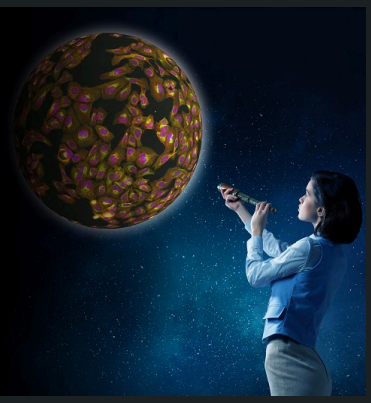
Microscopy Focus

Leica MICROSYSTEMS

See the Hidden: Spatial Proteomics
Gaining new disease insights through a better understanding of protein subcellular localization



Thursday, February 16th 2023
1pm London, 2pm Berlin, 5pm Dubai

Join us for this next virtual edition of our See the Hidden workshop series, which will continue to explore the topic of Spatial Biology – this time looking at the spatial localization of proteins.

Together with leading experts, we will examine how a deeper understanding of protein subcellular localization, using advanced microscopy techniques, can shed new insights into diseases such as metabolic disorders and cancer.

In this workshop, you will discover:

- Multiplexed imaging methods for spatial proteomics of cells and tissues
- Deep Visual Proteomics (DVP) for spatial molecular profiling in tissues at single cell resolution
- Novel golgi-nuclear interactions identified following analysis of genome-scale localization data from the Human Protein Atlas
- Advanced microscopy, laser microdissection, and AI-based techniques for studying protein subcellular localization

Through a series of scientific talks, our guest speakers from across Europe will present their research and discuss how specialized microscopy approaches are delivering unique insights into this exciting field. The program will also feature live panel discussions and microscopy showcases that focus on four specific areas in microscopy:

1. Laser microdissection
2. Multicolor microscopy (multiplexing)
3. AI-based image analysis
4. Confocal microscopy

Don't miss this exciting event or the chance to ask your questions to the experts and take part in interactive polls to share your experiences and views on Spatial Proteomics.

As a NEW addition to our See the Hidden workshop series in 2023, we are also delighted to offer you the opportunity to see some of the microscopy techniques you will hear about during this event, in more depth, in a short virtual follow-up workshop.

AGENDA

WELCOME AND INTRODUCTIONS

13:00 BST | 14:00 CET

Welcome & Introductions
Dr. Boris Zarda

PANEL DISCUSSION

13:05 BST | 14:05 CET

Dr. Boris Zarda, Prof. Andreas Mund, Dr. George Galea, Dr. Franco Klingberg, Dr. Christoph Greb, Dr. Falco Krüger, Dr. Charlotte Stadler, Dr. David Pointu, Dr. Jens Peter Gabriel

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DEEP VISUAL PROTEOMICS: UNLOCKING SPATIAL MOLECULAR PROFILING IN TISSUE AT SINGLE CELL RESOLUTION

13:25 BST | 14:25 CET

Prof. Andreas Mund

Single-cell omics technologies have greatly improved our understanding of cellular heterogeneity in complex samples. However, single-cell proteomics lags behind genomic technologies due to the technical challenges of amplifying and detecting the proteome. Spatial methods such as multiplexed immunofluorescence imaging can only measure a limited number of proteins, while imaging mass spectrometry is not yet sensitive enough for high spatial resolution. To address this, we have developed a novel technique called Deep Visual Proteomics (DVP) that integrates high-content imaging, AI, laser microdissection, and multiplexed mass spectrometry. DVP allows for single-cell analysis within intact tissues, preserving spatial information and providing a comprehensive view of the proteome. With a depth of 1,700 proteins, single-cell DVP (scDVP) can classify cells, assign functions, and even apply machine learning to infer the spatial proteome from imaging data alone. DVP is a powerful, unbiased method that is applicable to both healthy and diseased tissues and complements other spatial omics technologies in creating atlases of cellular abundance, distribution, and organization.

LASER MICRODISSECTION (LMD) AND AI SHOWCASE

14:00 BST | 15:00 CET

Dr. Christoph Greb

SPATIAL PROTEOMICS OF CELLS AND TISSUES USING HIGHLY MULTIPLEXED IMAGING

14:05 BST | 15:05 CET

Dr. Charlotte Stadler

To simultaneously visualize multiple markers within the same sample enables a more detailed view of cellular phenotypes and how they orient in space. This in turn brings deeper understanding of the function and interplay of different cell types in situ, of value for research related to many biological conditions. In this talk, Dr. Stadler will present methods for generating highly multiplexed imaging and show how her team is working on making these methods more easily adaptable. Furthermore, she will discuss the opportunities and challenges for implementing multiplexed imaging into clinical practice, and give an example of how multiplexed imaging was used to diagnose lung cancer biopsies using a panel of 7 markers. She will also share some data from a protocol developed in her lab to simultaneously visualize proteins and DNA loci using FISH in combination with multiplexed immunofluorescence (IF).

MULTIPLEX IMAGING SHOWCASE

14:40 BST | 15:40 CET

Dr. David Pointu

THE GOLGI COMPLEX AS A REGULATORY HUB FOR DNA REPAIR

14:45 BST | 15:45 CET

Dr. George Galea

The Golgi complex has long been recognised as an important homeostasis hub, where a multitude of signalling pathways and essential cellular processes intersect. Meanwhile, Golgi-nuclear communication and signalling dynamics remain largely unexplored. To this end, we have analyzed genome-scale localization data from the Human Protein Atlas which revealed an unexpectedly high number of Golgi and nuclear dual-localization proteins and several pathways including, surprisingly, DNA Damage Response (DDR). The latter is composed of regulatory proteins of various DNA repair pathways, including essential protein machinery for Homologous Recombination (HR), Non-Homologous End Joining (NHEJ), Mismatch Repair (MMR) and Base Excision DNA repair (BER), as well as other integral regulators of DNA repair cellular response such as chromatin cohesion, ubiquitination, cell cycle and signalling. These findings are the first report of DNA repair protein clusters localizing to the Golgi complex.

Through functional analysis of these dual-localization DDR proteins, we found that in response to specific DNA lesions, these proteins shift in localization either from the Golgi to the nucleus or from the nucleus to the Golgi, based on their role in the specific DDR pathway. Furthermore, we also have identified a class of Golgi proteins named Golgins that act as regulators and anchors of these DDR proteins at the Golgi. Exploring in more detail one of the major DNA repair proteins identified, RAD51C, confirmed a functional involvement of its Golgi population in the regulation of HR-mediated DNA repair. In response to double-strand DNA breaks, the Golgi protein population of RAD51C redistributes to form DNA repair foci. The Golgi localization of RAD51C was found to be dependent on the Golgin Giantin, with its depletion causing the disappearance of the Golgi localization and a nuclear redistribution of RAD51C independent of DNA damage induction and the recruitment of additional HR DNA repair machinery. This redistribution of RAD51C co-occurred with a significant increase in genomic instability and inhibition of DDR signalling response, both indicators of DNA repair disruption.

In this presentation, Dr. Galea will present evidence for a novel Golgi regulatory pathway for the coordination of HR-mediated repair through the activity of RAD51C and Giantin. The results also highlight that this regulation is not just restricted to HR-mediated DNA repair but also extends to other types of DNA repair mechanisms. Furthermore, he will propose that the Golgi, in its integrating function of several critical pathways, could act as a link to ensure that cellular homeostasis is maintained in response to DNA damage. This discovery has the potential to open new scientific fields and could significantly change the way we understand DNA repair regulation.

IMAGING MICROHUB SHOWCASE

15:20 BST | 16:20 CET

Dr. Falco Krüger

CONFOCAL MICROSCOPY SHOWCASE

15:25 BST | 16:25 CET

Dr. Jens Peter Gabriel

CLOSING REMARKS

15:30 BST | 16:30 CET

Dr. Boris Zarda

SPEAKERS

Dr. Boris Zarda
Advanced Workflow Manager
Leica Microsystems

Boris Zarda trained as a Microbiologist and has over 30 years of experience in multiple fluorescence microscopy techniques. He has been with Leica Microsystems for 24 years and currently manages their Advanced Workflow Specialist team. The proximity of Boris and his team to real-life science makes them ideally placed to facilitate the development of new technologies. Boris is dedicated to optimizing imaging techniques and workflows and strongly believes in knowledge sharing to improve results.

Prof. Andreas Mund
Associate Professor,
Clinical Proteomics, Novo Nordisk Foundation
Center for Protein Research

Prof. Andreas Mund is an expert in the field of clinical proteomics. As an Associate Professor at the University of Copenhagen, he is part of the team led by Prof. Matthias Mann at the Novo Nordisk Foundation Center for Protein Research. With a dual education in biotechnology engineering and protein biochemistry from the Anhalt University of Applied Sciences and University of Hamburg (Germany) respectively, Prof. Mund brings a unique skillset to his research, which focuses on understanding the molecular mechanisms of health and disease through the characterization of single cell identity and heterogeneity in tissue biobank samples. He uses cutting-edge techniques such as high parametric imaging, artificial intelligence, and ultrahigh sensitive proteomics to achieve this goal. He spearheaded the development of “Deep Visual Proteomics” - an innovative technology that allows unbiased quantification of thousands of proteins in single cells while retaining spatial context, providing new insights into the underlying mechanisms of disease.

Dr. George Galea
Research Scientist,
European Molecular Biology Laboratory
(EMBL) Heidelberg

George is a researcher working in the Pepperkok team at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. His research focuses on understanding how the Golgi complex interacts with other organelles to coordinate various cellular processes in response to physiologically relevant cues such as DNA damage events. To better understand these processes, he applies multi-omic approaches, including high-throughput imaging, to dissect the Golgi structure organization and DNA repair mechanics.

SPEAKERS

Dr. Franco Klingberg
Market Development Manager Aivia
Leica Microsystems

Franco Klingberg studied biotechnology (B.Sc. & M.Sc.) at the Brandenburg University of Technology. During his studies he worked on research projects in the United States and Australia. He obtained his PhD in Cell Biology from the University of Toronto. The project involved various microscopy techniques and image analysis challenges. After completion of his doctorate, Franco continued his career in a commercial role as Technical Sales Specialist for imaging and detection solutions with Thermo Fisher Scientific. In 2021, he joined Leica Microsystems supporting the launch of a novel Artificial Intelligence based software.

Dr. Christoph Greb
Application Scientist
Leica Microsystems

Christoph Greb studied cell biology at the Philipps University in Marburg. In the course of his dissertation he examined the vesicular transport of apically destined proteins in polarized epithelial cells utilizing biochemistry as well as TIRF and confocal microscopy. After his engagement for Novartis Vaccines & Diagnostics he started working for Leica Microsystems in October 2013 as a Scientific Writer, followed by positions as Workflow Manager, Application Manager and today, Application Scientist.

Dr. Falco Krüger
Manager Advanced Workflow Specialist
Leica Microsystems

Falco obtained his PhD in Plant Cell Biology in the group of Professor Karin Schumacher at the Centre for Organismal Studies in Heidelberg. Falco joined Leica Microsystems in 2018 and focused on advanced widefield microscopy. Since the launch of the THUNDER widefield imaging systems in 2019, he has hosted workshops demonstrating the power of THUNDER to the scientific community. More recently, he has also excelled at training researchers remotely.

SPEAKERS

Dr. Charlotte Stadler
Co-Director Spatial and Single Cell Biology Platform and Head of Spatial Proteomics, SciLifeLab

Charlotte Stadler is a co-director of the Spatial Biology platform at the Science for Life Laboratory. She is also Head of the National Spatial Proteomics facility. Charlotte received her PhD in 2012 within the framework of the Human Protein Atlas (HPA) project under Prof. Emma Lundberg and Prof. Mathias Uhlén, establishing many of the protocols and pipelines for image-based subcellular protein profiling that are used in the Human Protein Cell Atlas. Her team works mainly with highly multiplexed imaging using sequential immunofluorescence and barcoded antibodies using cutting-edge instruments.

Dr. David Pointu
Senior Application Manager Leica Microsystems

David Pointu has been application manager for Cell DIVE and translational research at Leica Microsystems since 2021 and has broad experience in light microscopy, including various aspects of cell and tissue imaging and analysis. After studying physical chemistry at the University of Strasbourg, he completed his PhD in 2002, followed by a postdoctoral fellowship at the Institut Curie. In 2004 he moved into industry, and has worked as an application specialist in high-end microscopy at several companies, including GE Healthcare.

Dr. Jens Peter Gabriel
Advanced Workflow Specialist Leica Microsystems

Jens Peter Gabriel obtained his PhD in Biology (Neurobiology) from the University of Cologne. He continued to work in this field as a postdoctoral researcher at the Max-Planck-Institute for Medical Research in Heidelberg/Germany and the Karolinska Institute in Stockholm/Sweden. His main interests were neuronal networks generating behavior, which he studied in zebrafish using methods like electrophysiology, multi-photon calcium imaging, and confocal microscopy. His passion for biological imaging was the reason why Jens joined Leica Microsystems in 2009. As Advanced Workflow Specialist he is now contributing to scientific progress in different ways: by helping researchers identify which microscope system best fits their requirements, and by supporting them through trainings and application advice.