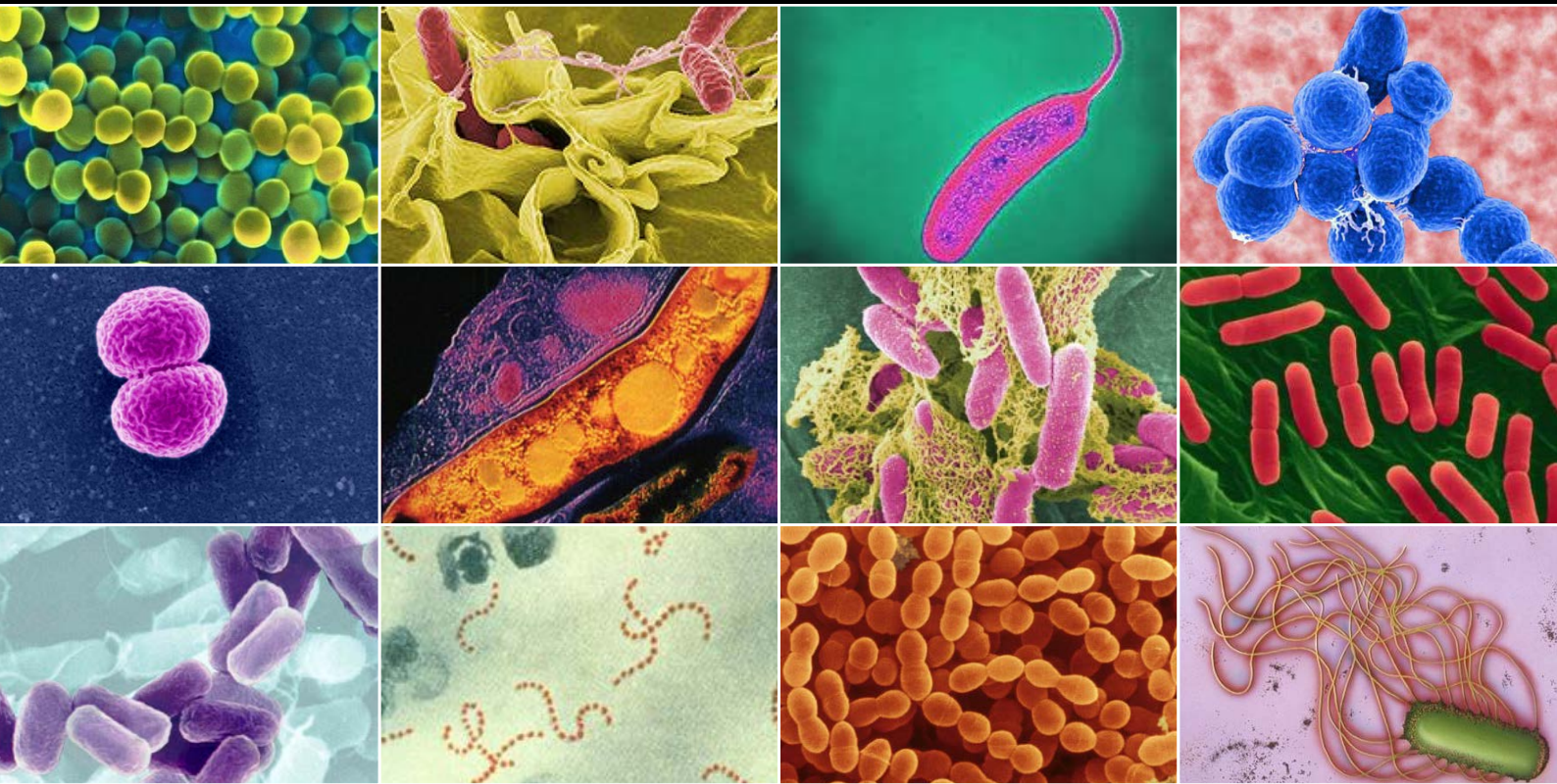
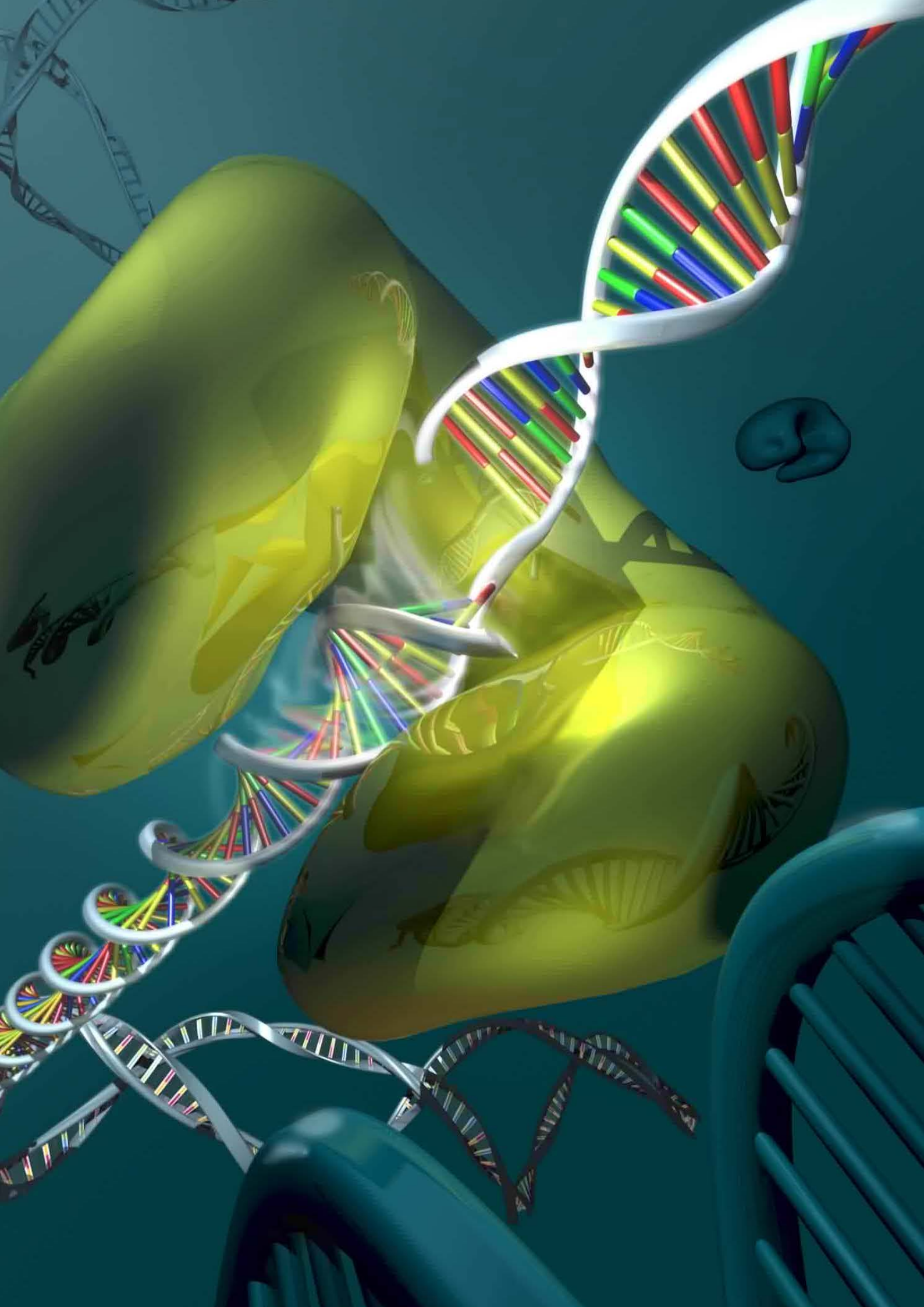


FEMS EMIF

The EFoST Annual
Conference, Bologna -
November 12 2013 at 14-18

PRE-CONFERENCE WORKSHOP
INFECTION DIAGNOSTICS
AND INFECTION BIOLOGY





From the organizers

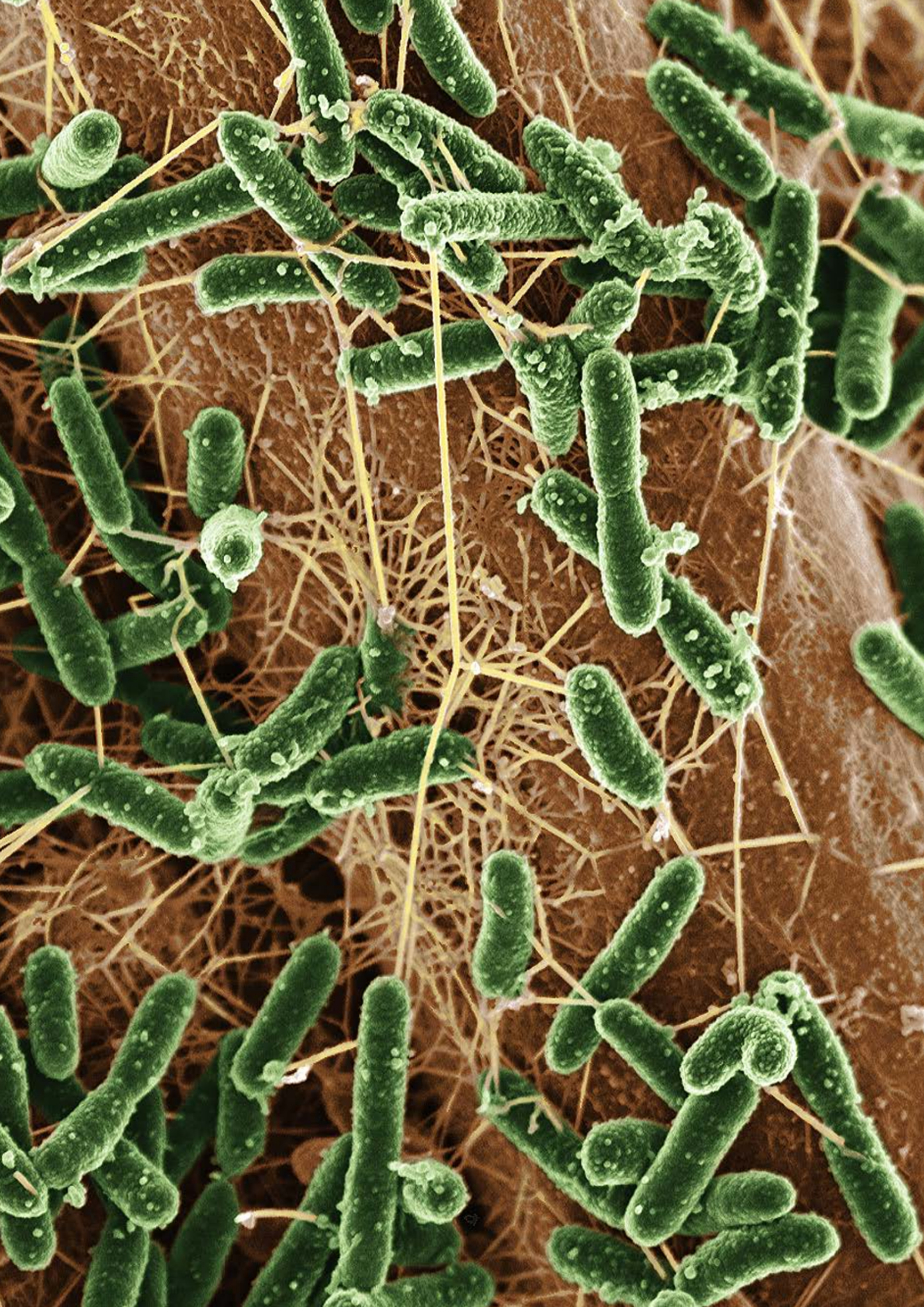
Welcome to the FEMS EMF-EFFoST pre conference meeting on infection diagnostics and infection biology! Presently microbes play an important but still underestimated role in life, while their role will only become more and more important in the future. Microbes impact on issues like well-being, healthy ageing and infectious diseases and thereby influence the growth of the population. In a wider context, climate change and depletion of energy resources, which are events that force society to explore and to use the potential of microbes for life in new ways. Where science and industry have revealed and applied many of the benefits of microbes in the past centuries, much remains still to be discovered.

The mission of the FEMS European Microbiology Forum (EMF) is to ensure that Microbiology is positively visible, thereby contributing to integrate Microbial Science and Technology in the decision-making process of European society, including public administration, private companies, educational institutions, media and the general public. The EMF is thereby the FEMS reference platform for the public understanding of Microbiology, ensuring recognition of the pivotal role of Microbiology in environment, industry, medicine and our overall well-being, hence the value of supporting Microbiology in education, research and innovation.

We are so pleased that world-leading scientists join us at this FEMS EMF- EFFoST pre-conference workshop to discuss the state-of-the-art and current perspectives on the role of microbiology related to food issues and life in general. Our aim is to address the relationship between microbes, their hosts and food relevant for food consumption, public health, healthy ageing and even sustainability and resource efficiency in society. Thus, this FEMS EMF-EFFoST pre-conference breaks new ground by addressing relevant gaps that exist in our understanding of the connections between microbes and food.

Tone Tønjum
FEMS EMF Secretary General





Programme

14:00 - 14:05	Marco Dalla Rosa, Italy, EFFoST chair: Welcome and focus on EFFoST - FEMS EMF interactions
14:05 - 14:30	Jean Claude Pifaretti, Switzerland, FEMS president: Quality control in microbial diagnostics
14:30 - 15:00	Jan van Impe, Belgium: Towards next generation predictivemodels: a systems biology approach relevant for food microbiology
15:00 - 15:30	Eliora Ron, Israel, FEMS EAM: Impact of the EHEC epidemic
15:30 - 16:00	Coffee break
16:00 - 16:30	Cesare Montecucco, Italy: Bacterial neurotoxins in infection biology
16:30 - 17:00	Brian B. Rudkin, France: Peptide aptamers: precision tools for dissecting signaling pathways
17:00 - 17:30	Tone Tønjum, Norway: Microbes and aging
17:30 - 17:50	Discussion
17:50 - 18:00	Tone Tønjum, Norway, FEMS EMF Secretary general: Closing remarks

Speaker

Abstracts



Jean-Claude PIFFARETTI
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Laboratory diagnostics in clinical and food microbiology: trends and quality assessments

Human health and food safety are often closely interlinked. Indeed, food can easily be the vector of infectious agents causing disease in humans. Hence, the microbiology diagnostics laboratory plays a central role in: i) identifying pathogens in clinical specimen; ii) assessing the qualitative and quantitative presence or absence of pathogens in food samples; iii) through the use of phenotypic or genotypic methods, establishing the potential link between a microorganism responsible of a disease (or an outbreak) and that isolated from a suspicious food. In the recent years, the diagnostic and typing methods have been steadily changing, with rapid molecular and automated techniques replacing the classical culture methods. These techniques, based mostly on nucleic acids (DNA), provide advantages, but can also raise a few problems related to the reliability of the results. Thus, validation and quality assessment of the diagnostic methods remain fundamental both in clinical and food microbiology.



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Systems biology for predictive food microbiology

Despite all efforts, more than 300,000 food poisonings are still reported in Europe each year, causing several hundreds of casualties and significant economic losses. Last century, food safety and quality research has prospered and the domain of predictive microbiology has gained significance. Predictive microbiology combines microbial knowledge and numerical techniques to generate mathematical models that describe and predict microbial behavior in food products.

First generation models accurately describe microbial dynamics under non-stressing conditions for liquid systems. However, these models fail (i) when applied to real, structured foods, and/or (ii) under stressing conditions. As a result, a quest for more mechanistically-based models has been initiated by considering single cells via Individual-based Models (IbMs) and Metabolic Network Models (MNM). Despite the promising potential of IbMs and MNMs, their widespread application in predictive microbiology is still lacking. This is due to (i) the detailed cell level information needed, and (ii) the complex nature of the models.

KU Leuven/BioTeC aims at building a novel generation of multi-scale predictive models by incorporating information collected at the micro- (cell), meso- (colony/subpopulation) and macro-scale (population). By combining multi-scale models with advanced computational strategies for large and uncertain systems, an innovative approach in quantitative food microbiology is being developed.

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<https://lirias.kuleuven.be/cv?u=U0013377> - complete list of publications of the author

www.cit.kuleuven.be/biotec - KU Leuven/BioTeC

www.kuleuven.be/optec - KU Leuven/OPTEC Optimization in Engineering Center

www.scores4chem.be - Knowledge Platform Chemical Industry & Life Sciences

www.AOPTimise.be - Knowledge Platform (Waste)Water Treatment

www.cpmf2.be - Flemish Cluster Predictive Modeling in Foods



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The impact of the EHEC epidemic of 2011

In the late spring of 2011 there was a major outbreak of pathogenic *Escherichia coli* O104:H4 that spread from Germany to other countries. Nearly 4000 persons were infected and more than 900 of them developed haemolytic uremic syndrome (HUS) resulting in 54 deaths. This epidemic was unusual in the number of infected people, the high proportion of HUS and the age distribution (median age, 42 years). This epidemic brought into focus important questions concerning rapid identification of the source of the infection and early warning systems as well as public health issues and prevention of future outbreaks.



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Safety aspect of food associated microorganisms

The genus *Clostridium* includes hundreds of species of anaerobic bacteria which are present in the environment as spores. They have a great importance in ecology, biotechnology and pathology. In fact few species produce exotoxins of great relevance for human health. One species produces a neurotoxin that acts within spinal cord neurons and causes the spastic paralysis of tetanus (tetanus neurotoxin, TeNT), whilst few species produce the botulinum neurotoxins (seven different serotypes: BoNT/A, /B, /C, /D, /E, /F and /G) that act on peripheral neurons and cause the flaccid paralysis of botulism. These neurotoxins intoxicate neurons via a four-step mechanism that includes: 1) binding, 2) endocytosis inside synaptic vesicles, 3) membrane translocation of a metalloprotease domain and 4) specific cleavage of the three major proteins forming the nanomachinwe that mediates the release of neurotransmitters. This causes a prolonged blockade of neuroexocytosis.

Here, I will discuss the recent acquisitions on the mechanism of entry of TeNT and BoNT inside nerve terminals and the identification of novel inhibitors of step 3) of the entry process.

In addition, I will discuss the possible advantages of the production of the BoNTs, which are the most potent toxins known, for the ecology of toxin-producing Clostridia.



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Peptide aptamers: precision tools for dissecting signaling pathways

Abstract

While systems biology approaches analyzing the genome, proteome, interactome etc. are increasing our understanding of complex regulatory networks, identification and modulation of the activity of key proteins in signaling pathways that regulate cellular responses, remains crucial for furthering our understanding of normal cellular processes and pathological perturbations thereof. Peptide aptamers, conceived to conceptually resemble antibodies, are small combinatorial proteins with a constant scaffold presenting a variable region. Implementation of peptide aptamer technologies allows identification and / or validation of targets, localization of the binding interface involved in the biological response and development of small molecules to mimic the peptide aptamer actions. Examples of identification of biologically-active peptide aptamers will be presented.

Bio

Dr. Rudkin is a Research Director at the CNRS, Head of a research group at the Ecole Normale Supérieure de Lyon, one of the top French academic research institutions, Laboratory of Molecular and Cellular Biology since 1990 and Co-Director of the Joint Laboratory on Neuropathogenesis at the ECNU along with Prof. ChongGang YUAN at East China Normal University (ECNU) in Shanghai since 2009. Prior to this, he was Senior Staff fellow at the National Institutes of Health (NICHD) USA, with G. Guroff (Nerve growth factor (NGF) signaling), subsequent to Post-Doctoral experience with G. Thomas (S6 Kinase) then J. Jiricny (G/T Mismatch binding proteins), at the Friedrich Miescher Institut of now NOVARTIS, Basel, Switzerland, after a PhD from the Department of BioChemistry & BioPhysics, University of Pennsylvania.

The group has dissected pathways involved in NGF signaling. Notably, they were first to describe those responsible for cell cycle phase-specific anti-mitogenic and differentiation responses. This led from the regulation of promoter function to trafficking, fate and identification of partners of NGF receptors that impact upon the signaling outcome from lipid rafts. The focus of applied research in the laboratory implements the peptide aptamers to identify novel therapeutic molecules towards existing validated therapeutic targets and to identify and validate novel targets for therapeutic intervention with particular focus on signaling pathway(s) involved in cancer and neurodegenerative diseases.

Dr. Rudkin is a member of the Executive committee for the coordination of the "Quality of Life and Aging" Research Cluster of the Rhone-Alps Region that encompasses research laboratories, small innovative companies, large multinationals, university hospitals and patient organizations to better serve the needs of society regarding these concerns. He is also on the investment committee of CREALYS, the regional incubator for accompanying innovative projects from research laboratories since its inception in 1999. Dr. Rudkin has accompanied a number of innovative companies in their creation and development over the years, as external advisor or partner.



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Microbes and ageing: Influence of DNA repair

One of the main theories of aging is based on the notion that macromolecular damage in DNA accumulates over time, and that these events could cause many of the phenotypical changes and genome instability seen with the aging process in mammalian organisms. A particular culprit is oxidative stress. Oxidative DNA damage induced by reactive oxygen species (ROS) is a major source of mutation load in living organisms and is believed to play a causative role in aging, neurodegenerative diseases and cancer. To counteract the potential harmful effects of oxidative DNA damage, cells primarily use the base excision repair (BER) pathway. BER is initiated by lesion specific DNA glycosylases which identify and excise the damaged base, leaving an abasic site in the DNA which is further processed by the other enzymes of the BER pathway.

Neisseria meningitidis, the meningococcus, is a leading cause of meningitis worldwide. This pathogen faces up to the environment in its exclusive human host with a small but hyperdynamic genome. We constructed meningococcal mutants inactivating genes involved in base excision repair, mismatch repair, nucleotide excision repair, translesion synthesis and recombinational repair pathways. Distinct differences between the meningococcus and the *E. coli* paradigm for DNA repair in the mutational profiles were identified.

In addition to defining roles for neisserial genome dynamics, these findings are important in the context of prokaryotic models linking bacterial mutator phenotypes to cellular fitness, survival under stress and disease. We are currently testing whether the corresponding DNA repair profile in humans develops or attenuates with normal aging and Alzheimer's disease. Correlating these findings with results of cognitive tests revealed a linkage of certain SNP combinations with memory and attention deficit. Collectively, these findings provide new insight into how both genetic variation and conservation generate a basis for maintaining genome stability and cellular function in the aging process.

NOTES

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UiO : **University of Oslo**



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