EURESTOP WG meeting

13 June 2023

Brussels, COST Association, 23rd floor of the Manhattan Center, Avenue du Boulevard – Bolwerklaan 21, 1210 Brussels Belgium

Scientific Committee:
Mattia Mori (Italy) - Action Chair
Patricia Rijo (Portugal) - Vice Chair
Cristina Nativi (Italy) - Science Communication coordinator
Priyanka Sahariah (Iceland) - Grant Awarding coordinator
Dana Reichmann (Israel) - WG1 Leader
Younes Smani (Spain) - WG2 Leader
Carole Devaux (Luxembourg) - WG3 Leader

PRACTICAL INFORMATION FOR MEETINGS AT COST ASSOCIATION: HOW TO GET TO HERE

COST Association is located on the **23rd floor of the Manhattan Center** (next to the Rogier square). The building entrance is entrance is between the Delhaize supermarket and Thon Hotel.

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Address : Rue des Croisades – Kruisvaartenstraat 19, 1210 Brussels – Belgium

Public parking : 2.80 € / hour – 18€ / 24 hours

Metro Station : Rogier (metro lines 2 & 6 tram 3, 4, 25, & 55)

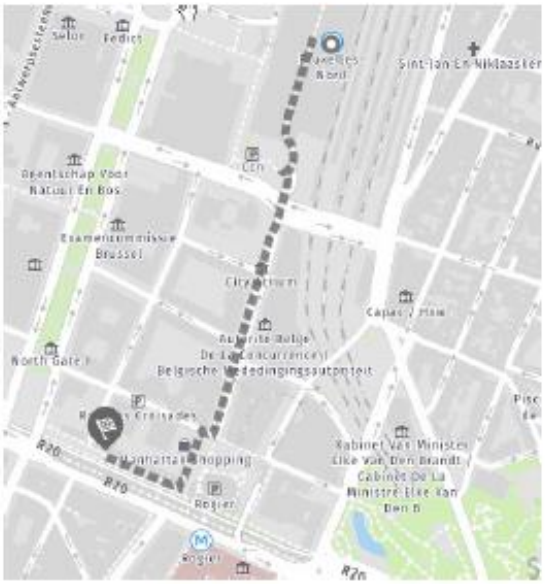
Transport from airport to COST Association

TRAIN:

Brussels North Station (5 minute walk)
Gives direct access from Brussels airport
Frequency: 4 trains per hour
Trip: 15 minutes
Price: 18.60 € return – 9.30 € single (2nd class)

TAXI:

Trip: round 35 to 40 min (morning 8 am and afternoon 5 pm)
Price: 45 € to 50 € (single trip)



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AGENDA

09:00 – 09:10	Welcome – **Mattia Mori**, Italy (Chair of the Action)
09:10 – 10:00	**Stephen Hawser** (CEO of IHMA Europe Sàrl, Switzerland): *Strategies for Monitoring and Combating Antimicrobial Resistance*
10:00 – 10:10	**Younes Smani**, Spain, WG2 leader
10:10 – 10:20	**Carole Devaux**, Luxembourg, WG3 leader
10:20 – 10:30	**Tomislav Mestrovic**, Croatia, Stakeholders coordinator
10:30 – 10:40	**Cristina Nativi**, Italy, Science Communication Coordinator
	10:40 – 11:10 Coffee break
11:10 – 11:20	**Priyanka Sahariah**, Iceland, Grant Awarding Coordinator
11:20 – 11:35	**Didem Şen Karaman**, Turkey, YR&Is Coordinator
11:35 – 11:50	**Giordano Rampioni**, University Roma Tre, Italy: *Novel therapeutic approaches against Pseudomonas aeruginosa.*
11:50 – 12:05	**Martijn Riool**, Amsterdam institute for Infection and Immunity, The Netherlands: *Novel Synthetic Antimicrobial and Anti-biofilm Peptides (SAAPs)-containing coatings to prevent biomaterial-associated infection.*
12:05 – 12:20	**Alexander Titz**, Saarland University, Germany: *Fighting ESKAPE bacteria: Lectin inhibitors as antibiofilm agents and probes for imaging/drug targeting*
	12:20 – 13:45 Lunch
13:45 – 14:00	**Ghadeer Suaifan**, The University of Jordan, Jordan: *Development of colorimetric biosensors for pathogenic bacterial detection*
14:00 – 14:15	**Maciej Kachanowski**, National Veterinary Research Institute, Poland: *Phenotypic and genotypic profiling of antimicrobial resistance in Streptococcus suis strains isolated from Polish swine populations.*
14:15 – 14:25	**Dana Reichmann**, Israel, WG1 leader
14:25 – 15:05	**Round Table #1** – *Creation of a virtual/physical EURESTOP chemoteque* (moderator: Mark Broenstrup)
	15:05 – 15:30 Coffee break
15:30 – 16:10	**Round Table #2** – *Enhancing WG2/WG3 interactions* (moderators: Younes Smani & Carole Devaux)
16:10 – 16:50	**Round Table #3** – *Creation of a virtual collection of strains* (moderator: Rossella Grande)
16:50 – 17:00	Closing remarks and next steps/events

ABSTRACTS (in order of presentation)

Strategies for Monitoring and Combating Antimicrobial Resistance

Stephen Hawser

CEO IHMA Europe Sàrl, Monthey, Switzerland

Antimicrobial resistance (AMR) continues to evolve and spread globally. As a result, infectious diseases become more challenging or even impossible to treat leading to an increase in morbidity and mortality. This emerging pandemic requires immediate and continual attention. Despite the failure of conventional, traditional antimicrobial therapy, in the past two decades no novel class of antibiotics has been introduced. Owing to this emergent situation, several novel alternative strategies to combat these drug resistant organisms, often multi- or even pan-resistant, have been identified. Traditional strategies such as novel synthetic and novel natural product antimicrobials are in development, but numerous other strategies are being applied or proposed as potential alternatives to traditional antibiotics. The current AMR situation, how to monitor and report, and status of new antimicrobials and alternative strategies will be highlighted.

Novel therapeutic approaches against Pseudomonas aeruginosa

Giordano Rampioni and Livia Leoni

Department of Science, University Roma Tre, Rome, Italy

Antivirulence drugs and antibiotic adjuvants could complement classic antibiotic therapies in the fight against MDR bacterial pathogens.
The ESKAPE Gram-negative pathogen Pseudomonas aeruginosa causes severe antibiotic-resistant infections in lungs, bladder, cornea and wounds and chronic lung infections in cystic fibrosis patients. Besides being intrinsically resistant to many antibiotics, it is prone to acquire resistance genes and to form hard to treat biofilms. In fact, P. aeruginosa is included in the WHO priority list of pathogens for which new therapic approaches are urgently needed, and has become a major model organism for studies focused on the identification of antivirulence agents and antibiotic adjuvants.
This talk will retrace the pre-clinical research about novel therapeutic approaches against P. aeruginosa carried out by our group, from the development of target-oriented screening systems to the discovery of antivirulence activities in old drugs, through their validation against clinical strains, up to the discovery of additional and unpredicted antibiotic adjuvant activities. Moreover, additional research lines carried out in our laboratory for the identification/characterization of new antivirulence target proteins, and for the investigation of gene expression at the single cell level will be briefly presented.

Novel Synthetic Antimicrobial and Anti-biofilm Peptides (SAAPs)-containing coatings to prevent biomaterial-associated infection

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The use of medical devices has grown significantly over the last decades, and has become a major part of modern medicine and our daily life. Infection of implanted medical devices (biomaterials), like catheters, prosthetic heart valves or orthopaedic implants, can have disastrous consequences, including removal of the device. For still not well understood reasons, the presence of a foreign body strongly increases susceptibility to infection. These so-called biomaterial-associated infections (BAI) are mainly caused by Staphylococcus aureus and Staphylococcus epidermidis. Formation of biofilms on the biomaterial surface is generally considered the main reason for these persistent infections, although bacteria may also enter the surrounding tissue and become internalized within host cells (Riool et al., Acta Biomater., 2014). Our work focuses on the development and characterization of novel antimicrobial agents and delivery systems, and their effectiveness in the prevention of BAI and other difficult-to-treat biofilm infections. The scarcity of current antibiotic-based strategies to prevent infections and their risk of resistance development prompted us to develop novel Synthetic Antimicrobial and Anti-biofilm Peptides (SAAPs) based on the primary sequences of the human antimicrobial proteins Thrombocin-1 and LL-37, and to test their potential in the fight against implant-associated and wound infections by multidrug-resistant bacteria. The lead peptide, SAAP-148, kills multidrug-resistant pathogens without inducing resistance, prevents biofilm formation and eliminates established biofilms and persister cells, and is effective against both acute and established skin infectionsde (de Breij & Riool et al., Sci. Transl. Med., 2018). Currently, we are developing improved SAAPs. As a next step, we aim to develop antimicrobial coatings, such as a new polymeric supramolecular scaffold material, exerting two important functions: preventing microbial adhesion - by incorporating SAAPs - and thereby preventing biofilm formation, and inducing endogenous (eukaryotic) cells to adhere and propagate, as a first step towards functional tissue repair.

Fighting ESKAPE bacteria: Lectin inhibitors as antibiofilm agents and probes for imaging/drug targeting

Alexander Titz

Saarland University, Germany

Bacterial biofilms are a severe problem for therapy. The Gram-negative bacterium P. aeruginosa is currently the most critical bacterial pathogen as defined by the WHO priority pathogen list. This bacterium is difficult to treat due to excessive development of resistance to antibiotics and its abundant biofilm formation. The latter is a major resistance determinant of this pathogen since the biofilm shields embedded bacteria from chemotherapy and host defence. Therefore, several approaches to identify new anti-infectives against this bacterium aim to block biofilm formation. P. aeruginosa utilises the two lectins LecA (PA-IL) and LecB (PA-IIL) for initial adhesion to the host, for biofilm formation and as virulence factors. These are promising drug targets that are addressed in our research for therapeutics, diagnostics and conjugates.
Various other ESKPAE pathogens have lectins that may serve as drug targets in the future.
Complementary to the lectins as targets, we exploited novel chemical matter as antibiotics against P. aeruginosa (PA) and Acinetobacter baumannii, the two most critical bacteria with extensive antimicrobial resistance.

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Development of colorimetric biosensors for pathogenic bacterial detection

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For thousands of years, microbial infections caused a wide range of ailments, from mild infections to potentially fatal diseases. Conventional detection approaches are frequently time-consuming, requiring experienced staff and lengthy processing time. As a result, new types of extremely sensitive, selective and low-cost nanostructured biosensors capable of detecting microbial infections in a number of applications (e.g., clinical diagnostics, food analysis, and environmental monitoring) were developed. These colorimetric biosensors involved the utilization of nanomaterials such as gold nanoparticles, quantum dots, graphene, magnetic nanoparticles, carbon nanotubes, plasmonic nanostructures and photonic crystals. Our work involves the development of a highly sensitive and specific colorimetric biosensor for pathogens spot detection by using a specific peptide probe for the detection of proteases secreted by the pathogen. Pathogen proteases precisely cleaved specific peptide substrates labeled with nano-magnetic beads and attached to a gold sensing surface. The superiority of this approach is based on its low-cost, simplicity being colorimetric, can be run by unskilled personnel and can be applied to real samples (without the need for isolation or purification) in a short time (1-5 minutes).

Phenotypic and genotypic profiling of antimicrobial resistance in Streptococcus suis strains isolated from Polish swine populations

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Streptococcosis, a severe disease in swine attributed to Streptococcus suis, is globally recognized. In Poland, this pathogen is identified in diseased tissues, including lungs, joints, heart, and brain, in a significant 30% of samples submitted for routine diagnosis. The disease prominently presents as septicemia, meningitis, pneumonia, bronchitis, pleurisy, and endocarditis, primarily affecting piglets and fattening pigs. Alarmingly, acute cases result in the death of previously asymptomatic pigs.
In addition to affecting swine, S. suis is a causative agent of invasive diseases in humans, predominantly meningitis, but also septicaemia, endocarditis, and arthritis. These sporadic infections are primarily encountered in certain occupational groups, notably abattoir workers and butchers. Moreover, exposure to raw or undercooked meat products poses a risk of S. suis infection, thus warranting its classification as a food-borne pathogen.
During 2021-2023, S. suis strains were isolated from swine demonstrating disease symptoms across numerous Polish farms. Their antimicrobial susceptibility was evaluated using disk diffusion, following the standard protocols of the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Using the Illumina NextSeq 500 technology, 91 S. suis strains underwent whole-genome sequencing. The resulting data were processed through an internal quality-control (QC) pipeline developed at the Technical University of Denmark (DTU), which eliminated low-quality and adapter sequences using bbduk2 and executed de novo assembly with SPAdes. In-depth sequence analysis was subsequently performed using in silico bioinformatics tools from the Center for Genomic Epidemiology (https://genomicepidemiology.org/).
The study discovered heightened resistance in S. suis strains to tulathromycin (56%) and oxytetracycline (49%). Other resistances were identified against lincomycin-spectinomycin (33%), doxycyclin (18%), gentamycin (14%), tiamulin (9%), and enrofloxacin (8%). Notably fewer resistant strains were detected for sulfamethoxazole-trimethoprim (4%), penicillin (4%), florfenicol (2%), and ampicillin (1%), with zero resistance noted for amoxicillin-clavulanic acid, and ceftiofur. Importantly, a third of these strains displayed resistance to three or more antibiotics. The most prevalent resistance genotypes were erm(B) and tet(O). Genotypes such as tet(M), tet(W), and lsa(E) were half as common, and genes tet(40), tet(W), tet(L), tet(T), tet(O/W/32/O), optrA, and lnu(C) were identified in singular isolates.
In conclusion, this study highlights a significant prevalence of antibiotic-resistant S. suis strains in Polish swine populations. Among these strains, resistance is most frequently observed against antibiotics from the tetracycline and macrolide groups, underscoring a potentially escalating challenge in the treatment of streptococcosis.
The combined analysis of both phenotypic and genotypic data provides a comprehensive understanding of antimicrobial resistance. It not only identifies the current resistance traits of the bacteria (phenotype) but also predicts their potential future evolution (genotype). This integrated approach is vital for informing the design of effective antimicrobial strategies, optimizing treatment protocols, and implementing targeted interventions to mitigate the public health impact of antibiotic-resistant S. suis strains.