

# 2012 Histopathology Event: Advances in research and techniques

30th March 2012, The Oak Suite, W12 Conferences, The Hammersmith Hospital, London, W12 0HS

This is the 9<sup>th</sup> Annual event (originally called Improving Immunohistochemistry), held in the centre of London, this meeting draws together international experts to discuss the need for technical-based updates in the areas of immunohistochemistry, clinical and research based histopathology and in situ hybridisation. This meeting gathers together workings from clinical, academic and pharmaceutical organisations.

We include a troubleshooting panel session in this event, so that delegates can discuss their work directly with a panel of experts.

Meeting Chair: *Dr Will Howat*, Cambridge Research Institute, Cancer Research UK

- 9:00 – 9:45      **Registration**
- 9:45 – 10:00    **Introduction by the Chair:** *Dr Will Howat*, Cambridge Research Institute, Cancer Research UK
- 10:00 – 10:30    **Immunohistochemistry and TMA's in the Target Discovery Process**  
*Arthur Lewis* MedImmune, Cambridge  
Establishing the link between target expression pattern and disease is a vital step in the drug discovery process. Here I will show how MedImmune is utilising immunohistochemistry (IHC) and Tissue MicroArrays (TMA) to frontload target expression analysis and build early human disease association data for novel and poorly validated therapeutic targets. For all potential antibody therapeutic targets it is important to demonstrate the target has a strong link with disease, has the right target tissue expression versus normal tissue, the right sub-cellular localisation suitable for targeting with an antibody and that correct distribution of antibody is achievable in vivo i.e. no significant antigen sink. This talk will give particular examples of how we are addressing these questions for targets expressed on tumour infiltrating immune cells to support our immune mediated killing therapeutic strategies and discuss the uses and limitations of TMA for this class of target.
- 10:30 – 10:45    **Innovation within Histology**  
*Dr Iris Nagelmeier*, Targos, Kassel, Germany  
This talk will discuss advances in Detection, Probes and Digital Pathology
- 10:45 – 11:15    **Immunohistochemistry/In Situ Hybridization in Neuropathology – Diagnosis & Research**  
*Dr Stephen McQuaid*, Queen's University Belfast, Belfast, UK  
Immunohistochemistry in diagnostic neuropathology is used in the assessment of neurosurgical biopsies, muscle and CSF cytology and in autopsies. Furthermore neuropathological studies on human and small animal tissues are a major contributor to basic and applied research in the neurosciences reflecting the complexity and diversity of neurological disease. For example, immunohistochemical and in situ hybridization studies in neuropathology have played a lead role in identifying and elucidating the pathogenesis of a wide range of neurological diseases (including variant CJD and multiple sclerosis). Examples from diagnostic surgical neuropathology, dementia and research (virus detection in the CNS and MS) will be used to illustrate the cardinal role that immunohistochemistry/ISH plays in neuropathology. While traditional formalin-fixed, paraffin-embedded tissues form the basis of much of the studies on neuropathology specimens, examples of the optimal use of snap-frozen tissue sections and vibratome sectioning/confocal scanning laser microscopy in research will also be described.
- 11:15 – 11:40    **Speakers' photo then mid-morning break and trade show**
- 11:40 – 11:55    **Development and Automation of Novel Assays on the Ventana Discovery Platform**  
*Dr Dan Gare*, Tissue Diagnostics, Roche, UK
- 11:55 – 12:25    **Virtual slides in medical research**  
*Dr Darren Treanor*, St James's University Hospital, Leeds
- 12:25 – 12:40    **Digital Pathology Enterprise (DPE) Solutions for Pathology and Tissue-Based Research**  
*Professor Peter Hamilton*, PathXL, Belfast, Ireland  
Digital pathology has been used in the past across various point applications for supporting tissue-based research, biomarker discovery and diagnostics. Modern approaches require full integration of application functionality together with interoperability with existing LIMS and IT systems in both the healthcare and research setting. PathXL has developed a Digital Pathology Enterprise (DPE) platform that captures these requirements. The solution underpins applications in education, EQA, biomarker evaluation, TMA management, image analysis, biobanking and clinical workflow. A powerful PathXL Management Engine integrates and shares data across the range of applications – facilitating workflow, data search, analytics and reporting. This engine underpins a range of user applications that make digital pathology an essential part of the modern pathology laboratory, facilitating tissue

archiving, the discovery and validation of companion diagnostics and health care delivery within a busy diagnostic laboratory.

- 12:40 - 13:10 **High throughput protein expression profiling of breast cancer: orders of probability**  
*Raza Ali*, CRUK Cambridge Research Institute, UK  
Breast cancer is not one disease but a collection of related diseases. Current histopathological evaluation of breast cancer does not encompass this variety, severely impairing therapeutic decision making. Gene expression experiments have generated an alternative molecular classification of breast cancer identifying subgroups of patients with tumours defined by characteristic gene expression signatures and different clinical outcomes. Although several of these signatures have been commercialised there are concerns as to their clinical utility. Immunohistochemistry (IHC) has several advantages over gene expression assays and is already widespread in clinical pathology. The challenge of translating complex gene expression signatures into IHC assays of just a few markers has only been partly met. I will describe recent work, including our own, in translating these signatures. I will also describe our strategy for refining this classification and staying abreast of emerging molecular studies including our strategy for antibody selection, optimisation and exclusion. Finally, I will discuss the current contribution of IHC to the molecular classification of breast cancer.
- 13:10 – 14:00 **Lunch and trade show**
- 14:00 – 14:45 **Question and Answer Session**  
Delegates will be asked to submit questions to a panel of experts. Questions can be submitted before the event or on the day
- 14:45 – 15:00 **Fully automated TMA production - an essential tool for any Biobank**  
*Dr Caroline Woolston*, Nottingham Health Science BioBank, UK  
Histopathology departments receive numerous tissue samples each day that require diagnostic analysis. Commonly this material is only available in small amounts, in particular tumour tissue, and may only be 2-5 mm thick which if sliced into tissue sections may only yield enough tissue for up to 100 arrays. For this reason the Nottingham Health Science Biobank which has approval for the use of excess archival material has opted to use the fully automated TMA GrandMaster tissue arrayer in conjunction with the Panoramic 250 slide scanner to produce reproducible and cost saving TMA which can yield about 300 times this number. The technique could therefore generate 100,000 assays compared to 100 assays if just sections of samples were utilised.
- 15:00 – 15:30 **Afternoon Tea/Coffee and trade show**
- 15:30 – 15:45 **Go forth and multiplex: Conquering the challenges of tissue imaging and analysis.**  
*Ms Roslyn Lloyd*, Caliper Life Sciences, UK  
Tissue-based approaches to research are increasingly popular. However, imaging tissue sections poses additional challenges. In fluorescence, qualitative and quantitative reliability are compromised by auto-fluorescence, problems of overlapping chromogenic signals pose similar imaging difficulties in brightfield and the analysis of tissue images is far more difficult than for cultured cells; reliable methods for dealing with these are required.  
A multispectral approach enables simultaneous imaging and quantitation of multiple analytes even when spatially and spectrally overlapping.  
Dedicated tissue analysis software can be readily trained to separate the image into appropriate morphologic regions, e.g., cancer, stroma and inflammation. The selected regions are further analysed for specific cellular/subcellular localization of markers, which is used for quantitation of molecular data.  
Combining these technologies within a slide sampling system allows the unsupervised high-throughput imaging, analysis, quantitation and scoring of tissues sections, either for whole slides or TMAs.
- 15:45 – 16:15 **Genetic profiling of tumours for systemic therapy: standard of care or a passing fad**  
*Dr Paul Wilkerson*, Chester Beatty Laboratories, The Institute of Cancer Research, London
- 16:15 – 16:30 **Using whole slide image analysis to address research applications in pathology**  
*Dr Kate Lillard*, Aperio, UK  
Aperio provides a complete solution for digitizing immunohistochemistry, from whole slide scanning to image analysis. Whole slide image analysis allows researchers to evaluate data objectively & consistently from slide to slide, without the bias associated with analyzing small snapshot images from the microscope. Aperio provides image analysis tools for analyzing all types of immunohistochemistry across whole slides, including nuclear markers, membrane proteins, colocalization of multiple stains, and microvessels. Dr. Lillard will discuss how Aperio image analysis can be used to quantitatively address common applications in experimental pathology.

16:30 – 17:00

### ***In situ* Proximity Ligation Assay (PLA) as a novel approach on breast cancer research**

Fabricio Barros, University of Nottingham, UK

Novel techniques such as *in situ* proximity ligation assay (PLA, Olink, Sweden) can be a useful tool for detecting, visualising and quantifying the frequency of protein expression or protein-protein interactions in archival formalin-fixed paraffin embedded tissue samples. Interactions can be either detected using fluorescent or brightfield microscopy and it is possible to perform PLA using high-throughput technologies such as Tissue MicroArrays (TMAs).

Protein or protein-protein interaction measurements can be used to explore sub-cellular processes helping to disclose both upstream and downstream pathways to be targeted for pharmaceutical intervention avoiding resistance development that occur in the current treatments.

We have successfully used PLA to investigate the heterodimerisation of the HER family of receptors in a large series of HER2+ breast cancer to understand their role in response to targeted therapy.

17:00

### **Chairman's summing up**

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*This meeting was organised by Euroscicon ([www.euroscicon.com](http://www.euroscicon.com)), a team of dedicated professionals working for the continuous improvement of technical knowledge transfer to all scientists. Euroscicon believe that they can make a positive difference to the quality of science by providing cutting edge information on new technological advancements to the scientific community. This is provided via our exceptional services to individual scientists, research institutions and industry.*

### Media partners



### About the Chair

**Will Howat** graduated with a BSc (Hons) in Immunology & Pharmacology from the University of Strathclyde, before gaining a PhD in Pathology from the University of Southampton. After two post-doctoral positions in Southampton, he moved to the Wellcome Trust Sanger Institute in Cambridge as the leader of Research & Development for the Immunohistochemistry group of the Atlas of Protein Expression project. He is now with Cancer Research UK as the head the Histopathology/ISH facility at the Cambridge Research Institute.

### About Our Speakers

**Stephen McQuaid** is a Principal clinical scientist in tissue pathology at the Royal Hospitals Trust, Belfast from 1990. Validated a wide range of immunocytochemical tests that are now used in diagnostic Neuropathology. Gained his MSc at QUB in 1991 for research into the optimization of non-radioactive *in situ* hybridization techniques and was awarded his PhD by QUB, for research into the neuropathogenesis of measles virus, in 1998. Main research interests are in tissue based studies in Multiple Sclerosis, paramyxovirus pathogenesis and high grade gliomas, for which he has been awarded or associated with more than £3 million in research funding. These studies are centered on histology, immunocytochemistry and confocal scanning laser microscopy. This work has been published widely >65 peer-review papers, and presented at a number of prestigious international conferences. Assessor for the UK-NEQAS immunocytochemistry organisation in London specialising in Neuropathology. He has supervised numerous MSc, MPhil, MD and PhD students.

**Roslyn Lloyd** is PerkinElmers European Applications Scientist for tissue imaging. With a multidisciplinary educational background she also has 10 years multispectral imaging experience.

**Iris Nagelmeier** is a Pathologist who works in Germany for Targos in Kassel. Roche Diagnostics have worked with Dr Nagelmeier for the past 3 years who recognise her expertise in the field of Histology who in turn will evaluate new products and offers a realistic, independent and ethical response. Roche Diagnostics value the opinion of Dr Nagelmeier and have been able to improve products and develop new products to add to our portfolio knowing that customers will benefit as we continue to provide consistent Patient Healthcare for all patients battling with cancer.

**Kate Lillard** received a PhD in molecular genetics from the University of Cincinnati Medical Center in Ohio in 2004. After spending four years as a postdoctoral fellow at the University of Texas Southwestern Medical Center, Kate joined Aperio as an Applications Scientist and in 2009 she relocated to Oxfordshire to manage global applications support for Aperio.UK.

**Fabricio Barros** is concluding his Phd based on examination of expression amongst the HER family in a large series of breast cancer cases examining the clinical effect of co expression of the receptors and respective ligands. This research study is being developed using not only the standard histopathological techniques as immunohistochemistry and in situ Hybridisation but also using a novel approach (in situ Proximity Ligation Assay) to characterise HER2+ invasive breast tumours. This study is being performed at University of Nottingham within the Breast Cancer Research Group led by Prof. Ian Ellis and Dr. Andrew Green.

**Arthur Lewis** has over 11 years experience working within a research focused IHC group within the biotechnology industry working at MedImmune and formerly Cambridge Antibody Technology prior to its acquisition and integration with MedImmune by AstraZeneca in 2007. Arthur is currently the Senior R&D Manager at MedImmune Cambridge leading the Research Histology Group. He has gained a wealth of experience using IHC to support antibody drug projects in many disease areas across the drug discovery process, from target discovery, through lead selection and pharmacology model characterisation as well as experience of working on GLP compliant tissue cross-reactivity studies. His group's current focus is to help drive new target identification and validation utilising IHC and other tissue based tools.

**Peter Hamilton** is the Founder of PathXL Ltd and is the Head of the Bioimaging and Informatics Research Group at Queen's University Belfast. For the past 25 years he has been leading research on computer vision and decision support in diagnostic cancer pathology and the identification of novel digital tissue and cell markers for diagnostics, prognostics and for predicting response to therapy in cancer. He has received multiple competitive grants, in excess of £7 million to support the research programme at Queens University. He sits on the committees of a number of major medical research organisations including the International Society for Cellular Oncology.

**Caroline Woolston** is a recent appointment as a Scientist to the Nottingham Health Science Biobank (NHSB). Her main role under the direction of the operations manager Dr Balwir Matharoo-Ball, is to manage the daily organisation of a section of the BioBank to include supervision of scientists and support staff including data and information services. Caroline will also liaise with members of the multi-disciplinary teams to establish procedures for the BioBank. Caroline has a wealth of experience, an established background in research and published in a number of peer-reviewed journals whilst working as a senior postdoctoral scientist with the University of Nottingham.

**Key words:** immunocytochemistry, in situ hybridization, confocal microscopy, TMA, Target Discovery, Validation, Human, Advances in Detection, Probes and Digital Pathology, image analysis, whole slide image analysis, pattern recognition, HER2, Dimerisation, Breast Cancer, Ligands, TMA, tissue micro array, slide scanning, Biobank, nottingham, Auto-fluorescence, multicolour immunohistochemistry, tissue segmentation.

Registration Web Site:

[www.regonline.co.uk/hist2012](http://www.regonline.co.uk/hist2012)

#### **NOTES ABOUT THIS EUROSCICON EVENT**

For your convenience we would like to bring your attention to the following

- You will be issued with a FULL delegate list within 14 days of the event, which will include the email addresses of the delegates (we are sorry that there is this delay in emailing the list, but we need to make sure that it takes into account any late arrivals). You will not be included in this list if you have opted out and you can do this by logging into your registration details. This list will not be sold or ever give out to third parties. Only people attending or sponsoring the event have access to the list
- There may be an independent meeting report published within a few months of this event. If this is published we will send you an email to let you know the reference details
- Notepads and pens are available from the Euroscicon reception desk
- We cannot give out the slides from our speaker's presentations as they are deleted immediately after each event. If you require a particular set of slides please approach the speaker
- Please remember that EuroSciCon is a small independent company with no subsidies from society memberships or academic rates for venues. We try to be as reasonably priced as possible and our delegate rates are substantially lower than comparable commercial meeting organisations
- To keep updated on our events and other Life Science News, please sign up for our newsletter at [www.eurosciconnews.com](http://www.eurosciconnews.com)
- We may take pictures during the meeting. These pictures will be used to promote our events and placed on our various websites and the closed Euroscicon group on Facebook. If you do not want your photograph distributed please let one of the Euroscicon staff know.