Universitari Mutua de Terrassa in Barcelona. His research includes community-acquired bacterial infections, antibiotic resistance and new antimicrobials.

Dr. Garau has published 230 articles in peer-reviewed journals on clinical microbiology and infectious diseases. He is an American Board of Internal Medicine and American Board of Infectious Diseases diplomat and an active member of numerous medical committees, professional societies and editorial boards of peer-reviewed journals. Dr. Garau served as the president of La Sociedad Espanola de Enfermedades Infecciosas y Microbiologia Clinica from 1990 to 1992 and as vice-president of the Spanish Society of Chemotherapy from 1988 to 1992 and as vice-president of the Spanish Society of Chemotherapy from 1988 to 1990. He also served as the ESCMID education officer and Secretary General, 2005-2009, and President of ESCMID (European Society Clinical Microbiology and Infectious Diseases), 2009-2010.

Antibiotic combination therapy

Abstract not available.

Dr. Luis Martinez-Martinez

He received his medical degree at the University of Córdoba (1983) and his doctorate from the University of Seville (1988). Residency in Clinical Microbiology at Hospital Puerta de Hierro, Madrid (1984-1987), and a fellow at the University of Seville (1988-1989). Postdoctoral education in the Department of Microbiology, University of Utrecht (1988-1989, Netherlands, Dr. Jan Verhoef) and in the Laboratory Research of the Infectious Disease Unit, Massachusetts General Hospital-Harvard University, Boston (1992-1993, USA, Dr. George A. Jacoby and Dr. David C. Hooper). He has been member staff of the Department of Microbiology of the University Hospital Virgen Macarena, Seville and Titular Professor of the Department of Microbiology, University of Seville (1989-2003), and Head of the Service of Microbiology, University Hospital Marqués de Valdecilla and Titular Professor, Department of Molecular Microbiology, University of Cantabria, Santander, Spain (2003-2016).
His primary research interest is antimicrobial agents, including mechanisms of resistance to antimicrobial agents in Gram-negative bacteria, molecular epidemiology of resistance, susceptibility testing of new antimicrobial agents, and evaluation of automatic-commercial methods for identification and susceptibility testing. He has been an author or co-author of 5 books, numerous book chapters, and 340 papers in peer-reviewed journals (H-index: 54). He is the current President of COESANT (Spanish Committee of the Antibiogram) and has been member of the Executive Committee of EUCAST and the Scientific Committee on Emerging and Newly Identified Heath Risks (SCENIHR), European Commission, Health and Consumers Directorate-General.

Do we really need new antimicrobials?

Antimicrobial resistance is a major current health problem. Since antimicrobial agents were introduced in clinical practice, bacteria (and other organisms) resistant to these agents have been recognized in clinical, animal and environmental samples. This is related to the presence of intrinsic or acquired biochemical mechanisms, encoded by a large variety of genes located in the chromosome or in mobile genetic elements. Antimicrobial usage at any level represents a Darwinian pressure selecting resistant mutants.

Considering just clinical consequences of antimicrobial resistance, this problem is related to increasing mortality and morbidity rates (with an additional economic impact). From the One-Health perspective, resistance is also relevant at animal, agricultural and environmental levels.

Resistance is increasing worldwide. The situation has evolved to a limit leading the WHO to define a priority list of antibiotic-resistant bacteria to guide research, discovery and development of new antimicrobial agents. Multidrug- and extensively drug-resistant bacteria head this priority list, but new agents are also needed for paediatric patients and for oral formulations to treat highly frequent community infections caused by resistant bacteria. Multiple approaches are being considered to fight against antimicrobial resistance, including the development of new agents. This has been a strategy considered for years by the pharmaceutical industry, but unfortunately, introduction of new compounds has been followed by selection and emergence of bacteria with new mechanisms of resistance.

Treatment of infections caused by multiresistant Gram-positive bacteria, particularly methicillin-resistant Staphylococcus aureus (MRSA) and glycopeptide-resistant Enterococcus, improved after the introduction of oxazolidinones, lipopeptides or new beta-lactams active against MRSA, but in all cases resistant mutants have already been identified, and in some cases (i.e. linezolid-resistant staphylococci) causing nosocomial outbreaks.

No agents are currently available against metallo-beta-lactamase-producing organisms, and very limited options can be considered for bacteria producing methylases involved in aminoglycoside resistance. Although several compounds or combinations have been developed to treat infections caused by carbapenemase-producing Gram-negative bacteria or multiresistant Pseudomonas aeruginosa or Acinetobacter baumannii complex, resistance is already documented against these new options. Resistance to ceftazidime-avibactam due to KPC variants or other beta-lactamases alone or combined with decreased intrabacterial accumulation has been reported in multiple centres. Resistance to ceftolozane-tazobactam in P. aeruginosa has been related to AmpC variants, OXA-type enzymes, etc. It is obvious that the problem is far from being solved and that new agents are still needed.
Olga Genilloud, Scientific Director at Fundación MEDINA, Granada, Spain

Olga Genilloud has more than 30 years of extended research experience in the discovery of novel microbial natural products, obtained in the academic and clinical environment and the pharmaceutical industry. She has a PhD in Chemistry from the Universidad Complutense de Madrid (1988) from her work in the biosynthesis of secondary metabolites (Hospital Ramón y Cajal, Madrid 1984-1988; Harvard Medical School, Boston, 1987). In 1989 she joined the Natural Products Discovery Research Centre at Merck Sharp and Dohme in Spain (1989-2008) where she led the bacterial natural products program and contributed to the discovery of key novel antibiotics such as platensimycin and kibdelomycin. In 2008 she assumed the leadership to establish Fundación MEDINA from the former MSD-Spain R&D Centre. Currently she is Scientific Director at Fundación MEDINA and Head of the Microbiology department, and she manages the discovery programs and international collaborations with academic centres, large pharma and biotechnology companies in the identification of novel drug leads and high value biotechnological products. Her main research interests are focused on the production of novel microbial natural products, the exploration of novel microbial diversity to deliver novel chemistry, and the development of molecular and chemical tools to support natural products drug discovery and the identification of potential new therapeutics. She has more than 135 publications and book chapters, and 18 international patents.

**Secondary metabolites with antibacterial activity**

Microbial natural products (NPs) are one of the most prolific sources of new leads for the discovery of novel antibiotics with a large number of molecules and analogues today in the clinic. NPs present a unique chemical space with potency and selectivity being the result of an extended evolutionary selection. Advances in genome sequencing and bioinformatic tools have revealed the broad biosynthetic diversity of certain microbial groups opening new opportunities to identify novel classes of compounds. New integrated NPs discovery approaches involving genome-driven and cultured-based strategies are playing a key role in the identification of new antibacterial secondary metabolites.

MEDINA is a research organization focused on the discovery of novel bioactive NPs with one of the richest and most diverse NPs collections that are at the origin of our collaborative drug discovery programs. Our research in microbial natural products is focused on the identification of novel compounds with biological activity as potential new leads to respond to unmet needs in infectious diseases. In the course of our screening programs, the combined use of our NPs libraries and phenotypic assay platforms, have permitted to identify different novel families of molecules with interesting new chemistry and biological activities. Different examples will be discussed in the context of our current discovery efforts and the exploratory research developed to support the prospection of new NPs.

Sara María Soto, Associate Research Professor at Barcelona Institute for Global Health (ISGlobal), Barcelona

Read bio in page 8.

**Oceans as natural source of antibiotics**

Nowadays, two millions of marine species are known and about 10,000 new species are discovered each year. It is estimated that about 100 millions of species could form part of our seas and oceans. The potential of the oceans has been discovered by the pharmaceutical/biological research trying to obtain from their habitants some chemical substances, known as active principles that could have effects against pathogenic microorganisms and/or other medical utilities. Nowadays, molecules obtained from marine species have been used against malaria, HIV, or cancer, among others clinical problems.

Domingo Gargallo-Viola, CSO at ABAC Therapeutics, Barcelona

Domingo Gargallo-Viola. PhD in Sciences from University of Barcelona. Over 30 years of experience in the pharmaceutical industry. Currently CSO at ABAC Therapeutics. Previously, Infectious Diseases Manager and Drug Discovery Director at Ferrer Lab. Before joining Ferrer in 2008, for a period of 18 years, Director of Drug Discovery Biology and Project Leader at GSK. Formerly, Research Associate at the Uniformed Services University of the Health Sciences, F. Edward Hébert School of Medicine,
Design of synthetic antibiotics

Since 1962 we have been unable to discover new classes of broad-spectrum antibacterial agents, possibly due to the combination of two conditions: 1) the Target Product Profile (TPP), looking for broad-spectrum compounds, and 2) the Drug Discovery Strategy (DDS) approach used. It is urgent to make a critical review of the objectives and strategies used so far. Regarding the TPP, the bacteria inhabit the earth for more than 3,000 years and reproduce every 15-30 minutes, giving them enormous genetic diversity. On the other hand, the available chemical diversity is restricted, and it has been used intensively to search for broad spectrum products. DDS strategies have focused on small molecules (abandoning natural products) and target-based essays (that do not include cellular envelopes and transport mechanisms).

Precision treatments using pathogen-specific drugs with novel MoA will constitute the next generation of anti-infective treatments, they will kill exclusively the infecting bacteria with a minimum impact on human microbiota and the selection of resistant strains. In addition, discover novel classes of antibiotics that target common features amongst phylogenetically very disparate species (broad spectrum) is far more difficult than exploiting selective targets specific of each species.

Regarding the DDS, it is important to highlight that compounds that reach the market represent a harmonious and coherent set of properties. PasNas is a novel DD platform, based on an algorithm engineered by the ABAC founders, designed to identify high quality leads (molecules that meets multiple developability criteria), reducing technical risk in the DD process. The anti-infectives of the future will likely be similar to the current oncology products, pathogen-specific drugs in combination with ultra-fast companion diagnostics tools.

Session 4

Sara María Soto, Associate Research Professor at Barcelona Institute for Global Health (ISGlobal), Barcelona

Chair of session 4.
Read bio in page 8.

Àlex Soriano, Head of Infectious Diseases at Hospital Clínic, Barcelona

Specialist in Internal Medicine and PhD in the University of Barcelona in 2006. My scientific contribution is focused in the treatment and management of bacteremia, infections in Intensive Care Units, and infections related to orthopedic implants. I have more than 200 articles in national and international journals with more than 7000 citations and an H index of 42 and i10 of 136. I am the current Head of Infectious Diseases Department of Hospital Clínic of Barcelona and the Leader of the Nosocomial Infection Group of Institut d’Investigació en Biomedicina Agustí Pi-Sunyer (IDIBAPS).

Microbiota as a therapeutic approach

Dysbiosis (alteration of the normal composition and function of the intestinal microbiota) has been associated with multiple illness, including Clostridiodes difficile infection (CDI), bowel inflammatory diseases, or obesity among others. However, the effectiveness of fecal microbiota transplantation (FMT) from a healthy donor has been documented in recurrent episodes of CDI with a very high (90%) success rate. The objective of the lecture is to describe the lessons learnt by using FMT as a therapeutic approach in CDI and how this experience can be applied to other entities.
Hasan Jafri, Senior Director, Clinical Research, Microbial Science, Clinical Head of Antibacterial mAb Program, Coordinator COMBACTE-NET & COMBACTE-MAGNET at AstraZeneca, Gaithersburg, USA

Dr. Hasan Jafri leads clinical development of the anti-bacterial monoclonal antibodies within the Serious Bacterial Infections Franchise at MedImmune, AstraZeneca. He has previously been involved in the design and conduct of multiple Phase 1-4 clinical studies to assess novel small and large molecules against bacterial, viral and fungal pathogens. Prior to joining MedImmune, Dr. Jafri served as a professor in the department of pediatric infectious diseases and the department of clinical science research at the University of Texas Southwestern Medical Center at Dallas. He was the Chief of Division of Clinical Pharmacology, director of the Pediatric Infectious Diseases fellowship program, and director of the NICHD Pediatric Pharmacology Research Center. He has also served at the US Center for Disease Control and Prevention (CDC). He has over 25 years of experience in clinical practice and research, especially in the area of serious healthcare associated and community acquired infections, respiratory viral infections and invasive fungal infections (in immunocompromised and immunocompetent hosts), and biomarker and translational research. Dr. Jafri serves as the industry lead on the Innovative Medicines Initiative (IMI) COMBACTE programs involving development of MedImmune, AstraZeneca’s novel antibacterial monoclonal antibodies, and serves as the overall Coordinator of the COMBACTE-NET and COMBACTE-MAGNET Public-Private consortia. He also serves as the AstraZeneca representative, and leads the clinical subteam within the Infectious Disease Strategic Governance Group (SGG), an industry committee tasked with advising the European Commission and IMI on EFPIA R&D priorities. He has authored over 70 peer reviewed journal articles and presented over 100 original research abstracts at National and International Conferences.

**Novel mAbs Against Serious *Pseudomonas aeruginosa* Infections: Are We Ready for a Paradigm Change?**

- *Pseudomonas aeruginosa* remains a major cause of morbidity, increased healthcare costs, and mortality in high-risk patients despite current infection control practices and the available antibiotics.

- Monoclonal antibodies (mAbs) targeting bacterial virulence factors are narrow spectrum, not likely to induce antibiotic resistance, and may help prevent dysbiosis. They have the potential to become a key component of antimicrobial stewardship by minimizing the overuse of antibiotics, thereby helping preserve antibiotics, thus reducing opportunities for emergence of antibiotic resistance.

- MEDI3902, a bi-specific monoclonal antibody by AstraZeneca, targets key virulence factors of *P aeruginosa*, and offers a novel opportunity to help prevent or treat serious pseudomonal infections in high-risk patients.

- Public-Private collaborations such as COMBACTE are critical to stimulate infectious disease R&D, especially in “Paradigm-Changing” areas and in challenging patient populations.

Eduard Torrents, Group Leader at Institute for Bioengineering of Catalonia (IBEC), Barcelona

I finished my PhD in 2001 at the Microbiology and Genetics Dept. of the Autonomous University of Barcelona (Spain). During that period, I visited Prof. P. Reichard’s laboratory at the Nobel Medical Biochemistry and Biophysics Dept. (Karolinska Institute, Stockholm, Sweden) (19 months) and I was also awarded with different fellowships (EMBO, FEBS, etc). After my PhD defence, I was granted with a post-doctoral fellowship (Spain, 2003) to join Prof. BM. Sjöberg’s team (Dept. Molecular Biology and Functional Genomics, University of Stockholm, Sweden). I returned to Spain (2007) with a Ramón y Cajal contract at the Institute for Bioengineering of Catalonia (IBEC), to initiate my own research line. In 2012, I got an IBEC Junior Group Leader position and promoted to Senior Group Leader (2016), after a very competitive international selection. My group is continuously funded through different competitive programs such as “Proyecto I+D, Retos” from MINECO, FIS (Instituto de Salud Carlos III), ERA-NET PathoGenoMics, “Patronage project” and “CaixaImpulse Programme” from Obra Social La Caixa, by the European Institute of Technology Health, etc. The recent Excellence mention of IBEC through the Severo Ochoa program (MINECO) contributes to increase the competitiveness and visibility of my group, which has been growing over the last years. I have published more than 70 original research articles. Notice that in my research lines there is an important translational research with four international patents, industry projects and grants specific to this point.
Overall, my scientific activity projection for the future relies on (i) understanding the molecular mechanism for bacterial infections and biofilm formation, (ii) to identify, characterize and study different antibacterial molecules including new targets and (iii) the bioengineering and nanomedicine applications in microbiology (new drug delivery systems based on nanoparticles).

**New drug delivery systems to treat bacterial infections**

Emerging concepts for designing innovative drugs (i.e., novel generations of antimicrobials) frequently include nanostructures, new materials, and nanoparticles (NPs). Along with numerous advantages, NPs bring limitations, partly because they can limit the analytical techniques used for their biological and in vivo validation. From that standpoint, designing innovative drug delivery systems requires advancements in the methods used for their testing, investigations and high efficiencies for drug delivering.

In this talk, we are going to talk about our recent advances in the use of nanotechnology and NPs for an efficient treatment of bacterial infections. First, we are going to talk about our new designed NPs based on PLGA, metallic and dextran-based scaffold. We focus our attention on using NPs for the disaggregation of bacterial biofilms.

Secondly, we will show our developed of a new methodology to evaluate metallic NP antibacterial activity. Finally, we will talk about the BiofilmChip, our new microfluidic device, which allows the growth and quantification of bacterial biofilms to determine the best therapeutic intervention for a specific patient (treatment adjustment to reduce antibiotic multiresistance and patient recurrence).

**Patrick Jault**, Freelance, Paris, France

Graduated since 1998 from Lyon (France) University, I served for Moree than 25 year as military physician first in paratroops in overseas campaigns then as intensivist in a burn unit (Percy Military Hospital). I was deployed in Kosovo, Africa, Afghanistan and Mali.

I was driven by these very specific conditions of clinical practices to be skilled in the management of infectious diseases. They are the last stage of evolution of severely injured patients whatever their age. In 2010 I met a start up engaged in the development of bacteriophages as new tools in the management of septic complications. In 2013 we have launched the PHAGOBURN project granted by the European Commission. The project ran from 2013 to 2017, it was the first clinical study of the use of bacteriophages in a randomized controlled double blind study. It was published in January 2019 in The Lancet infectious Diseases. I was retired from the army in 2016, I’m now anesthesiologist in a private clinic in Paris. In 2020 I expect to set up a new company with the aim to develop the use of bacteriophages in Europe in cooperation with National and European Regulators with a very pragmatic and clinical approach.

**Efficacy and tolerability of a cocktail of bacteriophages against Pseudomonas aeruginosa to treat Infected burn wounds**

Future medicine would be a more personalized and individualized medicine. Many potential applications of the therapeutic use of viruses occurred in the last decades: oncology virotherapy and phage therapy are promising tools with similar limits for their development.

Phage Therapy use the potential of natural lytic viruses to reduce a specific bacterial burden. In this area the first controlled randomized double-blind multicentric clinical trial was published in January 2019 (Lancet Infect Dis. 2019 Jan;19(1):35-45).

Efficacy and tolerability of a pre-assembled cocktail (PP1131) of 12 natural lytic anti-**Pseudomonas aeruginosa** bacteriophages were compared to standard of care (Silver Sulfadiazine). Adult patients from six European centres with confirmed burn wound infection were randomized through interactive web response system to daily topical treatment for 7 days with PP1131 (106 PFU/mL) or with thick layer silver sulfadiazine (SSD). Bacterial burden was assessed daily with semi-quantitative cultures of 2 swabs: one for the median time from inclusion to sustained reduction in semi-quantitative bacterial burden by at least two quadrants (primary endpoint); the other for ancillary studies analysing causes of success/failure of phage therapy.
FINDINGS: From July 2015 to January 2017, 27 patients were randomized, 26 analyzable for safety, 25 for efficacy. Primary endpoint was reached in 144 hours in PP1131 versus 47 in SSD arm (HR, 0.29 [95% CI, 0.10–0.79]; p<0.011). In PP1131 arm 6 [50%] of 12 analyzable patients had a maximal (4 quadrants) bacterial burden versus 2 [15%] of 13 in SSD arm. PP1131 titre decreased after manufacturing and patients received daily lesser phages than expected (102 PFU/mL). In PP1131 arm 3 (23%) of 13 analyzable patients developed adverse events versus 7 (54%) of 13 in SSD arm. The ancillary study showed that the bacteria isolated from patients with failed PP1131 treatment were resistant to low phage doses.

INTERPRETATION: PP1131 at very low concentration reduced bacterial burden within burn wounds at slower pace than SSD but seemed associated with fewer serious septic adverse events. Further studies using higher phage concentration and phagogram are warranted.

Joan Gavaldà, Senior Consultant Infectious Diseases Department and Coordinator Antibiotic Resistance Lab at Institut Recerca Vall d’Hebron (Hospital Vall d’Hebron), Barcelona

Dr. Gavaldà, Senior Consultant of Infectious Diseases Department at Hospital Vall d’Hebron (Barcelona) is the Coordinator of ‘Antimicrobial Resistance Research- VHIR Laboratory’. By the end of 2019, Dr. J.Gavaldà held 136 peer-reviewed publications and over 3,942 citations (h-index: 36).

Our Group has a long history of conducting therapeutic efficacy studies using animal models of infection. The philosophy of the Group with its studies in animal models is to try to find answers to the questions that are generated in clinical practice, so that from the results try to carry out clinical trials that, if satisfactory, can improve clinical practice. He started his projects in 1992 with models of endocarditis by S. aureus and E. faecalis. Subsequently, projects have been carried out with the models, invasive aspergillosis and recently in the model of catheter infection with S. aureus, Candida spp. and S. epidermidis. An example of the group’s findings is the treatment of E. faecalis endocarditis with or without high resistance to aminoglycosides. Based on a clinical situation detected in the mid-1990s in the clinic, two animal model studies of experimental endocarditis were conducted that demonstrated that the association of ampicillin and ceftriaxone is effective in treating this infection. A clinical trial was subsequently conducted and published in Annals of Internal Medicine, followed by a cohort study in Clinical Infectious Diseases. This therapeutic strategy is currently accepted in the Guidelines of the Reference Medical Societies and has recently been published in the latest editions of the reference books on Infectious Diseases (Mandell's Principles and Practice of Infectious Diseases) and Internal Medicine (Harrison’s Principles of Internal Medicine). For the past 6 years he has been leading the ThermoShot/FlashShot Project.

Nano technology for AMR Infections

ThermoShot is a new technology to treat and prevent infections caused by microorganisms resistant to antimicrobials and those related to medical devices produced by biofilms. In our laboratory we are creating two new ThermoShot devices: BioGel ThermoShot (for orthopedic infections) and Stent ThermoShot (for infections caused by biofilms from endotracheal tubes). Both devices are charged with thermosensitive nanoantibiotics (ThermoShot); silver nanoparticles (NP) (AgNP) that allow the union of amikacin on its surface acting as an Aptamer and, at the same time, act as a hyperthermia agent directed by thermotherapy. ThermoShot devices are new technologies, developed by clinicians and for clinicians, combining the participation of relevant experts in nanomedicine and industrial engineering. These innovative technologies, until now non-existent, can imply cost savings for public health systems in infections acquired in the hospital environment.

Session 5

Jordi Vila, Head of the Department of Clinical Microbiology at Hospital Clinic and Research Professor, Director of the Antimicrobial Resistance Initiative and Head of the Viral and Bacterial Infections Programme at ISGlobal, Barcelona

Chair of session 5.

Read bio in page 8.
Climent Casals-Pascual, Associate Research Professor at ISGlobal, Barcelona

Dr Casals-Pascual is clinical consultant in Medical Microbiology. He did his PhD at the University of Oxford (UK) studying the pathophysiology of severe malaria. He became an independent researcher in 2008 (MRC Clinician Scientist Fellowship) and his main research interests are biomarker discovery, microbiome analysis and artificial intelligence applied to infectious diseases.

Chair of session 5.

Francesc Rabanal, Professor of Organic Chemistry at University of Barcelona, Barcelona

Francesc Rabanal is a Professor of Organic Chemistry at the University of Barcelona. He carried out his PhD in the CID-CSIC in Barcelona and a postdoctoral stay in the School of Medicine of the University of Pennsylvania, first as an EMBO fellow and later as Johnson Research Fellow. His research focuses mainly in the design, synthesis and in vitro and in vivo studies of antimicrobial peptides, particularly polymyxins, with the long-term objective of developing them as future drugs for the treatment of multi-drug resistant infections. He has more than seventy international publications, an h index of 31 (Google Scholar), eight patent applications and, is a recipient of several grants. He has also been guest editor of the special issue “Polymyxins” in the journal Molecules and is a member of the editorial board of the journal Biomolecules. Finally, he is a member and programme leader in the ENABLE European consortium (European Gram-negative Antibacterial Engine; Innovative Medicines Initiative New Drugs 4 Bad Bugs programme) for the development of antibacterial drugs.

Antimicrobial cyclic peptides: the case of polymyxins

Antibiotic resistance is becoming a global health problem. The World Health Organization issued in 2017 a list of the most critical pathogenic bacteria for which new antibacterial agents are urgently needed, which included carbapenem-resistant Gram-negative bacteria (Enterobacteriaceae, Pseudomonas aeruginosa, Acinetobacter baumannii). Several approaches are available to address the development of new antimicrobial agents. In this sense, antibacterial cyclic peptides are a plausible approach. Some cyclic peptides have been available to treat infections for decades (polymyxins, bacitracin, daptomycin). In this talk, an overview of the field will be presented, focusing on strategies for the generation of new compounds particularly in the case of polymyxins where novel chemical designs are proposed to overcome the nephrotoxicity issues intrinsically related to this type of agents.

Els Beirnaert, PhD and CEO of Aelin Therapeutics, Leuven, Belgium

Els Beirnaert, PhD and CEO of Aelin Therapeutics, brings along 18 years of experience in drug development, venture and business development. Previously she was one of the start-up pioneers of Ablynx a company established in 2001 focused on biological therapeutics. She was leading multidisciplinary project teams and translating several drug development projects from discovery over pre-clinical development to clinical development (Phase 1 and 2). Since 2010, she was Head of New Ventures at VIB responsible for the establishment of start-up/spin-out companies in life sciences. She served in the board of directors of Confo Therapeutics, Q-Biologicals and Multiplicom. Dr. Beirnaert obtained a Master in Biotechnology at the University of Ghent and a PhD in Biochemistry at the Institute of Tropical medicine (University of Antwerp).

Harnessing the power of protein aggregation to develop new antibiotics

Aelin Therapeutics is a privately held Belgian biotherapeutics company that pioneers a novel modality in drug development in order to create a completely new class of antibiotics. The technology, branded PeptIns™, harnesses the power of protein aggregation to specifically induce functional knockdown of a target protein. The company was founded in December 2017 by VIB (KU Leuven, VUB and UGent), based on the ground-breaking work of renowned structural biologists Prof Joost Schymkowitz and Prof Frederic Rousseau. Building on the solid science and a convincing data set, Aelin Therapeutics has succeeded in raising 27 M€, bringing together a strong group of well-reputed investors (LSP, PMV, Fund+, BIVF).

The first high-priority drug discovery activities will focus on the development of a new class of antibiotics for the treatment of Gram-negative bacteria. Around the world bacteria are developing new strategies that render them resistant to existing
antibiotics. Most current antibiotics work according to only a few mechanisms of action and so when a bacterium becomes tolerant to one drug, it often becomes tolerant to the whole family. What we need is an entirely new class of drugs that shares no structural or mechanistic similarities with the existing antibiotics. Aelin Therapeutics goes one step further by developing a new way of designing antibiotic drugs that can give rise to many new antibacterial molecules. These first-in-class synthetic peptides can treat antibiotic-resistant Gram-negative bacterial infections by inducing toxic protein aggregation within bacterial cells. By harnessing this novel mechanism of action, Aelin Therapeutics could circumvent growing resistance to existing antibiotics.

Jean-Denis Docquier, Associate Professor of Microbiology at University of Siena, Siena, Italy

Dr. Docquier received an extensive training in both biochemistry and microbiology, and developed research projects focused on the molecular study of antibiotic mechanism of action and resistance, with a peculiar focus on β-lactamases, which he has been studying for over 20 years. He is an Associate Professor of Microbiology and teaches various aspects of Microbiology (including molecular microbiology, applied and pharmaceutical microbiology, and microbiology for drug discovery) to Chemistry, Pharmacy and Biotechnology students.

His research activities mainly focus (a) on the study of the molecular aspects of bacterial resistance to antibiotics, and (b) on the functional and structural characterization of β-lactamases, most importantly metallo-β-lactamases and serine-β-lactamases showing carbapenemase activity, as effectors of β-lactam resistance in clinically-relevant bacterial Gram-negative pathogens and as targets for enzyme inhibitors, and more recently, (c) on the discovery, optimization and characterization of novel compounds with antimicrobial properties.

Reversing β-lactam resistance with new β-lactamase Inhibitors

β-lactams are the most widely used antibiotics. However, clinically relevant bacteria acquired several mechanisms of resistance to these agents. The production of one or more β-lactamase(s) is one of the most important mechanisms of resistance to β-lactams, especially in Gram-negative opportunistic pathogens. Combining a β-lactamase inhibitor with a β-lactam antibiotic, such as in amoxicillin-clavulanate, is therefore a valuable and well-validated strategy to address β-lactamase-mediated resistance.

In the last decades, the emergence of β-lactamase variants showing resistance to commercially available inhibitors and/or the ability to inactivate a wider range of important β-lactam drugs, such as oxyiminocephalosporins and carbapenems, was and still is threatening the efficacy of such drugs.

The evolving epidemiology, and especially the global emergence and spread of carbapenemase-producing clinical isolates, revived the interest towards the discovery of β-lactamase inhibitors, and a new wave of β-lactam-β-lactamase inhibitor combinations reached the stage of clinical development, some being recently approved. This talk will cover the current status of and most recent advances in β-lactamase inhibitor research and development.

Younes Smani, Researcher at Institute of Biomedicine of Seville, Seville, Spain

Younes Smani graduated in Cellular Biology and Animal Physiology in 2002 at the University of Henri Poincaré, Nancy (France). He did his PhD thesis in 2006 in Haematology at the Physiology and Haematology department of University of Henri Poincaré, Nancy. In 2007, he joined the Infectious Department of University Hospital Virgen del Rocío of Seville (Spain) as postdoctoral researcher. Since 2016, he is a Senior Researcher at the Institute of Biomedicine of Seville. He has published 49 papers in scientific indexed journals and over 70 conference abstracts. His research lines are focused on the study of the bacterial pathogenicity and the development of non-antibiotic approaches to treat bacterial infections.

Antivirulence drugs

Compounding the problem of antimicrobial resistance is the immediate threat of a reduction in the discovery and development of new antibiotics, the dangers of which have recently been made clear by the World Health Organization
(WHO) and other European institutions. Consequently, a perfect storm is converging with regard to bacterial infections: increasing antimicrobial resistance with a decreased new antibiotic development. This context is likely the best example of the purported “Post-Antibiotic Era”. It is clear that effective solutions are urgently needed as stressed by various institutions. New policies and actions are necessary to avoid the figures predicted for 2050 that attribute ten million deaths worldwide to antimicrobial resistance. Therefore, the development of non-traditional therapeutic strategies for use alone or together with clinically relevant antibiotics has become exigent.

In this environment, antivirulence drugs have received considerable attention that specifically target bacterial virulence factors rather than growth. Despite this interest, only few antivirulence drugs are in clinical development. Here, we aim to systematically provide an overview on the scientific evidence on potential antivirulence drugs targeting Gram-negative bacteria. In specific, i) to discuss the therapeutic potential of this drug class, ii) to identify their potential targets, and iii) to summarize the outcome of their preclinical and clinical trials for treating MDR bacterial infections.

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**Brice Felden**, Professor and lab head at Rennes University, Rennes, France

Dr. Brice Felden has completed his MD and PhD in biochemistry & molecular biology on viral and bacteria RNAs at Strasbourg University (France) and postdoctoral studies from University of California (X-ray crystallography and Atomic Force Microscopy) and Human Genetics Institute (SLC, Utah, USA). He has worked as professor of Biochemistry at Rennes University and funded a research since 2000. He has published more than 90 papers in reputed journals and has been serving as a director of a Research Unit working on virulence regulations on various bacterial pathogens.

**Novel antibiotics effective against gram-positive and -negative multi-resistant bacteria with limited resistance**

Antibiotics are a medical wonder, but an increasing frequency of resistance among most human pathogens is rendering them ineffective. If this trend continues, the consequences for public health and for the general community could be catastrophic. The current clinical pipeline, however, is very limited and is dominated by derivatives of established classes, the “me too” compounds. Here, we have exploited our recent identification of a bacterial toxin to transform it into antibiotics active on multidrug-resistant (MDR) gram-positive and -negative bacterial pathogens. We generated a new family of peptidomimetics—cyclic heptapeptides—inspired from a natural bacterial peptide. Out of the 4 peptides studied, 2 are effective against methicillin-resistant *Staphylococcus aureus* (MRSA) in mild and severe sepsis mouse models without exhibiting toxicity on human erythrocytes and kidney cells, zebrafish embryos, and mice. These new compounds are safe at their active doses and above, without nephrotoxicity. Efficacy was also demonstrated against *Pseudomonas aeruginosa* and MRSA in a mouse skin infection model. Importantly, these compounds did not result in resistance after serial passages for 2 weeks and 4 or 6 days' exposure in mice. Activity of heptapeptides was explained by the ability of unnatural amino acids to strengthen dynamic association with bacterial lipid bilayers and to induce membrane permeability, leading to bacterial death. Based on structure determination, we showed that cationic domains surrounded by an extended hydrophobic core could improve bactericidal activity. Because 2 peptide analogs, Pep16 and Pep19, are effective against both MRSA and *P. aeruginosa* in severe sepsis and skin infection models, respectively, we believe that these peptidomimetics are promising lead candidates for drug development. We have identified potential therapeutic agents that can provide alternative treatments against antimicrobial resistance. Because the compounds are potential leads for therapeutic development, the next step is to start phase I clinical trials.
Discussion panel: Open discussion on new research strategies

**Javier Vega**, Business Creation Project Manager at EIT Health Spain, Barcelona

Javier Vega is a Biologist with a PhD in Immunology from the University of Barcelona, and has performed different post-doctoral stays in top level Research Institutions from Australia, Brazil and Barcelona. He has a wide experience in International biomedical Research, mostly in the fields of Immunology, infectious diseases and autoimmunity. Javier joined EIT Health Spain as Business Creation Project Coordinator in November 2018, working closely with Spanish Start-ups and SMEs to foster innovation and entrepreneurship in the health sector, providing advice and guidance, and promoting their success.

**Moderator**

**Brice Felden**, Professor and lab head at Rennes University, Rennes, France

Read bio in page 20.

**Domingo Gargallo-Viola**, CSO at ABAC Therapeutics, Barcelona

Read bio in page 13.

**Eduard Torrents**, Group Leader at Institute for Bioengineering of Catalonia (IBEC), Barcelona

Read bio in page 15.

**Olga Genilloud**, Scientific Director at Fundación MEDINA, Granada, Spain

Read bio in page 13.
Thursday, November 14, 2019

DAY 3: BEYOND THE DISCOVERY OF NEW ANTIMICROBIAL AGENTS

Session 6

**Rafael Vilasanjuan**, Policy and Global Development Director at ISGlobal, Barcelona

Chair of session 6.

Rafael Vilasanjuan is a journalist with a degree in Information Sciences from the Autonomous University of Barcelona (UAB). He is Director of Policy and Global Development of ISGlobal since March 2011. He was Deputy Director of the Centre for Contemporary Culture of Barcelona (CCCB) from 2006 to 2011.

He also worked for over 12 years with Médecins Sans Frontières (MSF), starting as Communication Director in 1995 and later as General Director of the Spanish section of MSF. In 1999, when the organization was awarded the Nobel Prize for peace, he was appointed General Secretary of MSF International until 2005. During this period, he worked in conflict areas such as Afghanistan, Chechnya, Somalia, Sudan, West Africa, the Democratic Republic of Congo and Colombia.

As General Secretary of MSF, he was a founder member of the Drugs for Neglected Diseases initiative (DNDi), which develops and delivers new drugs for diseases in developing countries. Rafael Vilasanjuan still collaborates with the DNDi.

**Jordi Vila**, Head of the Department of Clinical Microbiology at Hospital Clinic and Research Professor, Director of the Antimicrobial Resistance Initiative and Head of the Viral and Bacterial Infections Programme at ISGlobal, Barcelona

Chair of session 6 and moderator of the flash talks session.

Read bio in page 8.

**Flash talks**

- **Efficacy of lysophosphatidylcholine as direct treatment in combination with colistin against Acinetobacter baumannii in experimental murine peritoneal sepsis and pneumonia models**

  Authors: Miró-Canturri A., 1,2#, Ayerbe-Algaba R. 1,2#, Jiménez-Mejías ME. 1,2*, Rodríguez-Villodres A. 1,2, Pachón J. 2,3, Smani Y. 1,2*.

  Affiliations: 1 Clinical Unit of Infectious Diseases, Microbiology and Preventive Medicine, University Hospital Virgen del Rocío, Seville, Spain. 2 Institute of Biomedicine of Seville, Seville, Spain. 3 Department of Medicine, University of Seville, Seville, Spain.

- **The antimicrobial edge: Combining different antimicrobial domains for a more powerful tool**

  Authors: Ramon Roca-Pinilla, Adria Lópe-Cano, Cristina Saubi, Elena Garcia-Fruitós* and Anna Arís* (*co-corresponding authors)

  Affiliations: Department of Ruminant Production, Institut de Recerca i Tecnologia Agroalimentàries (IRTA), 08140 Caldes de Montbui, Spain

- **Disruptive strategy to overcome antimicrobial resistance by removing inhibitory antibodies causing enhancement of infections**

  Authors: Sara Olivera-Ardid, Daniel Bello-Gil, Pablo Madrazo, Rafael Mañez.

  Affiliations: RemAb Therapeutics. Feixa Llarga s/n. Edificio Modular, Campus de las Ciencias de Bellvitge, 08907, Hospitalet de Llobregat.
Visible Light Operated Photo-Switchable Antibiotics to Fight Resistances

Authors: Xavier Just-Baringo and Ernest Giralt
Affiliations: Institute for Research in Biomedicine (IRBBarcelona), Barcelona Institute of Science and Technology (BIST), Barcelona.

Novel antimicrobials based on gene expression inhibition

Authors: Javier Moreno-Morales*1, Salvador Guardiola2,3, Clara Ballesté-Delpierre1, Meritxell Teixidó2,3, Ernest Giralt2,3, Jordi Vila1.
Affiliations: 1 ISGlobal, Hospital Clínic – Universitat de Barcelona, Barcelona. 2 IRB Barcelona, Barcelona. 3 Department of Inorganic and Organic Chemistry, Universitat de Barcelona, Barcelona.

Determination of antimicrobial potential of recombinant Host Defense Peptides produced as soluble proteins and as protein nanoclusters

Authors: A. López-Cano, R. Roca, L. Gifre-Renom, F. Fàbregas, A. Arís and E. Garcia-Fruitós
Affiliations: Department of Ruminant Production, Institut de Recerca i Tecnologia Agroalimentàries (IRTA), 08140 Caldes de Montbui, Spain.

Jury members:

Domingo Gargallo-Viola, CSO at ABAC Therapeutics, Barcelona

Read bio in page 13.

Núria Martí, Director of Innovation at Biocat, Barcelona

Dr. Núria Martí Ras holds a degree in Veterinary Medicine (Autonomous University of Barcelona, UAB, 1993), a PhD in Microbiology (UAB, 1999), a Master's Degree in Sciences and Laboratory Animal Welfare (Cat D Felasa) (UAB, 2009) and a Master in R&D Management in Health at the Institute of Health Carlos III (University of Alcalá de Henares, 2016). She did the PhD thesis at Institut Pasteur in Paris at the Molecular Bacteriology Unit. After doing a post-doc at the Institut Pasteur in Brussels (Institut Scientifique Santé Publique Louis-Pasteur), she continued her career at Ferrer Internacional, working in the company's R&D center for more than 10 years managing drug-development projects in antiinfectious and in nervous central system fields. She also headed up the Innovation and Technology Transfer Office at the Institute for Health Science Research Germans Trias i Pujol (IGTP) for over 4 years. Since May 2018 she holds the position of Director of Innovation at Biocat where she is in charge of leading the new technology transfer and innovation projects that are at the core of Biocat’s new strategy. Author of scientific contributions published in international Journals in the field of Infectious diseases and scientific communications in international and national congress.

Seamus O’Brien, R&D Director at Global Antibiotic R&D Partnership, Geneva, Switzerland

Seamus O’Brien joined GARDP as R&D Director in July 2018 and is responsible for strategic development and delivery of the R&D portfolio of treatments for serious drug resistant infections.
Prior to joining as GARDP’s R&D Director, Seamus was responsible for building and leading R&D collaborations and networks to address industry commitment to develop treatment options for antibiotic resistant infections. He played a leading role in establishing novel partnerships for AstraZeneca with the US government’s Biomedical Advanced Research and Development Authority and with the Innovative Medicines Initiative (IMI) New Drugs 4 Bad Bugs programme within Europe as leader of the COMBACTE-CARE consortium addressing carbapenem resistance.

Seamus has extensive experience in pharmaceutical drug development from antibiotic to vaccine clinical development, to leading medical affairs support for a number of product launches.

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**Joan Bigorra**, Director of Innovation at **ISGlobal**, Barcelona

Director of Strategy and Innovation at Barcelona Institute of Global Health, Senior Advisor of Innovation at University of Barcelona Clinic Hospital, Associate Professor at the Universitat Pompeu Fabra (UPF), and Scientific Director of the Official Master on Leadership & Management of Science and Innovation (Barcelona School of Management, UPF).

Former Director of Innovation at University of Barcelona Clinic Hospital from 2009 to 2014, Managing Director of the Fundació Clinic for Biomedical Research from 2006 to 2008. Former General Manager of Novartis Pharma Spain, former Medical Director and Head of R&D of Bayer Healthcare, Boehringer Ingelheim and Sandoz Pharma in Spain.

Graduate (M.D.) and Ph.D. in Medicine by Universitat Autònoma de Barcelona; Board Certified Specialist in Clinical Pharmacology and Therapeutics; Graduate in Law by the National Distance Learning University and Master in Biomedicine, Biotechnology and EU Law; Graduate in Health Economics by the University of Tromso, Norway. Senior Management Development Program by IESE Business School.

**How to stimulate innovation in the public and private sectors?**

Innovation is about using the best available knowledge to challenge and improve the status quo in a way that is perceived and valued by users. There is a direct correlation between the capacity of a society to innovate and the wellbeing of its members. So, in theory, it should be quite easy to stimulate innovation, but reality shows that this in not always the case, mostly because of the “non-invented here syndrome”, the conflicting priorities and the resistance to change. And yet, there is an obligation to stimulate innovation in it broader sense. It is estimated that the annual budget gap of what is nowadays invested in order to fulfil the 17 Sustainable Development Goals by 2030 is around $2,5 trillion. Realistically, innovation seems to be the only way to win the SDG race.

In the case of Health Innovation, where most of the knowledge is generated by publicly funded research while most of the development work is done by the private sector, we need to address the issue of focusing innovation on the real medical and social needs and stimulating cooperation to innovate fast and efficiently. Some initiatives like Research Impact Assessment, Open Science or the creation of highly targeted PPPs go in the right direction. But besides these trends there seems to be the need to create and overall context, through regulations but also through market conditions, where the best players, both public and private, could find enough incentives to share common goals and accelerate medically and socially valuable innovation.

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**Laura Marin**, Head of Secretariat at **JPIAMR**, Stockholm, Sweden

Laura Marin heads the Executive office Secretariat of the Joint Programming Initiative on Antimicrobial Resistance hosted by the Swedish Research Council. JPIAMR, is an international member states platform that coordinates national funding and supports collaborative research action on antimicrobial resistance. Previously she was responsible for Science Policy and Member Relations at the European Science Foundation. Earlier on she was also team leader of the European Science Open Forum in 2008 in Barcelona (ESOF2008) and Director of Operations at the Catalan Foundation for Research and Innovation. She has several years of experience in Brussels and Germany managing research and innovation projects and facilitating numerous fora on science policy and governance issues.
Science and policy interface: JPIAMR

With increasing policy and research funding initiatives in the area of AMR, it is more relevant than ever to better connect the research community with those funding strategies, especially in the area of therapeutics. The talk will focus on what kind of opportunities such initiatives present and on mechanisms to get better involved in policy and funding activities through the JPIAMR-Virtual Research Institute. JPIAMR Strategic Research and Innovation agenda and its joint research priorities and gap analysis roadmap that guide future funding lines will be presented as well as the landscape of main running research projects and networks in the area.

Seamus O’Brien, R&D Director at Global Antibiotic R&D Partnership, Geneva, Switzerland

Read bio in page 23.

Public-Private Partnership to address the public health challenge of antibiotic resistance

Partnerships are essential to address the challenges of antibiotic resistance. Increasingly there are limited or no treatment options for infections caused by the WHO priority pathogens. These infections disproportionately impact vulnerable populations due to both a lack of access to effective antibiotic and the lack of new antibiotics developed to meet the need. This is a public health issue which needs a public-private framework and partnership to address key R&D and access challenges.

The presentation will outline the impact of public-private partnerships to date and the opportunities and remaining challenges that remained to be address by partnerships such as the Global Antibiotic Research and Development Partnership (GARDP).

Gemma Buckland-Merrett, Science Lead Drug Resistant Infections Programme at Wellcome Trust, London, UK

Dr Gemma Buckland-Merrett is the Science Lead for Drug-Resistant Infections priority programme at Wellcome. In her role, she is shaping and delivering Wellcome’s antimicrobial resistance strategy, bridging the gap between science and policy.

Gemma joined Wellcome in 2019 from Public Health England where she was the lead epidemiologist for travel-associated infections. Gemma has over ten years of experience in multi-disciplinary research roles leading projects spanning public health, epidemiology and infectious diseases. She worked as a research manager for Health Action International, an NGO focused on access to medicines, where she led a multi-country research project on access to sexual and reproductive health commodities in Africa. Prior to this Gemma spent four years in academic research at the University of Sussex Centre for Global Health Policy focusing on antimicrobial resistance and access to medicines.

Gemma has a PhD in Immunology from Imperial College, an MSc in Global Health and Development from University College London and an MSc in Controlling Infectious Diseases from the London School of Hygiene and Tropical Medicine.

Wellcome Trust Initiatives to tackle antimicrobial resistance

Wellcome established its Drug-Resistant Infections programme in 2017 to help drive a step-change in the global response to AMR. The Programme has a budget of £175m – about $225m – and is entirely global in its scope. Structured around four pillars that reflect the key challenges that were identified in the global response to AMR – or at least the challenges which were identified as presenting the greatest opportunities for Wellcome to make a difference.
These are:
- Evidence for decision-making – focused on improving the surveillance and epidemiology data that is available to inform decision-making, globally at all levels – from the patient and clinic level, up to national- and international-level decision-making by policymakers.
- New treatments – recognizing that the pipeline of new antibiotics and other technologies needed to respond effectively to the challenges of drug resistance are inadequate.
- Faster clinical trials – looking at what can be done to support faster, more effective clinical trials for antibiotics, so they can be brought to global markets as cheaply and as rapidly as possible.
- Global governance – working to ensure that there is an effective global policy response to drug resistance, and that we see change to the structures in place globally to ensure a collective, collaborative, multi-sectoral response to drug resistance.

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Dr Gaetano Castaldo is from Research Executive Agency (REA) of the European Commission. After 12 years working as scientist with a PhD in Pharmaceutical Biochemistry, he has served the European Commission first as Scientific and Policy Officer and, since 2017, at REA working as Project Adviser and coordinator of Life Science proposals evaluation. He coordinates together with his team, the entire project life cycle of Marie Skłodowska-Curie Individual Fellowship, from proposals evaluation to the monitoring of project implementation and their final assessment. He has organised in June 2019 a dedicated cluster event on Antimicrobial Resistance bringing together researchers, policy makers and entrepreneurs.

**The role of Marie Skłodowska-Curie actions in the fight against Antimicrobial Resistance**

Marie Skłodowska-Curie actions (MSCA) are one of the most prestigious programmes for boosting scientific research in Europe. The MSCA Individual Fellowship schemes support career and training of experienced researchers through the funding of scientific projects up to 36 months. Amongst all scientific fields funded through MSCA, Antimicrobial Resistance (AMR) represents a very important research area with several projects focusing on this urgent global concern. Bringing together different actors involved in the fight against AMR is of a pivotal importance to join forces towards finding innovative solutions. The first cluster event on Antimicrobial Resistance was held in June 2019 with 14 selected MSCA projects tackling AMR from different research perspectives. This event involved also external experts, policy makers from European Commission, the European Institute of Innovation & Technology (EIT) Health and entrepreneurs. The selection of projects and external speakers has allowed a 360-degree vision of the current EU policy and MSCA research on AMR together with future opportunities for researchers to continue the fight against this global challenge.

**Discussion panel: Open discussion on the discovery of new antimicrobial agents**

**Jordi Vila**, Head of the Department of Clinical Microbiology at Hospital Clinic and Research Professor, Director of the Antimicrobial Resistance Initiative and Head of the Viral and Bacterial Infections Programme at ISGlobal, Barcelona

Moderator.

Read bio in page 8.

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**Joan Bigorra**, Director of Innovation at ISGlobal, Barcelona

Read bio in page 24.
Laura Marin, Head of Secretariat at JPIAMR, Stockholm, Sweden

Seamus O’Brien, R&D Director at Global Antibiotic R&D Partnership, Geneva, Switzerland

Gemma Buckland-Merrett, Science Lead Drug Resistant Infections Programme at Wellcome Trust, London, UK

Gaetano Castaldo, Life Science Coordinator and Project Adviser at European Commission-Research Executive Agency, Brussels, Belgium
PRACTICAL INFORMATION

Venue: CosmoCaixa Barcelona

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

Conference room
Àgora (-2 floor)

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

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

Contact person during the event

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www.bdebate.org | www.biocat.cat
SUGGESTED READING

- **Current landscape in the discovery of novel antibacterial agents.**
  Vila J, Moreno-Morales J, Ballesté-Delpierre C.
  *European Society of Clinical Microbiology and Infectious Diseases*. (2019).

- **Grand Challenges in Marine Biotechnology.**
  First chapter written by Sara Soto.

- **Analysis of the clinical antibacterial and antituberculosis pipeline.**
  Theuretzbacher, U., Gottwalt, S., Beyer, P., Butler, M., Czaplewski, L., Lienhardt, C., ... & Silver, L. L.
  *The Lancet Infectious Diseases, 19*(2), e40-e50. (2019).

- **Microbiota transplantation and/or CRISPR/Cas in the battle against antimicrobial resistance.**
  Vila, J.
OUTCOMES

B·Debateca

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

Contents of the meeting: “Reversing a dystopian future. New strategies to discover antibacterial agents”

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**ORGANIZERS**

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

The debates are top-notch international scientific meetings featuring a selection of experts of renowned international prestige and scientists 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

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**ISGlobal**

The Barcelona Institute for Global Health (ISGlobal) is a public-private centre that is the result of an innovative alliance between "la Caixa" and various academic and government institutions, including the Spanish Government, the Catalan Government and the Barcelona City Council. It was set up to contribute to the efforts of the international community to address health challenges in a globalised world. With a track record in global health stretching back more than 30 years, ISGlobal has consolidated a hub of excellence in research and medical care that has its roots in work first started in the world of health care by the Hospital Clinic and the Mar Health Park and in the academic sphere by the University of Barcelona and the Pompeu Fabra University. The pivotal mechanism of its work model is the transfer of knowledge generated by scientific research to practice, a task undertaken by the institute's Education and Policy and Global Development departments. Its ultimate goal is to help close the gaps in health disparities between and within different regions of the world. ISGlobal a member of the CERCA Programme of the Generalitat de Catalunya.

More info: www.isglobal.org
COLLABORATORS

REIPI is a Research Network aimed at improving developing high quality basic, translational and clinical research in the area of clinical microbiology and infectious diseases. REIPI is formed by 17 Spanish leading research groups in the field, and is funded by Ministerio de Ciencia, Innovación y Universidades, Instituto de Salud Carlos III, co-financed by European Development Regional Fund “A way to achieve Europe” ERDF.

More info: http://reipi.org/

WITH THE SUPPORT OF

EIT Health is a network of best-in-class health innovators backed by the European Union. We collaborate across borders to deliver new solutions that enable European citizens to live longer, healthier lives.

As Europeans tackle the challenges of increasing chronic diseases and multi-morbidity, they seek to realise technology's potential to move beyond conventional approaches to treatment, prevention and healthy lifestyles. To succeed, Europe needs thought leaders, innovators and efficient ways to bring innovative healthcare solutions to market.

EIT Health addresses these needs. We connect all relevant healthcare players across European borders – making sure to include all sides of the “knowledge triangle”, so that innovation can happen at the intersection of research, education and business for the benefit of citizens.

We give health innovators access to the market, funding and the expertise of our network. We facilitate innovation through programmes, workshops and initiatives. We collaborate on international projects and disseminate our findings to the public. We create new products and services for healthy lives in Europe. And we educate, through citizen engagement activities, innovation programmes and skills training.

More info: https://www.eithealth.eu/home

The Ministry of Science, Innovation and Universities is the department of the Government of Spain responsible for the execution of the Government's policy regarding universities, scientific and technical research, technological development and innovation in all sectors, including the management of international relations in this area and the Spanish representation in programs, forums and international organizations, and the European Union of its competence.

More info: http://www.ciencia.gob.es/
SEIMC is a non-profit scientific society that brings together professionals working in the field of infectious disease and clinical microbiology, including clinical management, treatment, microbiological diagnosis and prevention. For over 35 years, SEIMC has been collaborating with Health Authorities to promote and develop health initiatives such as the National Plan to Combat Antimicrobial Resistance, the National AIDS Plan, Flu Recommendations, Guidelines for HCV, Guides for Ebola and others.

More information: https://seimc.org/

MSD es un líder de salud global que trabaja para contribuir a la salud mundial. Nuestra Compañía tiene una historia rica y dilatada de trabajo por mejorar la salud y el bienestar de las personas. Durante años, nuestros investigadores han ayudado a encontrar nuevas formas de tratar y prevenir enfermedades, desde el descubrimiento de la vitamina B1 hasta la primera vacuna contra el sarampión, medicamentos para el resfriado y antiácidos, o la primera estatina para tratar el colesterol elevado. Nuestros científicos también han contribuido al desarrollo de muchos productos de salud animal, como vacunas y antibióticos.

A la vez que nos enorgullecemos de nuestro pasado, vemos con entusiasmo el futuro y nos apasiona contribuir a crear un mundo más saludable y mejorar la vida de las personas en todo el mundo.

Y además los valores que reflejan nuestra cultura son:
 - Continuar en la búsqueda de nuevos retos en salud para mejorar la calidad de vida de las personas en todo el mundo, es nuestro compromiso
 - Estamos comprometidos con los más altos estándares de ética e integridad. Este compromiso se extiende a nuestra relación con los clientes y proveedores, con nuestros empleados, con el medioambiente y en definitiva, con la sociedad.
 - Perseguimos el más alto nivel de excelencia científica.
 - Identificamos las necesidades en salud más críticas y a través de la investigación continua. Nuestro reto es dar respuesta a esas necesidades innovando en todo lo que hacemos.
 - Trabajamos para ofrecer, a través de programas de largo alcance, soluciones sostenibles que mejoren la salud y la calidad de vida de las personas en todo el mundo.
 - Fomentamos y reforzamos entre nuestros empleados, la inclusión, la diversidad, la creatividad y el trabajo en equipo


Shionogi is a company dedicated to health funded about 140 years ago by Gisaburo Shiono SR. He founded the organization (1878) in Doshomachi, Osaka, Japan. Nowadays, the headquarters are still in Osaka and the company has become a major pharmaceutical company primarily dedicated to research to provide the best possible patient care.

In 2012, Shionogi Europe opened its headquarters in London, United Kingdom, and marked the beginning of a new era for the organization.
At Shionogi Europe, we are committed to working in a different way and closer to patients in the areas in which we focus both in Europe, the Middle East and in Africa (EMEA region). We aspire to become leaders in the field of health care through the discovery and supply of medicines that meet the expectations of patients, their families and healthcare professionals, and that contribute to improving their quality of life.

More information: https://www.shionogi.eu/

**Pfizer** is a research-based global biopharmaceutical company. The Company is engaged in the discovery, development and manufacture of healthcare products. Its global portfolio includes medicines and vaccines. The Company manages its commercial operations through two business segments: Pfizer Innovative Health (IH) and Pfizer Essential Health (EH). IH focuses on developing and commercializing medicines and vaccines. IH therapeutic areas include internal medicine, vaccines, oncology, inflammation and immunology, rare diseases and consumer healthcare. EH includes legacy brands, branded generics, generic sterile injectable products, biosimilars and infusion systems. EH also includes a research and development (R&D) organization, as well as its contract manufacturing business.

More information: https://www.pfizer.com/