Stretch & Hold Forth

Innovation Academy

7th December 2018

viapath
pioneers in pathology

Programme

INTRODUCTION

9.15 Registration

9.45 Welcome

Joy Milne

'NOSE'

MORNING SESSION

Chair - Rob Dunn

10.00 **Prof Perdita Barran**
Nose to Diagnose – The search for volatile biomarkers of Parkinson disease in sebum

10.30 **Dr Meera Chand**
Application of nanopore technology

11.00 **Olivier Usher – Nesta**
Flying High

11.30 BREAK

Chair – Prof Neil Dalton

11.55 **Prof Hal Drakesmith - University of Oxford**
The importance of being iron-ic

12.15 **Prof Josephine Bunch – National Physical Laboratory**
The Google earth of cancer

12.45 **Panel Discussion**

1.00 LUNCH

Excellence in Pathology – 2018 finalists and voting

2.00 **Terry Hunter**
Quantitative assessment of NFKB transcription factor activity in health and disease

2.05 **Younis Khan**
Luminex-based detection of complement-fixing antibodies using HLA antigens isolated from donor cells – An alternative to the CDC crossmatch

2.10 **Rachel Mayhew**
Functional characterisation of genetic variants using red blood cell ektacytometry

AFTERNOON SESSION

Chair – Alan Dunlop

2.15 **Marie-Jose Weber – PRUH**
OSNA at the PRUH

2.45 **Dr Sally Brady, Karolina Witek, Erin Emmett**
An introduction to analytical continuous quality improvement: 3 case studies

3.15 **Dr Gary Moore - Viapath**
Viapath and Venom

3.45 **Winner of Excellence in Pathology announced**

4.00 CLOSE

Dr Dominic Harrington

CHIEF SCIENTIFIC OFFICER, VIAPATH

It gives me great pleasure to welcome you all to our eighth Innovation Academy Scientific Symposium, 'Stretch & Hold Forth'.

At our seventh symposium we focussed on the advances made in the provision of healthcare since the founding of the National Health Service 70 years ago. We noted that the big issues of 1948 were often a consequence of overcrowded unsanitary living environments. This contrasts starkly with the health service of 2018 which faces the considerable challenges of obesity, diabetes, coronary heart disease, cancers and dementia. Conditions driven partly by lifestyles favoured by those living in the 21st century which if left unresolved threaten the viability of healthcare delivery as we know it.

There is a long standing dependency on scientists to provide innovative solutions that allow us to dodge impending calamity. There is certainly no shortage of stretching challenges that require the implementation of innovative solutions today. Fortunately, I find myself this morning introducing an Innovation Academy symposium program that may have seemed like 'Science Fiction' had I presented it at our first symposium. The art of the impossible is increasingly possible.

Welcome: Joy Milne

HONORARY LECTURER IN ANALYTICAL OLFACTION

I am the "NOSE" that started the present research into the smell of Parkinson's. My husband, who was a Consultant Anaesthetist, was the person who had Parkinson's. I smelt PD on him 12 years before he was diagnosed, at the age of 33.

Twenty years later I stood up at a Parkinson's UK research meeting at the MRC, Centre for Regenerative Medicine in Edinburgh and asked Dr Tilo Kunnath about the smell of Parkinson's and why it was not being used for early diagnosis. At that moment I did not realise that I would travel through this incredible journey which I have undertaken for the last 8 years.

As a consequence of Tilo's dedication and his foresight in seeing the potential for this research, he invited Prof Perdita Barran to assess the possibilities. Under her auspices, the research the Department of Biotechnology at Manchester University and with the help from Anatune in Cambridge, we have discovered the bio-markers for PD which Prof Barran will be discussing.

I will be talking about how I realised this smell, how in discussion with my husband we realised the potential, as a Doctor and a nurse, how I have developed this ability and how I detect it on the swabs and portal.

I have been awarded an Honorary Lectureship in Analytical Olfaction at Manchester University Chemistry Department which I very much appreciate.

Morning Session

Chair: Rob Dunn

HEAD OF CYTOGENETICS

I began my career in Cytogenetics at Guy's Hospital, initially in constitutional disease, but soon moved into the fascinating and rewarding world of acquired genetics. The chromosomes may be more difficult to analyse, but the knowledge is quite limitless as we understand more about the genetic fabric of cancer. I gained my Part 1 FRCPath in Clinical Cytogenetics and then furthered my career as Deputy Head of the Haematology Cytogenetic laboratory at the Royal Free Hospital. I have since moved jobs south of the river and now run the Cytogenetics laboratory at King's College Hospital as part of the Haematological Malignancy Diagnostic Centre.

Having always appreciated the importance of Quality within a diagnostic setting, I am an assessor for the Genomics Quality Assessment service (GenQA). I am also a module tutor for the IBMS in their Molecular Pathology Certificate of Expert Practice, aiming to inspire those working in pathology to utilise the ever-expanding molecular technologies for advanced diagnostics of their samples. Process improvement is also a pursuit of mine, having a yellow belt in Lean Six Sigma techniques, as we drive towards balancing higher throughput with more complex analysis to pursue better outcomes for our patients.

Prof Perdita Barran

MANCHESTER INSTITUTE OF BIOTECHNOLOGY

Professor Barran holds a Chair of Mass Spectrometry in the School of Chemistry and is Director of the Michael Barber Centre for Collaborative Mass Spectrometry at the Manchester Institute of Biotechnology, The University of Manchester, UK.

She is Theme Leader for Biological Mass Spectrometry for the Rosalind Franklin Institute.

Her research interests include: Biological mass spectrometry; Instrument and technique development; Protein structure and interactions; Dynamic and Disordered Systems; Parkinson's disease Diagnostics; HDX-MS; Proteomics; and Molecular modeling.

Parkinson's disease (PD) is a progressive, neurodegenerative disease that presents with significant motor symptoms, for which there is no diagnostic test We have serendipitously identified a hyperosmic individual, a 'Super Smeller' that can detect PD by odour alone, and our early pilot studies have indicated that the odor was present in the sebum from the skin of PD subjects.

This presentation will detail our research program that has arisen from this observation, and the use of mass spectrometry based metabolomics to identify and quantity diagnostic biomarkers for PD.

Authors
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Dr Meera Chand

CONSULTANT MICROBIOLOGIST

Dr Meera Chand is a consultant microbiologist in the respiratory and immunisations teams of the National Infection Service at Public Health England. She also works at Guy's and St Thomas' and in the NIHR Heath Protection Research Unit in Respiratory Infections at Imperial College London. Her specialist interests are in the clinical and public health aspects of severe acute respiratory infection and in the application of nanopore sequencing to clinical and public health services.

Nanopore sequencing is a new technology which allows long DNA fragments to be analysed and identified in real time. Currently primarily used in research, it offers the possibility of rapid yet pathogen-agnostic diagnosis of infectious diseases if translation to clinical service can be achieved. Six months into our evaluation, we describe the early results and challenges of trialling nanopore sequencing in the NHS environment for the rapid diagnosis of bacterial infections through amplicon-based and metagenomic approaches.

Olivier Usher

RESEARCH MANAGER, NESTA'S CHALLENGE PRIZE CENTRE

Oli is Research Manager in Nesta's Challenge Prize Centre. At Nesta he has participated in the development of a range of prizes, from driving innovation in aquaculture in India, to the Open Up Challenge for small business fintech solutions in the UK.

He leads the Challenge Prize Centre's work to identify and scope out new topics, and has worked on projects ranging from the safety of infrastructure to assistive technology for people with paralysis to the introduction of drones in cities.

He previously worked in science public relations, including a period as Public Information Officer for an ESA centre in Munich, where he coordinated European media relations for the Hubble Space Telescope. He has also worked in journalism and co-authored a popular science book, The Universe through the Eyes of Hubble.

Drone technology has come on in leaps and bounds. From being an expensive technology used for niche purposes, primarily by the military, drones have become cheap enough to use for a wide array of civilian, commercial and recreational uses.

In 2017 and 2018, Nesta carried out Flying High, a research programme to understand the implications of and aspirations for drone technology for UK cities. Working with five cities (London, Bradford, Southampton, Preston, West Midlands), we explored what further advances could be feasible in the coming years, what use cases have public and political support, and what the implications for regulation and safety could be.

Alongside uses in infrastructure and construction, and uses by the emergency services, our research identified the health service as a potential key market for drone services. This could involve niche services such as ferrying medical supplies to inaccessible or remote locations such as islands. Or it could involve more ambitious efforts to redesign medical logistics in dense urban cores. In this talk I will discuss the key findings from the Flying High project, and in particular the potential opportunities and pitfalls we found around the use of drones in medical logistics.

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Chair: Prof Neil Dalton

DIRECTOR OF WELLCHILD LABORATORY

In 1975, Neil was appointed as a probationary clinical biochemist in the routine Clinical Chemistry laboratory at Guy's Hospital and has successfully managed to survive, in situ, various NHS and academic re-organisations over the last 40 plus years.

Neil is currently a Consultant Clinical Scientist, Director of the WellChild Laboratory at the Evelina London Children's Hospital, a founding director of SpOtOn Clinical Diagnostics Ltd, and Emeritus Prof of Paediatric Biochemistry at King's College London. His current clinical interests include the rapid diagnosis of acutely ill babies and children, using tandem mass spectrometry (MSMS) based targeted metabolic profiling, and the measurement of renal function decline (the HTA funded eGFR-C study).

Academic projects are focussed on the early diagnosis of diabetic complications (AdDIT, SUMMIT, and JDRF biomarker consortia) and understanding the fundamental biology leading to increased cardiovascular risk. SpOtOn, a University and Trust spin-out company, provides the conduit for commercialization of intellectual property: currently c.400,000 babies are tested p.a. in the UK and Europe, using the SpOtOn kit for newborn dried blood spot (DBS) screening for sickle cell disease and thalassaemia.

A kit that facilitates haemoglobinopathy, biotinidase deficiency, and type-1 tyrosinaemia screening simultaneously on a single DBS has been successfully trialed in Berlin and will be marketed in 2019. The company is expanding its range of MSMS based diagnostic kits, advancing the metabolic and proteomic panels for acute diagnostics in ITU and A&E, and developing a remote micro-sampling personalised medicine approach to the early detection of chronic diseases and their clinical complications.

Prof Hal Drakesmith

WEATHERALL INSTITUTE OF MOLECULAR MEDICINE AT OXFORD

Hal Drakesmith trained at the University of Cambridge, University of Kyoto and UCL before moving to the Weatherall Institute of Molecular Medicine at Oxford. The lab has worked at the intersection of iron homeostasis, immunity and haematology for over ten years, mostly focusing on the biology of the iron regulatory hormone hepcidin.

We have made breakthroughs in understanding the molecular basis of iron homeostasis in physiological and pathophysiological states including iron deficiency, haemochromatosis, thalassaemia, viral, bacterial and malarial infections, and inflammatory disorders. Our research ranges from mechanistic analysis of hepcidin regulation and iron homeostasis to testing the effects of experimental manipulation of iron transport on infection and immunity in animal models.

We have developed new tools to investigate iron biology, including inducible hepcidin knock-out mice, and agonists and antagonists of erythroferrone, a key suppressor of hepcidin. Analysis of samples from controlled human infection experiments, population surveys of iron deficiency, a variety of disease cohorts, and clinical trials, informs our mechanistic work.

Iron is required for the growth of almost all infectious organisms but is also needed for host immune function. The iron regulatory hormone hepcidin controls both total body iron levels and the distribution of iron. Hepcidin expression is regulated by the balance of several signals, chief among them being iron status, inflammation, and erythropoietic drive. Interestingly, iron appears to be the only nutrient that is controlled by a hormone that responds both to nutrient levels and to infection, underscoring the importance of iron in host-pathogen interactions. Furthermore, hepcidin is evolutionarily related to microbicidal defensins that target bacteria and yeast infections. Here I will discuss the role of hepcidin and iron in infectious diseases and the immune response. Emerging evidence is revealing marked heterogeneity in how hepcidin is regulated during different types of infection, and the effect of hepcidin and altered iron distribution on the progression of infections is also highly variable. One of the best-studied infections in this field is malaria. Epidemiological evidence in humans shows that iron is a critical determinant for the outcome of malaria, and experiments in mice show that hepcidin controls growth of the liver-stage of Plasmodium infection. The innate immune response to most infections (including malaria) involves an acute and profound hepcidin-mediated decrease in serum iron levels. Furthermore iron deficiency is the most common micronutrient deficiency worldwide; recent genetic evidence links lack of iron acquisition by lymphocytes from serum to severe immunodeficiency. Therefore, a currently underappreciated important aspect of iron and hepcidin in the context of infection is that iron levels may directly regulate the adaptive immune response.

Prof Josephine Bunch

PRINCIPAL SCIENTIST

Professor Josephine Bunch is a Principal Scientist and Co-Director of the National Centre of Excellence in Mass Spectrometry Imaging (NiCE-MSI) at the National Physical Laboratory and Chair of Biomolecular Mass Spectrometry at Imperial College London.

At NPL, Josephine is the science area leader for mass spectrometry imaging, leading a team of around 30 scientists. She is currently delivering a Cancer Research UK Grand Challenge programme.

Developing a google-earth view of cancer: Multiscale mass spectrometry imaging of tumours

Rory T. Steven[1]; Adam J. Taylor[1]; Andrew D. Campbell[2]; Yulia Panina[1,3]; Alex Dexter[1]; Chelsea Nikula[1]; Spencer A. Thomas[1]; Tingting Fu[1]; Efstathios Elia[1]; James S. McKenzie[4]; Stephanie Ling[5]; Paolo Inglese[4]; Arafath K Najumudeen[2]; Jean-Luc Vorng[1]; Gregory Hamm[5]; Rasmus Havelund[1]; Renata Filipe-Soares[4]; David Gay[2]; Kenneth N. Robinson[1]; Teresa Murta[1]; Bin Yan[1]; Ala Al-Afeef[1]; Robin Philip[1]; Ian S Gilmore[1]; Richard J.A. Goodwin[5]; Zoltan Takats[4]; KevinBrindle[6] Mariia O. Yuneva[3]; Owen J. Sansom[2]; Josephine Bunch[1,4]

1National Physical Laboratory, Teddington, United Kingdom; 2Cancer Research UK Beatson Institute, Glasgow, United Kingdom; 3The Francis Crick Institute, London, United Kingdom; 4Imperial College, London, United Kingdom; 5AstraZeneca, UK, Cambridge, United Kingdom. 6University of Cambridge, Cambridge, United Kingdom.

Mass spectrometry (MS) is one of the most powerful techniques for chemical analysis and when combined with an imaging modality allows molecular chemistry to be visualised in 2D and 3D, from the nano- to the macroscale, in ambient conditions and in real-time. There are numerous techniques each having different modes of operation including label-free and labelled analyses

Cancer Research UK has identified that building an understanding of the inter- and intra- heterogeneity of tumours and their evolution over time and in response to therapy will require greater insight into the underlying biology, using in vivo and in vitro models and integrating biomarkers into both early- and late-phase trials. In 2017 the Grand Challenge programme was launched. Our collaborative action involves NPL, Imperial College London, The Beatson Institute, ICR, Barts Cancer Institute, The Francis Crick Institute, The University of Cambridge and AstraZeneca. Together we are developing a validated pipeline for multi-scale imaging of tumours collected from mouse models and patients.

By pursuing this multiscale and multi-omics approach with a range of mass spectrometry imaging (MSI) techniques (MALDI, DESI, SIMS and ICP MS), we aim to deepen our understanding of the interplay of genes, proteins, metabolites and the role of the immune system in cancer development and growth.

This presentation will review early results from pilot studies of mouse models of breast, CRC and pancreatic cancer. A review of the performance of the different techniques across the consortium will be included.

Excellence in Pathology 2018

Excellence in Pathology 2018

Terry Hunter

Terry is a Clinical Scientist in the Clinical Immunology and Allergy Department. He has over 10 years' experience in Laboratory Medicine with over 4 years here at Viapath. Terry is a PhD candidate in the School of Immunology and Microbial Sciences at King's College London. Identifying genetic mutations in human disease is not only useful for clinical practice, it can inform basic science. Terry's research theme focuses on identifying mutations that lead to primary immunodeficiency diseases, to inform diagnostic decisions not just in Immunology, but across disciplines. Terry's work involves devising and developing various cellular, molecular, immunological and biochemical tests that measure gene expression. These tests are useful for the functional validation of gene defects in patients with immunodeficiencies, immune mediated inflammatory diseases, as well as samples undergoing whole genome sequencing as part of the national 100 thousand genome project. Terry's aim is to develop novel molecular and cell functional immunology tests based on gene sequencing and the range of technological varieties. This includes whole exome sequencing, gene panel sequencing, sanger sequencing of candidate genes, commenting on clinical exome and genetic variants, in terms of likelihood of pathogenicity and clinical significance, and providing the correct interpretation for these tests.

Quantitative Assessment Of Nfkb Transcription Factor Activity In Health And Disease

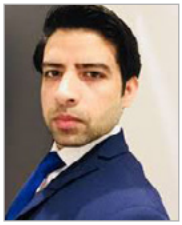
Terrence T J Hunter [1,2,] David Fear [1,]
Paul Lavender [1,] Jo Spencer[3] Mark Peakman[3]
Mohammad A A Ibrahim[1]

Background and Aims
Common Variable Immunodeficiency (CVID) is a prevalent cause of immunodeficiency in adults. Many cases are due to single immune gene defects. Nuclear factor kappa B (NFkB) is an important signalling pathway in immune processes. It comprises canonical and non-canonical components. Single gene defects in the NFkB pathway are described in a number of CVID patients, all of whom have functional abnormalities in mature B cells. How genetic defects in this pathway affect the function of B cells is not well defined. Here we describe a method for accurately quantifying the functional activity of the NFkB pathway and show that CVID patients with single gene defects in the non-canonical NFkB pathway have reduced DNA binding by the relevant transcription factors in the nucleus.

Methods
Peripheral blood mononuclear cells (PBMCs) where stimulated over several days, with a combination of anti-IgM antibody and multimeric CD40 ligand. Nuclear proteins where thereafter extracted and tested for the presence of activated transcription factors, with potential to bind known DNA motifs.

Results
There was a significant increase in the translocation of both canonical (P50 and P65) and non-canonical (Rel B) NFkB transcription factors to the nucleus, with the potential to bind specific immobilised oligonucleotides after stimulation. Healthy people could be segregated into i) low, absent or slow (LAS), ii) normal and iii) high responders. CVID patients with single gene defects that affect the pathway were LAS responders. Conclusion

Activation of NFkB signalling can be functionally measured accurately to distinguish between low and high responders.



Younis Khan

Younis is a pre-registration clinical scientist in histocompatibility and immunogenetics. He joined Viapath after completing NHS Scientific Training Programme (STP) at Clinical Transplantation laboratory, Guy's hospital. Prior to STP, Younis worked as a research scientist at Prof Sir Steve Bloom laboratory on obesity and diabetes, Imperial College London. Younis holds a BSc in Medical Genetics, Master's in Research, MSc in Clinical Sciences and PhD in molecular cell biology. He has published many research articles in high impact journals. Younis enjoys travelling and yoga.

Luminex-based detection of complement-fixing antibodies using HLA antigens isolated from donor cells – An alternative to the CDC crossmatch.

Younis Khan, Chloe Martin, Louise Howe, Olivia Shaw

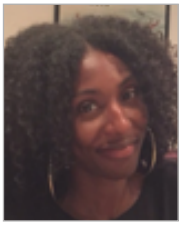
Clinical Transplantation Laboratory, Guy's Hopsital, Viapath, London, UK

Donor HLA specific antibodies (DSA) are associated with kidney allograft failure. Evidence suggests that complement-fixing antibodies carry the greatest risk. Historically, DSA were detected using complement dependent cytotoxicity (CDC) assay. However, it has low sensitivity and requires high titre antibodies and viable cells. Intact HLA antigen can be isolated from donor cells and immobilised onto polystyrene beads for Luminex based DSA analysis, utilising the Immucor DSA bead kit. In addition, variations to the single antigen beads (SAB) kit have allowed the identification of complement-fixing antibodies through detection of C3d fixation to the beads. We propose that combining the donor HLA isolation of the DSA bead kit with the C3d fixation of the SAB kit would allow the creation of a Luminex based, alternative to the CDC crossmatch.

Eight highly sensitised renal patients sera were analysed for both pan IgG and C3d fixing antibodies using the Immucor SAB kit. HLA antigens from selected donors were isolated and fixed on to polystyrene microbeads following manufactures instructions. The presence of both IgG and C3d fixing DSA was assessed using the donor HLA coated beads and a modified methodology.

The results obtained from the modified-C3d DSA results are in agreement with results derived from LIFECODES C3d and SAB assay. The sensitivity and specificity of the modified-C3d DSA assay is 75% and 62.5% respectively when compared with the conventional LIFECODES C3d assay.

This proof of concept study provides an alternative to traditional CDC crossmatch with increased sensitivity and without the requirement for viable donor cells.



Rachel Mayhew

I am a pre-registration Clinical Scientist working in the Molecular Pathology department at King's College Hospital. Before joining Viapath I completed my BSc in Biomedical Science at the University of Surrey and my MSc in Genomic Medicine at St George's University of London. I have a particular interest in the role of genomics in the treatment and diagnosis of red blood cell disorders. I am currently a member of the Future Leaders in Innovation and enjoy running projects that encourage young people to choose science as a career.

Functional characterisation of genetic variants using red blood cell ektacytometry

Red blood cell membranopathies are a heterogeneous group of disorders that impair the cells' deformability and permeability. Membranopathies cause increased red cell fragility and destruction resulting in anaemia requiring transfusion or splenectomy.

A long-standing technique for the assessment of such disorders is osmotic gradient ektacytometry which measures the deformability of red cells under an increasing osmotic gradient. Its utility however, has been limited by the availability of the instrumentation, complex analysis and interpretation. In recent years, targeted next-generation DNA sequencing has played an important role in the diagnosis of such disorders, but often identifies variants of uncertain clinical significance (VUS) that are difficult to interpret.

With help from the innovation fund, we have harnessed next generation ektacytometry to provide much-needed functional evidence for the interpretation of such genetic variants detected by our Red Cell Gene Panel. To-date, the ektacytometer has been informative in 46 Red Cell Gene Panel cases. During our validation, trio analysis has identified a potential case of digenic inheritance. The proband, who is affected with membranopathy was found to have a SLC4A1 VUS inherited from his father, and a pathogenic SPTA1 variant inherited from his mother. Ektacytometry on this family revealed normal profiles for both parents, yet a significantly abnormal profile for the proband, suggesting a pathogenic effect when these variants are present together but not in isolation.

Routinely using ektacytometry for functional characterisation, alongside genetic analysis allows more accurate interpretation of genetic variants and thus, a more informative diagnosis for the referring clinician and the patients.

Afternoon session

Chair: Alan Dunlop

SENIOR BIOMEDICAL SCIENTIST

Alan began working for Viapath in December 2014 as a Senior Biomedical Scientist before being quickly promoted to his current position as Head of Immunophenotyping in February 2015.

He spent 5 years at the Royal Marsden Hospital/Institute of Cancer Research working in the Immunophenotyping Laboratory, where Alan was responsible for performing and reporting diagnostics and monitoring for a wide range of haematological malignancies and enumeration of stem cells to assist the bone marrow transplant team. During this time he undertook some research in the multiple myeloma targeted therapies team looking at ways to try to improve existing therapies.

Alan also spent 6 years at Great Ormond Street Hospital (GOSH) initially working in the immunology laboratory, where he gained experience in the diagnosis of a range of rare immunodeficiencies and monitoring of patients following bone marrow transplants and gene therapy. He gained experience in a number of cellular therapy procedures which complemented his existing knowledge of leukemia and lymphoma diagnosis and monitoring.

Following this, Alan took up a Senior Biomedical Scientist role in the flow cytometry section of the Haematology, Cellular, and Molecular Diagnostics Service (HCMDS) where he was responsible for the day to day running of the laboratory. The role involved diagnosing and performing disease monitoring for children suffering from a range of haematological diseases, patient samples received came from patients across the UK and worldwide.

Marie Jose Weber

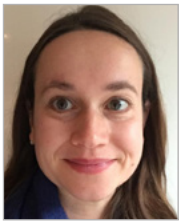
TISSUE SCIENCES AT THE PRINCESS ROYAL UNIVERSITY HOSPITAL

Marie-Jose Weber is the Service Delivery Manager for Viapath Pathology Tissue Sciences (histology and cytology) at King's College Hospital on the Princess Royal University Hospital (PRUH) site. Marie-Jose has a proven track record in change management. In 2006, Marie-Jose project managed the transition from conventional smears to monolayer liquid-based cytology by introducing the hub and spoke model to deliver an integrated processing service for South East London Trusts across three sites. In 2011, Marie-Jose was able to successfully implement a new intra-operative service for the detection of metastatic cancer in sentinel lymph nodes of breast cancer patients. More recently Marie-Jose set-up the first Rapid On Site Evaluation (ROSE) thyroid clinic in radiology at PRUH to assess sample adequacy, thereby reducing the number of inadequate tests and avoiding unnecessary patient recalls.

Marie-Jose is a Fellow of the Institute of Biomedical Sciences – specialist examination (MSc equivalent) in Cellular Pathology and a Chartered Scientist of the Institute of Biomedical Sciences. She is the holder of a diploma in management and a member of the Chartered Institute of Management.

Sentinel lymph node biopsy (SLNB) is a standard method in the UK for assessing the axillary nodal status in patients with breast cancer, to avoid unnecessary axillary node clearance. SLNB is conventionally done by frozen section, touch imprint, cytological smear or routine paraffin sections. Sentinel lymph nodes are removed at the time of surgical excision of the tumour and are subject to histological analysis for the presence or absence of metastasis, an important aspect of tumour staging. The turnaround for the histopathology is 7-14 days and following a positive result the patient would require readmission and further surgery in the form of an axillary clearance.

Intra-operative assessment of axillary lymph nodes by one-step nucleic acid amplification (OSNA) is an advanced molecular technique which was introduced at the PRUH in February 2011. The sentinel lymph node(s) are removed by the breast surgeon from the patient in theatre under anaesthetic and sent fresh on ice to the histopathology laboratory for analysis. The test is carried out by the quantitative measurement of CK19 mRNA copy numbers using the Sysmex RD100i analyser. The process takes 40 to 50 minutes to assess up to four lymph nodes. OSNA provides standardised whole node analysis in an intraoperative framework, in line with NICE guidance. A positive OSNA result allows immediate surgical decisions to be taken whilst the patient is still under anaesthesia, thereby effectively eliminating second surgeries. It removes patient post-operative stress and anxiety and advises on the subsequent treatment pathway. The correlation between the copy number and the number of metastatic cells allows the concept of a quantitative analysis of "nodal tumour burden" with the possibility to predict non-sentinel lymph node involvement.

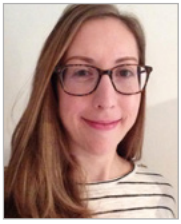


KAROLINA WITEK
PRINCIPAL CLINICAL SCIENTIST

Karolina is a Principal Clinical Scientist working at Viapath. She graduated from King's College University of London in 2004 and trained as a Clinical Scientist in North Bristol NHS trust. She joined Inherited Metabolic Laboratory at Viapath in 2007 and has a particular interest in application of mass spectrometry in diagnosis of inherited metabolic disorders.

DR SALLY BRADY
CONSULTANT CLINICAL SCIENTIST

Sally is a Consultant Clinical Scientist in our Blood Sciences Department at Guy's and St. Thomas' Hospital. She trained at North West London Hospitals and took her first substantive post at The Hillingdon Hospital. She then spent 3 years at UCLH specialising in Point of Care Testing (POCT) and Endocrinology prior to joining Viapath. Her area of interest in the delivery of a high quality, high-throughput, short turnaround time analytical service required for Central London's leading Teaching hospitals. She is a POCT champion and encourages design of clinical workflows to utilise POCT effectively. Her other passion is in developing junior members of the profession. She is a supervisor for the NHS Scientist Training Program (STP) training scheme and a London Regional Tutor, and has also organised/delivered a master's degree in Clinical Laboratory Practice at the University of Jimma in Ethiopia.



ERIN EMMETT
PRINCIPAL CLINICAL SCIENTIST

Erin has been working as a Clinical Scientist in the Inherited Metabolic Disease Laboratory at St Thomas' Hospital for five years. Prior to this she undertook her Clinical Scientist training in Southampton after graduating from Oxford University with an undergraduate Master's degree in Biochemistry. Erin has been involved in a number of CQI initiatives in the department and is in the process of identifying a suitable topic for her next improvement project.

Dr Gary Moore

CONSULTANT SCIENTIST

Dr Gary Moore is the Consultant Scientist for the Diagnostic Haemostasis and Thrombosis Laboratories of Viapath Analytics at Guy's and St. Thomas' Hospitals, London, UK, which he has led since 1997. Prior to this he trained in diagnostic haematology at the Hospital for Sick Children at Great Ormond Street, spent seven years at the Royal London Hospital, and then took charge of Bart's coagulation laboratories for three years. He received his Doctorate in Biomedical Science from the University of Portsmouth in 2003 for a thesis on lupus anticoagulant detection. Dr Moore is Chief Examiner in Haematology for the Institute of Biomedical Science and member of their haematology scientific advisory panel. He is also a visiting specialist lecturer at four UK universities and doctoral examiner for the University of Portsmouth.

Dr Moore's main areas of interest and research are antiphospholipid antibody detection, thrombophilia testing, and diagnostic applications of snake venoms. He has published over 50 papers on laboratory haemostasis/thrombosis diagnostics, published two text books, co-authored guidelines with more at various stages of the publication pathway, and is a regular peer reviewer for various journals. The 'Haematology' textbook he co-authored is widely used as a course text for undergraduate and postgraduate biomedical science courses throughout the UK and the 2nd edition won the Royal Society of Biology best undergraduate textbook award in 2016. In 2017 he received the International Eberhard F. Mammen Excellence in Thrombosis and Haemostasis Award. He is also a regular presenter at national and international meetings, an external consultant to DSM Pentapharm in Switzerland, and member of advisory boards for diagnostic and pharmaceutical companies.

Viapath and Venom

Snake venoms are modified digestive juices containing zootoxins that function as offensive weapons to incapacitate and immobilise prey, as defensive weapons to protect from predators, and to aid digestion. Broadly, venoms can be neurotoxic, cytotoxic, cardiotoxic or haemotoxic, and it is intriguing that evolution of the latter unravelled many steps of vertebrate haemostasis long before human study did the same. Not to be outdone, albeit a few million years later, human study continues to unravel the complexities of snake venoms and knowledge gained thus far has permitted us to employ snake venoms in diagnostic haemostasis testing for some decades

Venoms directly activating coagulation enzymes are the most commonly employed of the haemotoxic venoms in the diagnostic setting i.e. Common Lancehead (Bothrops atrox) to check for heparin contamination, Southern Copperhead (Agkistrodon contortrix contortrix) for assaying protein C, and Russell's Viper (Daboia russelli) for lupus anticoagulant (LA) detection. Publications from St. Thomas' Hospital Haemostasis & Thrombosis laboratories on use of Russell's viper venom for LA detection have informed recent guidelines on best diagnostic practice.

Therapeutic anticoagulant therapy interferes with most LA assays so the St. Thomas' laboratories additionally employ venoms from Coastal Taipan (Oxyuranus scutellatus) and Saw-scaled Viper (Echis carinatus) in their LA assay repertoire as they are unaffected by some of the more widely used anticoagulant drugs. Publications from the St. Thomas' laboratories informed inclusion of these assays in two of the current guidelines and an international, multi-centre study being co-ordinated at Viapath will validate them for adoption by more centres.

Close

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