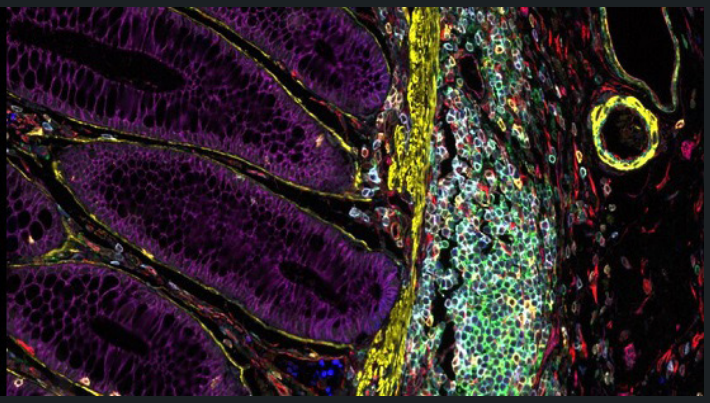
Microscopy Focus

Leica MICROSYSTEMS

See the Hidden
LIVE ONLINE WORKSHOP

Translational Cancer Research

Thursday 28th October 2021
LONDON 10:00 - 15:00 I BERLIN 11:00 - 16:00 I DUBAI 13:00 - 18:00



Understanding cancer biology has become increasingly dependent on imaging. High-resolution imaging is vital for studying genetic and cell signaling changes that underlie cancer, whereas live-cell imaging is crucial for a deeper understanding of disease mechanisms. Microscopy techniques are also essential for the study of spatial relationships between different types of tumor cells. They are also critical to understanding the immune system's role in combating cancerous cells. For the latter, researchers rely on multiplexing imaging solutions for a faster rate of discovery.

Leica Microsystems is pleased to invite you to the 3rd Virtual Edition of our See the Hidden Workshop, this time focused on Translational Cancer Research, hosted by Microscopy Focus. The workshop is centered on scientific sessions covering a broad range of first-hand applications of our workflows, encompassing sample preparation, multiplexing, imaging, and analysis. In addition, participants will have the opportunity to join instrument demonstrations and Q&A discussions.

This is an excellent opportunity to hear from leading researchers and industry experts, to learn about the innovative imaging systems and workflows that are available in order to address the critical challenge of tumor heterogeneity, to gain a deeper understanding of the mechanisms of cancer development, and translate these discoveries into information that can be used to advance therapeutics.

AGENDA

Each presentation will be followed by a Q&A session and technical demonstration from a member of the Leica Microsystems team.

WELCOME

10:00 BST I 11:00 CET

Welcome & Overview
Dr Falco Krüger

SESSION 1: SAMPLE PREPARATION FOR TRANSLATIONAL RESEARCH

10:10 BST I 11:10 CET

Tumor cell heterogeneity and its transcriptional bases in pancreatic cancer
Dr Giuseppe Riccardo Diaferia

Laser Microdissection Application Showcase
Dr Mauro Baron
Dr Christoph Greb
Dr Falk Schlaudraff

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SESSION 2: MULTIPLEXING AND CANCER TISSUE ANALYSIS

11:00 BST I 12:00 CET

Single-cell phenotyping and spatial analysis of cancer and immune cells with quantitative protein multiplex imaging
Dr Alison Cheung

Cell DIVE Application Showcase
Dr David Pointu

LUNCH

12:00 BST I 13:00 CET

SESSION 3: CONFOCAL IMAGING IN TRANSLATIONAL CANCER RESEARCH

13:00 BST I 14:00 CET

When genome stability is bad for you: How resolution of R-loops promotes DNA replication and maintains cancer cell proliferation
Dr Manolis Papamichos Chronakis

The STELLARIS Workflow Application Showcase
Mr Paul McCormick

SESSION 4: THE APPLICATIONS OF CORRELATIVE MICROSCOPY

13:45 BST I 14:45 CET

Cryo Light Microscopes – the essential tool for your Cryo EM Workflow
Dr Jan De Bock

SESSION 5: PANEL DISCUSSION

14:15 BST I 15:15 CET

Dr Falco Krüger moderates a panel discussion with todays speakers
Dr Giuseppe Riccardo Diaferia
Dr Mauro Baron
Dr Alison Cheung
Dr David Pointu
Dr Manolis Papamichos Chronakis
Mr Paul McCormick
Dr Jan de Bock

ABSTRACTS

Tumor cell heterogeneity and its transcriptional bases in pancreatic cancer

Dr Giuseppe Riccardo Diaferia

Pancreatic ductal adenocarcinoma (PDAC) is a highly heterogeneous tumor with different types of cancer cells that coexist in the same patient. Standard analyses of tumor transcriptomes average the data obtained from heterogeneous tumor cells, which usually display varying growth properties and chemoresistance potential, thus contributing to therapeutic failure. In contrast, single-cell analyses provide detailed information on gene expression profiles of individual cells after dissociation of the tumor tissue, thus being not informative of the spatial relationship between tumor cells and non-tumor components. Using next-generation sequencing techniques coupled to laser microdissection, we performed gene expression analysis of defined tumor anatomical areas to maintain the spatial information of the anatomical structures. This study helped us understand the mechanisms governing pancreatic tumor heterogeneity, and the spatial relationship between tumor cells with different gene expression profiles, to identify new molecular targets for precision medicine.

Single-cell phenotyping and spatial analysis of cancer and immune cells with quantitative protein multiplex imaging

Dr Alison Cheung

The extent of intra-tumoural heterogeneity—the variation in the composition of cells in a given tumor and those in the local tumor microenvironment—could potentially impact diagnosis, treatment planning, and subsequent response to treatment. To evaluate the extent of cancer cellular heterogeneity, we conducted quantitative protein marker multiplex imaging to study the variations in protein marker expression patterns on individual cells and spatial localizations. A multiplexed immunofluorescence imaging platform (MxIF, Cell DIVE™) was used to measure the cellular expression of Estrogen Receptor (ER), Progesterone Receptor (PR), Epidermal Growth Factor Receptor 2 (HER2), Ki67, p53, p21WAF1, and p16INK4A in cancer epithelium. Analysis was conducted on a tissue microarray (TMA) representing subtypes classified as Luminal A-like, Luminal B-like (HER2-negative), Luminal B-like (HER2-positive), HER2-positive (non-luminal), or Triple-negative based on tumor grade and immunohistochemical staining according to the St. Gallen surrogate classification. Of the 101 cores from 59 cases studied, high levels of heterogeneity were observed in ER and PR expression among the hormonal receptor-positive tumors. Spatial visualizations illustrated that cells with similar expression signatures tend to be clustered together. In addition to using MxIF to quantify the extent of heterogeneity in the cancer epithelium, we also investigated the composition and spatial arrangement of immune cells in ovarian cancers. The co-expression patterns of T-cell markers CD3 and CD8, macrophage marker CD68, immune checkpoint proteins PD-1 and PD-L1, together with the proliferative marker (Ki67) and cancer-specific marker PCK (pan-Cytokeratin) was studied. Densities of immune subsets were quantified using thresholding with levels defined by comparing positive and negative control tissues. Spatial relationship was evaluated by quantifying the most common neighboring cell type with co-occurrence matrices. Our work demonstrates the application of MxIF in quantitative imaging analysis of cancer and the tumor microenvironment in assessing their heterogeneous phenotype and spatial distributions.

When genome stability is bad for you: How resolution of R-loops promotes DNA replication and maintains cancer cell proliferation

Dr Manolis Papamichos Chronakis

Collisions between the DNA replication machinery and co-transcriptional R-loops can impede DNA synthesis and are a major source of genomic instability in cancer cells. How cancer cells deal with R-loops to proliferate is poorly understood. Here we show that the ATP-dependent chromatin remodeling INO80 complex promotes resolution of R-loops to prevent replication-associated DNA damage in cancer cells. Depletion of INO80 in prostate cancer PC3 cells leads to increased R-loops. Overexpression of the RNA:DNA endonuclease RNAse H1 rescues the DNA synthesis defects and suppresses DNA damage caused by INO80 depletion. R-loops co-localize with and promote the recruitment of INO80 to chromatin. Artificial tethering of INO80 to a LacO locus enabled turnover of R-loops in cis. Finally, counteracting R-loops by INO80 promotes proliferation and averts DNA damage-induced death in cancer cells. Our work suggests that INO80-dependent resolution of R-loops promotes DNA replication in the presence of transcription, thus enabling unlimited proliferation in cancers.medicine.

SPEAKERS

Falco Krüger
Leica Microsystems

Dr Giuseppe Riccardo Diaferia
IEO Research

Giuseppe obtained an MSc in Medical Biotechnologies and PhD in Molecular Medicine at the University of Milan. He developed a solid theoretical and technical background in developmental biology during his PhD training at the National Council of Researches in Milan and at the University of California San Diego, UCSD (USA), where he continued to work on pancreatic development in health and disease. In Italy, he focused his research on pancreatic tumor grading by reverse epigenomic approaches at Humanitas University and the European Institute of Oncology in Milan. His research interests currently focus on studying the molecular basis of pancreatic cancer heterogeneity and its clinical implications. Giuseppe is also a member of the Italian Pancreatic Cancer Community (IPCC) that brings together all the young Italian scientists involved in this field and some no-profit patient organizations to foster collaborations among researchers and raise awareness on this aggressive cancer.

Dr Mauro Baron
Leica Microsystems

Mauro joined Leica Microsystems Italy in 2000 as Product Manager Microscopy covering all aspects of microscopy applications, particularly those related to Laser Microdissection (LMD). In 2009, he became European Field Support Specialist for the Life Science Research Division, primarily responsible for all microdissection-related topics in Europe.

Dr Alison Cheung
Sunnybrook Research Institute

Alison completed her PhD training at the Department of Medical Biophysics, University of Toronto, studying the role of breast cancer gene BRCA2 in cancer development. After her PhD, she continued her research work at Sunnybrook Research Institute and Princess Margaret Hospital in Toronto, focusing on monitoring cancer progression and therapeutic response in preclinical models using imaging. Alison is currently a research associate at the Biomarker Imaging Research Laboratory led by Dr. Martin Yaffe at the Sunnybrook Research Institute. Her research interests include the quantitative analysis of high-dimensional data in protein multiplexing to examine cellular and spatial heterogeneity in cancer, and the integration of radiological imaging features and molecular signatures to improve disease characterization.

SPEAKERS

Dr David Pointu
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 Manolis Papamichos Chronakis
University of Liverpool

Manolis gained a PhD in Molecular Biology at the University of Crete / IMBB, followed by a postdoctoral fellowship at the University of Massachusetts Medical School. In 2010, he became Appointed Group Leader at Curie Institute, and then joined the University of Newcastle as a Research Fellow in 2015. In 2020 he was appointed as Lecturer at the University of Liverpool. Manolis' research interests include how chromosome structure controls genome function and stability and how its dysregulation can lead to cancer. Specifically, he aims to understand how chromatin is integrated into the gene regulatory and genome stability networks, promoting DNA replication and gene expression. Using a combination of functional genomics, single-cell imaging, and high-throughput technologies in budding yeast and human cells, he aims to illuminate the interplay between the multiple machineries that keep our genome intact and maintain its functionality and the chromatin structure of DNA.

Mr Paul McCormick
Leica Microsystems

Paul is the Advanced Workflow Manager at Leica Microsystems (UK). The Advanced Workflow Specialist Team are application experts in all things microscopy related. Working across the whole EMEA region, they specialize in confocal and widefield microscopy and sample preparation techniques specifically for life science research. Their mission is to work alongside scientists, providing guidance and helping to share knowledge throughout the microscopy community via webinars, workshops, and training programs across a wide variety of disciplines, from live-cell microscopy, through to lifetime measurements and deep tissue imaging all the way down to super-resolution and CLEM microscopy applications. The team's proximity to real science means they are ideally placed to facilitate the development of new technologies and help integrate new innovations into research the environment as quickly as possible.

SPEAKERS

Dr Jan De Bock
Leica Microsystems

Jan studied biology and gained his PhD in the field of olfaction, characterizing olfactory neurons in their response to odorants. He has worked as a microscopy expert in different roles since 2003. He joined Leica Microsystems in 2011 as a product specialist for confocal microscopy. In 2017, he became a member of the newly formed Workflow and Application Team responsible for correlative workflows, in particular involving sample preparation and imaging under cryogenic conditions.