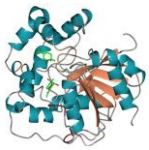
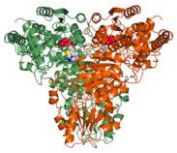
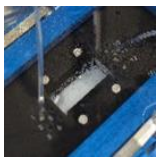


ESAB
European Society of Applied Biocatalysis

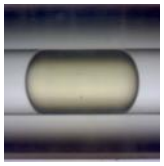
SKB
Schweizerischer Koordinationsausschuss für Biotechnologie
Swiss Coordination Committee for Biotechnology





ESAB - SKB Webinar

Biocatalysis and Molecular Medicine



July 29th 2022

09.00-11.00 British Summer Time (BST)
10.00-12.00 Central European Time (CET)
16.00-18.00 China Standard Time (CST)
17.00-19.00 Japan Standard Time (JST)

Chairs: Jennifer Littlechild (University of Exeter)
Roland Wohlgemuth (Lodz University of Technology)
Antonio Ballesteros (CSIC, Madrid)
Thomas Sauter (Université du Luxembourg)

PROGRAMME

10.00 CET Prof. Dr. Thomas F. Meyer, Max Planck Institute for Infection Biology, Department of Molecular Biology, Berlin, and Laboratory of Infection Oncology, Institute of Clinical Molecular Biology, Christian Albrecht's University of Kiel and University Hospital Schleswig Holstein – Campus Kiel, Germany

Critical mechanisms in the pathogenesis of persistent bacterial infections

The generation of vaccines is a prime strategy to protect against infectious diseases. However, some infections so far escaped effective prevention or therapy by vaccines due to either sophisticated escape mechanisms by such pathogens or inappropriate practicality. Similarly, antibiotic treatment regimens may not always be feasible due to collateral effects, e. g. with respect to the general microbiota. Future efforts will need to overcome pathogens' evasion strategies and be aimed to precisely target pathogenic traits. Here, I will discuss two bacterial pathogens implicated in human carcinogenesis which call for innovative approaches of disease prevention.

Gastric infections with H. pylori are characterized by a remarkably strong inflammatory response along with the ability of the bacteria to persist in the inflamed gastric mucosa. While our analysis of the first phenomenon revealed an entirely novel cellular pathway, involving alpha kinase 1 (Alpk1) and TIFA being triggered by the bacterial ADP-heptose in a type 4 secretion system (T4SS) dependent manner (Zimmermann et al. 2017), H. pylori withstands the resulting antibacterial response by effectively suppressing IFN and IL22 signaling of the infected epithelial cells by glucosylating and extracting the cholesterol from host cells (Wunder et al. 2006; Morey et al. 2018). Thus, the two essentially antagonistic features enable H. pylori to establish immune-protected micro-niches in the gastric mucosa within a strongly inflamed surrounding mucosal environment. These micro-niches provide H. pylori the proficiency to colonize the human stomach essentially life-long, thus, driving host cells to acquire carcinogenic properties.

The bacterial genotoxin colibactin is known to be a potent inducer of DNA damage in epithelial cells in vitro. Infection with E. coli harboring the pks island, which encodes the biosynthesis gene cluster of colibactin, has also been linked to increased tumorigenesis in various mouse models. Two recent independent in vitro studies from our lab (Dziubańska-Kusibab et al., 2020) and Clevers' lab (Pleguezuelos-Manzano et al., 2020) have revealed the preferential target sites of colibactin in the DNA. Colibactin's damage at this motif gives rise to a mutational signature that can be identified in the genomes of a subset of colorectal cancers. Our subsequent work (Iftekhar et al., 2021) provided clues on how failure of proper repair of cross-linked DNA constitutes a risk factor of colon cancer.

Having recognized the mechanistic basis of carcinogenesis in the course of these two persistent bacterial infections, this propels innovative approaches for early cancer prevention that will be discussed.

PROGRAMME

10.30 CET Prof. Dr. Grzegorz Węgrzyn, Department of Molecular Biology, Faculty of Biology, University of Gdansk, Wita Stwosza 59, 80-308 Gdansk, Poland

Mucopolysaccharidoses - molecular mechanisms and treatment options of disorders caused by defects in biocatalysis of glycosaminoglycan decay

Mucopolysaccharidoses (MPS) is a group of 14 diseases belonging to lysosomal storage disorders (LSD) that occur with cumulative frequencies of all their types of about 1 per 40,000 – 50,000 live births. These diseases are caused by mutations in genes coding for enzymes involved in biocatalysis of degradation of glycosaminoglycans (GAGs) (formerly called mucopolysaccharides). Their impaired hydrolysis leads to continuous accumulation and storage of these compounds in cells of patients, which results in a damage of the affected tissues, including the heart, respiratory system, bones, joints and central nervous system. MPS are usually fatal diseases (especially neuronopathic forms of MPS), with average expected life span of one or two decades. MPS are monogenic diseases, which are often considered model genetic diseases in studies on mechanisms of genetic disorders and development of novel therapeutic strategies. Despite monogenic nature of MPS, recent studies demonstrated that their pathomechanisms are significantly more complex than primary effects of GAG storage on functions of lysosomes. It appeared that expression of hundreds of genes is changed in MPS cells and many cellular processes are significantly affected. This causes further changes in function of tissues, organs and the whole body. Nevertheless, our knowledge on molecular processes occurring in MPS cells, and disease-specific changes relative to normal cells, is still limited. On the other hand, understanding molecular pathomechanisms of the disease, especially molecular aspects of various interactions between biologically active macromolecules, is crucial for both gaining basic knowledge on regulation of various biological processes and developing new therapeutical strategies for genetic diseases which are particularly difficult to cure. In fact, previous studies on MPS allowed to achieve spectacular progress in understanding principles of genetic disorders and to propose many sophisticated therapeutical options, including enzyme replacement therapy, substrate reduction therapy, modifications of gene therapies, and many others.

11.00 CET Prof. Dr. Leonardo Scapozza, School of Pharmaceutical Sciences, University of Geneva, and Institute of Pharmaceutical Sciences of Western Switzerland, University of Geneva, Switzerland

Biocatalysis in Cells through Proteolysis Targeting Chimeras (PROTACs): How to Improved Cell Permeability and Achieve Successful Protein Degradation

Proteolysis Targeting Chimeras (PROTACs) are heterobifunctional degraders that specifically eliminate targeted proteins by hijacking the ubiquitin-proteasome system (UPS) and fostering ubiquitination in situ of the protein to be degraded and eliminated. This modality has emerged as an orthogonal approach to the use of small-molecule inhibitors for knocking down classic targets and disease-related proteins classified, until now, as “undruggable”. In early 2019, the first targeted protein degraders reached the clinic, drawing attention to PROTACs as one of the most appealing technology in the drug discovery landscape. Despite these promising results, PROTACs are often affected by poor cellular permeability due to their high molecular weight (MW) and large exposed polar surface area (PSA). Herein, we will report using several case studies a comprehensive record of PROTAC design, pharmacology and thermodynamic challenges and solutions, as well as some of the available strategies to enhance cellular uptake, including suggestions of promising biological tools for the in vitro evaluation of PROTACs permeability towards successful protein degradation.

PROGRAMME

11.30 CET **Prof. Dr. Adil Mardinoglu, Science for Life Laboratory, KTH - Royal Institute of Technology, Stockholm, Sweden, and Centre for Host-Microbiome Interactions, Faculty of Dentistry, Oral & Craniofacial Sciences, King's College London, London, United Kingdom**

The use of systems biology in treatment of liver diseases

To develop novel strategies for prevention and treatment as well as to gain detailed insights about the underlying molecular mechanisms of liver diseases, it is vital to study the biological functions of liver and its interactions with other tissues and gut microbiota. Biological networks can provide a scaffold for studying biological pathways operating in the liver in connection with disease development in a systematic manner. In my presentation, I will present our recent work where biological networks have been employed to identify the reprogramming in liver physiology in response to NASH/NAFLD. I will further discuss how this mechanistic modelling approach can contribute to the discovery of biomarkers and identification of drug targets which may lead to design of targeted and effective personalized medicine.

Key points of my presentation

- Omics technologies are used in detailed characterization of human liver tissue in health and disease states.
- Biological network models are functional tools for exploring and integration of multi-omics data.
- Systems biology uses a holistic and integrative approach for comprehensive analysis of the biological functions in healthy and diseased states
- Systems Biology approaches have been successfully employed in hepatology to identify biomarkers and drug targets.
- These integrative tools can be used for simulation of liver tissue functions and its crosstalk with other tissues for prediction of therapeutic and side effects.

ABOUT THE SPEAKERS

Prof. Dr. rer. nat. Thomas F. Meyer **Curriculum Vitae**

1971-1979	Biology, University of Heidelberg; 1977 Diploma, 1979 Ph.D. ('summa cum laude')
1979-1980	Junior Scientist, Max Planck Institute (MPI) for Medical Research, Heidelberg.
1980-1981	Research Fellow (DFG), Cold Spring Harbor Laboratory
1981-1982	Visiting Scientist (MPG), Public Health Research Institute of the City of New York
1982-1983	Staff Scientist, Max Planck Institute for Medical Research, Heidelberg
1983-1985	Group Leader, Centre for Molecular Biology at Heidelberg University (ZMBH)
1985-1990	Head of Research Unit ('C3' tenured), Max Planck Institute for Biology, Tübingen
1990-2006	Adjunct ('apl.') Professor University of Tübingen, Biology Faculty
1990-2000	Director, MPI for Biology, Department of Molecular Biology, Tübingen
1994	Co-Founder, Max Planck Institute for Infection Biology, Berlin
1994-2020	Director, Department of Molecular Biology, MPI for Infection Biology, Berlin
2003-2017	Managing Director (rotating 2-year periods), MPI for Infection Biology, Berlin
2009	Founder & Director, Center for Systems Biomedicine, Steinbeis Innovation GmbH
2014	Foundation Focus Biomed for Research on Infection, Remote Sequels and Cancer
2019-2021	Senior Professor, Charité University Medicine Berlin
2020 (01.09.)	Director Emeritus, Max Planck Institute for Infection Biology, Berlin
2020 (01.09)	Senior Professor, Christian Albrecht's University of Kiel (CAU), Med. Faculty (UKSH)

Awards

1980	Carl Clemm - Carl Haas - Research Award, University of Heidelberg
1981	Otto Hahn Medal, Max Planck Society
1986	Heinz Maier Leibnitz Award, Federal Minister for Science and Education
1989	Main award, Foundation of the German Society for Hygiene and Microbiology
1989	Elected Member, European Molecular Biology Organisation (EMBO)
1993	Max Planck International Collaboration Award of the Alexander van Humboldt Foundation
1996	Aronson Award of the Federal State of Berlin
2001	Elected Fellow of the German Academy of Naturalists Leopoldina
2004	Honorary Professor Humboldt University Berlin
2005	Honorary Professor Charité University Medicine Berlin
2016	Elected Member European Academy of Microbiology
2017	Honorary Professor Zhengzhou University, Fifth Affiliated Hospital, China
2018	Member of the American Association of Cancer Research
2019	Honorary Professor Jilin University, Changchun, China
2020	ERC Advanced Grant Award (2.5 M€, 5 y)
2020	Robert Koch Medal in Gold 2020 of the Robert Koch Foundation

Publication statistics

Researcher unique identifier - ORCID: 0000-0002-6120-8679, Total: Meyer TF >400 original peer-reviewed articles (without book chapters), H-Index (Meyer TF): Web of Science: 87, Pubs. Top Journals (IF >=10): Total (>70)

Research interests at a glance

Active homepage: https://www.mpiib-berlin.mpg.de/1911472/molecular_biology

Genetic basis of microbial behaviors and virulence mechanisms (1978 – 1998)

From insights into host cell mechanisms of infection towards host-directed therapy (1991 – 2020)

Impact of chronic bacterial infections on human cancer and remote sequels (2000 – ongoing)

ABOUT THE SPEAKERS

Grzegorz Węgrzyn, Ph.D., D.Sc., Professor, graduated from University of Gdansk, Poland. In 1987 he obtained MSc degree in biology, and in 1991 PhD degree in molecular genetics. His PhD thesis was focused on the regulation of DNA replication in starved cells. Then (in 1991), he was a research fellow at the Department of Biochemistry, University of Nottingham Medical School (UK), where he worked on the mechanisms of gene expression regulation in bacteria. In 1992 he was a post-doctoral researcher at Center for Molecular Genetics, University of California at San Diego (USA), where he investigated regulation of viral DNA replication. Since 1996 he is a head of Department of Molecular Biology at the University of Gdansk (Poland). In his laboratory, several projects are conducted, which are focused mainly of gene expression and DNA replication, and mechanisms and new treatment methods of human genetic diseases. Grzegorz Wegrzyn is a co-author of over 400 scientific articles in peer-reviewed journals and over 600 communications on scientific conferences. He is a member of American Society for Biochemistry and Molecular Biology, American Society for Microbiology, International Society for Plasmid Biology, and Society for Experimental Biology and Medicine. He is an editor of several scientific journals, including FEMS Microbiology Reviews, Microbial Cell Factories (Editor-in-Chief), Metabolic Brain Disease (Deputy-Chief-Editor), Plasmid, Scientific Reports, and Acta Biochimica Polonica (Editor-in-Chief). He supervised 54 PhD theses and has experience in leading teams, being the Principal Investigator in 11 international and 28 national research grants), and having functions of Head of Department of Molecular Biology, Dean of Faculty (2002-2008), and Vice-Rector for Research (2008-2016).

ABOUT THE SPEAKERS

Prof. Dr. Leonardo Scappozza is a pharmacist by training and received his PhD in pharmaceutical chemistry at the ETH. He spent 3 years as postdoctoral fellow in Switzerland and in the USA (Texas A&M University) working in the field of pharmaceutical chemistry and structural biology. 1996 he returned at the ETHZ as "Oberassistent" in Pharmaceutical Chemistry by Prof. Folkers where he became Assistant Professor in February 2001. In October 2004 he was appointed Full Professor of Pharmaceutical Biochemistry/Chemistry at the University of Geneva. His research focuses on molecular recognition for a better understanding of ligand-macromolecule interactions to develop therapeutic strategies in the therapeutic area of Rare Diseases, Cancer & Antibiotics involving new chemical entities and targets. The approach is based on the combination of biochemistry/biophysics, medicinal chemistry, molecular pharmacology, and computational chemistry/molecular modelling techniques. He is a member of the editorial board of a number of scientific journals, has won three Phoenix prizes for innovative scientific work in pharmaceutical chemistry and published more than 150 papers in peer-reviewed journals. He is an inventor on 10 patents and has obtained an orphan drug designation on the use of tamoxifen in Duchenne muscular dystrophy granted by EMA in 2017. Through drug repurposing his group has brought Tamoxifen to phase 3 clinical trial (TAMDMD) for Duchenne Muscular Dystrophy. He is a member of the UNIGE SNF commission and a member of the board of the Swiss Society of Experimental Pharmacology (SSEP) as well as the Division of Medicinal Chemistry and Chemical Biology (DMCCB) of the Swiss Chemistry Society (SCS). He is co-founder of Adoram Therapeutics, a UNIGE-spin-off company.

ABOUT THE SPEAKERS

Prof. Dr. Adil Mardinoglu is an expert in the field of Systems Medicine, Systems Biology, Computational Biology and Bioinformatics. He has been recruited as a Professor of Systems Biology in the Center for Host-Microbiome Interactions, King's College London, UK where he leads a computational group. He also works as a group leader in Science for Life Laboratory (Scilifelab), KTH-Royal Institute of Technology in Sweden and led a team of 25 researchers working in the area of computational biology, experimental biology and drug development to develop new treatment strategies for Metabolic diseases, Neurodegenerative diseases and certain type of cancers.

Professor Mardinoglu received his Bachelor's degree from Istanbul Technical University, Turkey in Electronic and Telecommunication Engineering and his Ph.D. from Waterford Institute of Technology, Ireland in magnetic drug targeting applications. He worked as a postdoctoral researcher at Trinity College Dublin, Ireland and Chalmers University of Technology, Gothenburg, Sweden. His recent research activities include the generation of the context-specific genome-scale metabolic models (GEMs) for human cell-types including liver, adipose, muscle, heart, kidney and brain as well as certain types of cancer e.g liver, kidney, colon, prostate and brain (glioblastoma) cancers. His research team also focuses on the integration of GEMs with the other biological networks including regulatory, protein-protein interactions and signaling networks.

He employs comprehensive biological networks for revealing the molecular mechanisms of complex diseases, identification of novel biomarkers and drug targets and eventually developing efficient treatment strategies. Professor Mardinoglu has contributed to the creation of human tissue, subcellular and pathology atlas within the Swedish Human Protein Atlas program and cell atlas within the international Human Cell Atlas program. He has published around 100 research and review papers in different journals including Science, Cell Metabolism, Nature Communications, PNAS, Cell Reports, Molecular Systems Biology and EbioMedicine. He is also co-founder of three different biotech companies focusing on the development of novel drugs for fatty liver disease and different cancer types.

NEXT ESAB WEBINARS

ESAB aims to promote the development of Applied Biocatalysis and takes initiatives in areas of growing scientific & industrial interest in the field.

Schedule and Topics of the next ESAB webinars:

26th August 2022 14.00-16.00 CET	Synthetic Biology and Metabolic Engineering Tools and Methodologies, organized by Frangiskos Kolisis and Roland Wohlgemuth
23rd Sept. 2022 14.00-16.00 CET	Advances in the Analysis of Enzymatic Reactions, organized by Jennifer Littlechild and Roland Wohlgemuth
21st October 2022 14.00-16.00 CET	Biocatalytic Process Engineering, organized by Polona Žnidaršič-Plazl and ESAB Working Group Biocatalytic Process Engineering

HOW TO JOIN ESAB

You are cordially invited to join ESAB by completing the membership application form online *via* https://esabweb.org/Join+us/Application+form.html

Personal membership is free.

Institutional membership is welcome and is currently being established as new membership category.

ESAB has been founded in 1980 and has the mission of promoting the development of Applied Biocatalysis throughout Europe. The aims of ESAB are to promote initiatives in areas of growing scientific and industrial interest of importance within the field of Applied Biocatalysis.

Further information on ESAB Conferences and other activities can be found on the ESAB website www.esabweb.org

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