UPPSALA UNIVERSITET

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LÄNSSTYRELSEN UPPSALA LÄN

INTERNATIONAL CONFERENCE

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The scientific liaison Office of Wallonia Brussels in Sweden

6th edition

Wallonia – Uppsala University Symposium :

Antibiotic Resistance

Uppsala, 9th - 10th of March 2017

Venue:

Biomedical Center
Room C8:301

Program Thursday 9th March

8.50-9.00	Introduction and welcome

Session I - Drug development (Chair Dan Andersson)

9.00-9.25	**Anders Karlen**: Finding starting points for antibacterial drug discovery
9.25-9.50	**Moreno Galleni**: Structural studies of metallo-beta-lactamases and their inhibitors
9.50-10.15	**Stephane Vincent**: Antivirulence and antiadhesive strategies to combat bacterial pathogens: a chemist´s perspective
10.15-10.40	**Ulf Göransson**: Antimicrobial compounds with endless opportunities: discovery and design of macrocyclic peptides
10.40-11.10	COFFEE BREAK
11.10-11.35	**Caroline Stevigny**: Medicinal Plants: A tool to overcome antibiotic resistance?

Session II - Diagnostics (Chair Anders Karlen)

11.35-12.00	**Johan Elf**: Fast Antibiotic Susceptibility Testing based on single cell growth rate measurements
12.00-12.25	**Leonid Irenge**: Whole-genome sequences of multidrug resistant E. coli in Democratic Republic of Congo: characterization of phylogenomic changes, virulence and resistance genes
12.25-13.30	LUNCH

Session III - Resistance mechanisms and evolution (Chairs Linus Sandegren and Diarmaid Hughes)

13.30-13.55	**Pierre Bogaerts**: Carbapenemase-producing multidrug-resistant Enterobacteriaceae : Epidemiology in Europe and development of novel diagnostic technologies
13.55-14.20	**Linus Sandegren**: Influence of gene amplifications on carbapenem resistance evolution in E. coli
14.20-14.45	**Jean-Francois Collet**: How bacteria protect their cell envelope
14.45-15.10	**Pierre Smeesters/Anne Botteaux**: Antibiotic resistance among paediatric streptococcal infections: From mechanism to clinical diagnostic
15.10-15.40	COFFEE BREAK
15.40-16.05	**Hervé Nicoloff**: Heteroresistance in bacteria
16.05-16.30	**Laurence Van Melderen**: Toxin - antitoxin systems and persistence
16.30-16.55	**Diarmaid Hughes**: The importance of mutation supply and relative fitness
16.55-17.20	**Veronique Fontaine:** The PDIM lipid virulence factor in mycobacteria antibiotic resistance: impact in drug screening and diagnostic
19.30	DINNER

Program Friday 10th March

Session IV-- Pharmacokinetics and pharmacodynamics (Chair Herve Nicoloff)

09.30-09.55	**Elisabet Nielsen**: Understanding the PKPD of antimicrobial resistance
09.55-10.20	**Francoise Van Bambeke/Marie-Paule Mingeot-Leclerq**: Cellular and molecular pharmacology of antibiotics: from bench to bedside
10.20-10.45	**Lena Friberg**: PKPD modeling to reach the target
10.45-11.15	COFFEE BREAK

Session V-- Environmental aspects of antibiotic resistance (Chair Herve Nicoloff)

11.15-11.40	**Lorenzo Proia**: Role of natural aquatic ecosystems in the dissemination of antibiotic resistance. A case study: the Zenne River in Brussels
11.40-12.05	**Dan Andersson**: Selection of resistance in the environment
12.05-12.30	**Josef Järhult**: Antibiotic resistance in the human/animal/environment interface
12.30-13.45	LUNCH
13.45-15.15	Discussions with coffee
15.15-15.30	Conclusion

PRESENTATION OF SPEAKERS

First name, NAME : Anders KARLEN

Function : Professor Uppsala University

Mail : Anders.Karlen@orgfarm.uu.se

Presentation : Finding starting points for antibacterial drug discovery

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Summary of the talk

The pipeline of new antimicrobials is today almost dry and there is a need to boost development and innovation in this area. The Innovative Medicines Initiative (IMI) with support from the European Commission and major pharmaceutical companies (through EFPIA) recently launched the ENABLE project. The goal of ENABLE is to increase the overall pipeline in the antibacterial area and to progress a variety of antibacterial programmes through preclinical discovery and to complete by 2020 phase 1 trials of at least one novel anti-bacterial for systemic Gram-negative infections. ENABLE has been in operation for three years and an update on the Programme and where we are at the moment will be presented.

Career path

Anders Karlén is presently the overall medicinal chemistry project leader for drug discovery efforts currently directed at five different anti-bacterial targets at Uppsala University. Since February 2014 he is the Leader of the Managing Entity and co-coordinator of the €85 million, 6 year, Innovative Medicines Initiative (IMI) project ENABLE (European Gram Negative Antibacterial Engine). The ENABLE project, within IMI's New Drugs for Bad Bugs (ND4BB) programme, is working to advance the development of potential antibiotics against Gram-negative bacteria. The ultimate goal is to take at least one clinical candidate into a Phase I clinical study.

First name, NAME : Moreno GALLENI

Function : Professor ULG

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Presentation : Structural studies of metallo-beta-lactamases and their inhibitors

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Summary of the talk

The most worrying resistance mechanism displayed by Gram negative bacteria concerns the β-lactam antibiotics. Among them, carbapenems have the broadest activity spectrum and are considered as one of the last resort drugs to treat life-threatening nosocomial infections. While combination therapies (treatment with a β-lactamase inhibitor such as clavulanic acid or tazobactam to prevent inactivation of prescribed β-lactam antibiotics) are useful to deal with bacteria producing active site serine β-lactamases, metallo-beta-lactamase inhibitors are not currently available for clinical applications. In addition, the interplay between the decrease permeability of the outer membrane combined to the production of beta-lactamase favored the emergence of highly resistant Gram negative bacteria.

Career path

Graduating in chemistry from the University of Liège in 1984, Moreno Galleni, then began a PhD focusing on the resistance of bacteria to antibiotics. He finished his thesis in 1989 and started his study on dust-mite proteins at ULg's Protein Engineering Centre. Nominated 1st assistant in 1999, and professor in 2002, he is currently conducting research on dust-mite allergies, among other things, at the Biological Macromolecule Laboratory.

First name, NAME : Stéphane VINCENT

Function: Professor Unamur

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Presentation : Antivirulence and antiadhesive strategies to combat bacterial pathogens: a chemist´s perspective

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Summary of the talk

The emergence of resistant or extremely resistant pathogenic bacterial strains calls for the development of novel strategies to combat infectious diseases. Among them, antivirulence and antiadhesive strategies seem very promising. Our laboratory has been involved in these two approaches by the synthesis of carbohydrate-derived molecules. For the antivirulence strategy, the bacterial heptose biosynthetic pathway has been targeted. For the antiadhesion strategies, we are developing multivalent molecules as antagonists of the host/pathogen interaction.

Career path

Stéphane Vincent received his Master and PhD degrees in bioorganic chemistry from the Université Louis Pasteur (Strasbourg, France) with Charles Mioskowski.After postdoctoral studies first at The Scripps Research Institute in the research group of Prof. Chi-Huey Wong and then in Strasbourg with Prof. Jean-Marie Lehn, he took up a permanent position as a CNRS researcher in 2001 at the Ecole Normale Supérieure (Paris).In 2004, he began an appointment at Université de Namur (Belgium), as Assistant Professor then Full Professor in 2014. His research interests include the glycosciences, biocatalysis, and mechanistic enzymology.

First name, NAME : Ulf GÖRANSSON

Function : Professor Uppsala University

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Presentation : Antimicrobial compounds with endless opportunities: discovery and design of macrocyclic peptides

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Summary of the talk

In my talk I will give an overview of a unique family of antimicrobial peptides, the plant cyclotides, their effects and how they have inspired to the design of stabilized peptides derived from the human cathelicidin LL-37. The ultra stable cyclotide scaffold is based on three disulfide bonds and their characteristic seamless chain of amino acids; this cyclic backbone appears to give endless opportunities.

Career path

I obtained my PhD in 2002 at the Faculty of Pharmacy, Uppsala University. After post doctoral studies in structural biology at the Institute of Molecular Bioscience, University of Queensland, I returned to Uppsala in 2004. My research group focuses on discovery of biologically active peptides from plants and animals, and the production and use of stabilized peptide structures.

First name, NAME : Caroline STEVIGNY

Function : Associate professor ULB

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Presentation : Medicinal plants : a tool to overcome antibiotic resistance ?

Summary of the talk

The present talk will start with a global presentation of the PlantNut laboratory activities. Regarding our specific activities in the field of the antibiotic resistance, a phytochemical study, direct and indirect antimicrobial activities of African plants selected based on an ethnobotany survey will be presented in details

Career path

Caroline Stévigny is Pharmacist, PhD (Pharmaceutical Sciences, Natural Products), postdoc experience (Food and Agriculture, Italy). Since 2006, associate professor at Université Libre de Bruxelles – Laboratoire de Pharmacognosie, Bromatologie et Nutrition Humaine (PlantNut) (field: characterization and evaluation of biological activities of natural products isolated from ethnopharmacological selected plants).

First name, **NAME** : Johan ELF

Function : Professor Uppsala University

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Presentation : Fast Antibiotic Susceptibility Testing based on single cell growth rate measurements/

Summary of the talk

I will present a fast antibiotic susceptibility test where we capture individual bacterial cells in nanofluidic channels and monitor their response to different antibiotics based on direct imaging. By averaging the growth rate over a few hundred cells we can determine the susceptibility to several antibiotics in less than 15 min even at cell densities as low as 10^4 CFU/mL . The sensitivity, speed and low cost can make the test practically useful for guiding the primary antibiotic treatment in of several types of infections.

Career path

Johan Elf is Professor of Physical Biology at the Department of Cell and Molecular Biology at Uppsala University.

His research group studies dynamical processes in bacterial cells using sensitive optical measurement methods and quantitative modeling.

First name, NAME : Leonid IRENGE

Function : Senior Researcher UCL

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Presentation : Whole-genome sequences of multidrug resistant E.Coliin Democratic Republic of Congo : characterization of phylogenomic changes, virulence and resistance genes

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Summary of the talk

Whole genome sequencing data of multidrug-resistant *Escherichia coli* isolates (n=16) from a tertiary care hospital in the Democratic Republic of Congo have revealed that the virulent ST131-O25b:H4 and ST405 Extended Spectrum Beta-Lactamase (ESBL)-producing pandemic clones harboring plasmids with the CTX-M-15 gene were present in the country. Our data warrant a continuous surveillance of antimicrobial resistance in the DR Congo.

Career path

Leonid Irenge Mwana Wa Bene is Senior scientist with extensive experience in Microbiology and Molecular Biology. He is a Medical Doctor of the Université de Kinshasa (The Democratic Republic of Congo) a PhD of the Université catholique de Louvain (Belgium). During the past 4 years, he managed a project funded by the Belgian Cooperation, aimed at strengthening capabilities in clinical microbiology at the local level in the DR Congo (Bukavu, South Kivu Province).

First name, NAME : Pierre BOGAERTS

Function : Head of department UCL

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Presentation : Carbapenemase -producing multidrug-resistant Enterobacteriaceae : Epidemiology in Europe and development of novel diagnostic technologies

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Summary of the talk

Antimicrobial resistance including the emergence of extensively resistant Gram–negative bacteria has become a major public health issue worldwide. The enormous diversity of enzymes conferring resistance to beta-lactams, including to the last resort carbapenems, is still increasing and represent an important challenge for the diagnostic in clinical laboratory. We propose an overview of the current situation in Europe with a focus on Belgium epidemiology and present two innovative carbapenemase detection systems developed in our laboratory.

Carreer path :

Pierre Bogaerts is bioengineer and PhD in molecular biology from the UCL, Louvain-la-Neuve, Belgium.

Since 2002, he is the head of the molecular biology at the laboratory of microbiology of the teaching hospital CHU UCL Namur headed by Prof Youri Glupczynski. He is in charge of the molecular diagnostic of the routine laboratory and of the Belgian national reference center for antibiotic resistant Gram-negative bacteria and coordinator of R&D projects in the field of the Gram-negative resistance.

First name, NAME : Linus SANDEGREN

Function : Researcher Uppsala University

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Presentation : Influence of gene amplifications on carbapenem resistance evolution in E. coli

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Summary of the talk

Extended Spectrum Beta-lactamase (ESBL), or carbapenemase-producing Enterobacteriaceae such as *Escherichia coli* and *Klebsiella pneumonia* are at the top of the global priority pathogens list of antibiotic-resistant bacteria by the World Health Organisation. Carbapenems have become the last resort antibiotics for ESBL-producing bacteria and their increased use has created selection for increased carbapenem resistance.

We have studied the effect of ESBL-production on development of carbapenem resistance in and *K. pneumoniae* and found that both readily develops reduced carbapenem susceptibility and clinical resistance by combination of porin loss and β-lactamase over-expression, especially towards ertapenem. All three β-lactamases tested CTX-M-15, TEM-1 and OXA-1 can contribute to reduced carbapenem susceptibility in the absence of porin expression. Spontaneous amplifications of plasmid borne beta-lactamase genes had a major effect on resistance levels. However, the inherent instability of gene amplifications coupled with a fitness cost makes them unstable in the bacterial population and their prevalence is most likely underestimated in clinical isolates.

Career path

Linus Sandegren, Ph.D., Associate professor, is a molecular biologist/bacteriologist with a special interest in mobile genetic elements and antibiotic resistance evolution. His group studies fundamental aspects of how resistant bacteria evolve during antibiotic treatment in patients and hospital settings and how resistance plasmids are maintained and disseminated and serve as platforms for evolution of antibiotic resistance.

First name, NAME : Jean-François COLLET

Function : Professor UCL

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Presentation : How bacteria protect their cell envelope

Summary of the talk

The cell envelope of Gram-negative bacteria is an essential organelle that is in direct contact with the environment; proteins involved in its assembly are therefore attractive targets for new antibacterials. However, basic, important features of the envelope remain unknown. The long-term objective of our laboratory is to delineate and ultimately harness the mechanisms underlying the assembly and maintenance of the bacterial cell envelope. In my talk, I will explain how we recently discovered a new system rescuing envelope proteins from oxidative damages

Career path

During his PhD thesis in the lab of E. Van Schaftingen (UCL), Jean-François Collet discovered one of the largest families of phosphotransferases. In 2001, he moved to the lab of J. Bardwell (Michigan), where he became interested in the pathways of disulfide bond formation in the bacterial cell envelope. The major contribution of his postdoctoral stay was the engineering of a new pathway for the formation of disulfide bonds in the bacterial periplasm. In 2005, he started his own lab at the *de Duve Institute* (UCL, Brussels), where his group aims at understanding how envelope proteins fold and how they are protected from damages caused by environmental stresses. Important contributions of his lab include the identification of a new periplasmic reducing system that protects single cysteine residues from oxidation by reactive oxygen species, the discovery of a novel methionine sulfoxide reductase system rescuing periplasmic proteins from oxidative damage as well as the unraveling of the elegant mechanism used by the stress sensor RcsF to sense peptidoglycan and OM damages and to turn on the Rcs signaling system.

First name, NAME : Pierre SMEESTERS & Anne BOTTEAUX

Function : Head of department & associate professor

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Presentation : Antibiotic resistance among paediatric streptococcal infections: From mechanism to clinical diagnostic

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Summary of the talk

Our laboratory is interested in characterising the antibiotic resistance from paediatric clinical isolates with special focus on *Streptococcus pyogenes*. Key questions are: 1) Why is *Streptococcus pyogenes* never resistant to penicillin?; 2) What is the link between macrolide prescription and the induction of macrolide resistance by either efflux pump or ribosomal methylation?; 3) How can we develop new point of care diagnostic tools for better and faster diagnostic of antibiotic resistance in a clinical setting? A multidisciplinary laboratory with both basic scientists and clinicians has been set up to further elucidate these questions.

Career path

Anne Botteaux is a biologist, associate professor and PI of the Molecular Bacteriology Lab at the Free University of Brussels (ULB). After 10 years working on deciphering the activation mechanism of the bacterial Type 3 secretion systems and a brief time spent in the pharmaceutical industry, she is now working with Pr. Smeesters on understanding the virulence mechanisms of Group A *Streptococcus* .

Pierre Smeesters is a paediatrician acting as the head of the paediatric department from the Academic Children's Hospital Queen Fabiola at the Free University of Brussels (ULB) in Belgium. He is also leading a research group in Microbiology and Infectious Disease at the Free University of Brussels. His research interests include Group A Streptococcus, vaccination and new diagnostic tests.

First name, NAME : Hervé NICOLOFF

Function : Researcher Uppsala University

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Presentation : Heteroresistance in bacteria

Summary of the talk

Heteroresistance (HR) is the propensity of some bacterial isolates to display a heterogeneous susceptibility pattern where a subpopulation of cells displays a higher resistance than the main population. HR is not easily detected and is a cause of concern in the clinic. We performed a large-scale study and detected HR in about 30% of the tests performed, revealing that HR was a very frequent phenotype. We also found that spontaneous genetic amplifications were frequently involved in the subpopulations unstable increased resistance

Career path

Hervé Nicoloff is a researcher in Microbiology at the Department of Medical Biochemistry and Biology at Uppsala University. I obtained my PhD in Molecular and Cellular Biology from the University of Strasbourg, France, where I studied metabolic pathways in lactic acid bacteria. After two postodoctoral positions in the USA working on antibiotic resistance and on sigma factors, I joined the laboratory of Dan Andersson where I pursue my work on antimicrobial resistance.

First name, NAME : Laurence VAN MELDEREN

Function : Professor ULB

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Presentation : Toxin - antitoxin systems and persistence

Summary of the talk

My lab is working on toxin-antitoxin (TA) systems and persistence. TA modules are widespread in bacterial genomes and very diverse. We aim at discovering new toxins with new activities. Regarding persistence, although it was propose to be linked to TA systems, recent data from our lab and others showed that it is not the case. We are analyzing various aspects of persistence notably the involvement of stress responses such as the SOS system.

Career path

PhD in Molecular Biology, Université Libre de Bruxelles (ULB), Belgium
Professor and director of the Laboratory of Bacterial Genetics and Physiology (ULB)
Research interests: prokaryotic toxin-antitoxin systems and their impact on genome plasticity and physiology; molecular mechanisms of bacterial persistence and adaptation.

First name, NAME : Diarmaid HUGHES

Function : Professor Uppsala University

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Presentation : The importance of mutation supply and relative fitness

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Summary of the talk

The Importance on Mutation Supply and Relative Fitness in the Evolution of Resistance to Ciprofloxacin. We identified the order in which specific mutations are selected in the clinical genotype, showed that the high frequency genotype could be selected over a range of drug selective pressures, and that its probability of selection was strongly influenced by the relative fitness of alternative mutations and factors affecting mutation supply. Our data map for the first time the fitness landscape that constrains the evolutionary trajectories taken during the development of clinical resistance to ciprofloxacin and explain the predominance of the most frequently selected genotype.

Career path

Diarmaid Hughes is Professor of Medical Molecular Bacteriology at Uppsala University. His research is focused on the evolution or resistance to antibiotics, and on the discovery and early development of novel antimicrobial drugs to treat Gram-negative bacteria. His group uses experimental evolution, whole genome sequencing, genetic reconstructions, and measurements of physiological parameters to probe the trajectories of antibiotic resistance evolution.

First name, NAME : Veronique FONTAINE

Function : Professor ULB

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Presentation : The PDIM lipid virulence factor in mycobacteria antibiotic resistance : impact in drug screening and diagnostic

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Summary of the talk

Tuberculosis is still a cause of major concern, partly due to the emergence of multidrug-resistant strains. New drugs are therefore needed. We use a vancomycin susceptibility assay to detect drugs hampering lipid synthesis in *Mycobacterium bovis* BCG and in *Mycobacterium tuberculosis*, as we previously showed that a synergistic combination of vancomycin and cerulenin can inhibit MDR and XDR clinical strains. Among several tested drugs, tetrahydrolipstatin (THL) was able to synergize with vancomycin on *M. bovis* BCG and on *M. tuberculosis*. Lipid and proteomic analyses allowed us to identify several modifications in the treated *M. tuberculosis* and to assess the mechanisms of action of these drugs on *M. tuberculosis*.

Career path

Veronique Fontaine is a University Teacher since October 2009 in the Faculty of Pharmacy, she is at the Head of the Unit « Pharmaceutical Microbiology and Hygiene in the laboratory of Medical and Biological Chemistry and Pharmaceutical Microbiology.
Ph.D
She finished a Ph.D in January 1992 at the Institut Pasteur du Brabant
The title of the thesis was : identification, by mutagenesis, of sequences required for the interaction of the human IL-6 with its receptor

She does performing analyses in pharmaceutical microbiology (agreement of the AFMPS in 2012). She makes environmental analyses (water, air, surfaces, operators) ,bacteria and fungus analyses (cells counting) bactericidal and biofilm analyses for solutions or surfaces and challenge tests.

First name, NAME : Elisabet NIELSEN

Function : Assistant Professor

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Presentation : Understanding the PKPD of antimicrobial resistance

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Summary of the talk

The presentation will focus on techniques used to understand the relationship between drug exposure and antimicrobial resistance. The experimental setup, data produced and methods used to analyze and present the data will be discussed, both for currently used and novel methodologies. An example related to the assessment of efficacy and resistance for *E. coli* exposed to ciprofloxacin will be presented.

Career path

Elisabet Nielsen graduated in 1998 with a Master in Pharmaceutical Sciences, and in 2011 she received her PhD in the field of Pharmacokinetics and Drug Therapy, at the Faculty of Pharmacy, Uppsala University. Currently, she holds a position as senior lecturer in Clinical pharmacy. Dr. Nielsen co-leads the pharmacometric antibiotic research group at Uppsala University in collaboration with Prof. Lena Friberg and Prof. Mats Karlsson. The focus of her research is to advance the understanding of pharmacokinetics and pharmacodynamics for antibiotics and how to utilize pharmacometric methods to optimize treatments in the individual patient.

First name, NAME : Marie-Paule MINGEOT-LECLERCQ & Françoise VAN BAMBEKE

Function : Professor UCL & professor UCL

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Presentation : Cellular and molecular pharmacology of antibiotics: from bench to bedside

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Summary of the talk

Our team is studying the pharmacology of antibiotics with the aim to decipher the mechanisms responsible for their activity or their cellular toxicity, and to optimize their use in the clinics.

Our current research topics include the study of (a) the mechanism of action of original molecules targeting the membrane, (b) the role of active efflux in antibioresistance, (c) the pharmacokinetic (PK) and pharmacodynamic (PD) parameters contributing to impair antibiotic activity in persistent infections (intracellular infection, biofilm), (d) the mechanism of cellular toxicity of antibiotics accumulating in eucaryotic cells (lysosomal theraurismoses, mitochondrial alterations, apoptosis), (e) the optimization of antibiotic dosing based on PK/PD concepts. Disciplines involve biophysics, biochemistry, microbiology, cellular and molecular biology.

Career path

Francoise van Bambeke : pharmacist (1991); PhD (1995); University thesis (2005); Senior Research Associate of the Belgian FNRS and extra-ordinary Professor at the U*niversité catholique de Louvain* (pharmacology & pharmacotherapy), Brussels, Belgium.
research interests: PK/PD of antibiotics in persistent infections; resistance by efflux; new drugs
ORCID: http://orcid.org/0000-0002-0052-7991; Google scholar: http://scholar.google.com/citations?user=qc8SkV4AAAAJ&hl=fr

Marie paule mingeot – Leclercq is a full professor at the Catholic University of Louvain since 2008. She achieved a Ph.D in Pharmaceutical Sciences in 1988. She is at the Head of the

Louvain Drug Research Institute. Her Main Research Interest are Caracterization of the interactions between drugs (mostly antibacterials) and lipid membranes, the consequences of the interactions between drugs and lipid membrane on the biophysical properties of membranes (permeability, ability to fuse, lateral and transversal organization of lipids, bending modulus….) , the passage of peptides or drugs through membranes , the lysosomal phospholipase activity and the integrity of subcellular organites (lysosomes)

First name, NAME : Lena FRIBERG

Function : Professor Upssala University

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Presentation : PKPD modeling to reach the target

Summary of the talk

The dosing regimen of an antibiotic, i.e. both the dose amount and the dosing interval, can have a large impact on the rate and degree of bacterial killing as well as for emergence of resistance. The talk will focus on how clinical dosing regimens are defined today, the drawbacks of the current approach of defining the target, and how PKPD-models, i.e. mathematical descriptions of the time-course of bacterial kill and growth, can facilitate during drug development and for bridging between preclinical and clinical, and between different groups of patients who may have different PK.

Career path

Dr. Lena Friberg is since 2014 a Professor of Pharmacometrics in the Department of Pharmaceutical Biosciences at Uppsala University in Sweden. Her research has mainly focused on Pharmacokinetic-Pharmacodynamic (PKPD)-modeling of desired and unwanted effects of antibiotics and anticancer drugs. The developed models are intended for translation of the time-course of drug effects from preclinical (*in vitro* and *in vivo*) to patients, from early to late clinical drug development and between different patient populations.

First name, NAME : Lorenzo PROIA

Function : Researcher ULB

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Presentation : Role of natural aquatic ecosystems in the dissemination of antibiotic resistance. A case study: the Zenne River in Brussels area.

Summary of the talk

The importance of the aquatic ecosystems in the spread of antibiotic resistance will be shown through the presentation of the results obtained in four sampling campaigns carried out during 2016 in the Zenne River (Brussels, Belgium). The Zenne River is a paradigm of sewage-impacted river which receives the discharge of the two wastewater treatment plants (WWTPs) of Brussels. As a consequence the discharge of the river doubled after crossing the city of Brussels (half of the water downstream comes from WWTP effluents) making Zenne River a good model to study the influence of treated wastewater release on the spread of antibiotic resistance in freshwater ecosystems.

Career path

I was born in Rome (Italy) the 31st October 1978. I got my degree in Biology at the University of Rome “Tor Vergata” in 2005. In 2007,I got a Marie Curie research fellowship to start my PhD at the Institute of Aquatic Ecology of the University of Girona (Spain) working on the effects of multiple stressors on river ecosystems. I obtained my Ph.D. degree in 2012 afterwards I worked as postdoc in different Spanish research institutes. Since October 2015 I continued to work in the field of antimicrobial resistance in the interface of environment, animals, and humans - both regarding influenza and antibiotic resistance. He is engaged in the "One Health" approach to research and the build-up of "Zoonosis Science Center" at Uppsala University. I started my research at the Ecology of Aquatic Systems group of the University of Brussels (Belgium) granted by the Fund for Scientific Research – FNRS working on the antibiotic resistance in river microbial communities.

First name, NAME : Dan ANDERSSON

Function : Professor Upssala University

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Presentation : Selection of resistance in the environment

Summary of the talk

Antibiotic use results in generation of antibiotic concentration gradients and pathogenic bacteria are often exposed to non-lethal (sub-MIC) drug concentrations in humans, animals and the environment. Recent evidence suggest that sub-MIC exposure may accelerate the emergence and spread of antibiotic-resistant bacteria among humans and animals.

Career path

Dan Andersson is a geneticist and evolutionary biologist who studies various evolutionary processes using mainly experimental evolution approaches. Particular interests include evolution of antibiotic resistance and new genes and proteins.

First name, NAME : Josef JÄRHULT

Function : Researcher Uppsala University

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Presentation : Antibiotic resistance in the human/animal/environment Interface

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Summary of the talk

The occurence of antibiotic resistance is well documented in the environment as well as in both wild and domestic animals. However, the extent and direction of transmission of resistance in between those compartments is poorly understood. This talk will give a brief overview and then focus on two case studies: i) experimental evidence of prerequisites for wild birds as reserviors and spreaders of antibiotic resistance; and ii) descriptive evidence of a pronounced similarity in antibiotic resistance genes in humans and domestic animals in a low-income setting.

Career path

Josef Järhult works 50% as a consultant physician in Infectious Diseases and 50% as a researcher. He did his PhD on development of resistance in influenza A viruses in Mallards exposed to the antiviral Tamiflu. He has continued to work in the field of antimicrobial resistance in the interface of environment, animals, and humans - both regarding influenza and antibiotic resistance. He is engaged in the "One Health" approach to research and the build-up of "Zoonosis Science Center" at Uppsala University.