**Principal Investigator:** Professor Ian Weeks

**Institution:** Cardiff University

**Title:** The All Wales Molecular Pathology Node: The translation of discovery research to comprehensive clinical service delivery

**Summary:**

Wales enjoys the commitment of the Welsh Government in establishing a vibrant life science sector as a means of increasing health and wealth. Underpinned by the quality of research and innovation in the HEI sector together with University Health Boards and Life Science companies, it provides the ideal environment for the establishment of a Molecular Pathology Node. Cardiff University (CU) is a member of the Russell Group of research-intensive universities and the University Hospital of Wales is the largest hospital in Wales serving the local population and is a Wales-wide tertiary referral centre. We will leverage CU’s internationally recognised discovery expertise in psychiatric genetics, neuroscience, and immunity and infection to develop novel platforms and diagnostics. We will:

1. apply recent advances in psychiatric genetics to develop new approaches to diagnosing and stratifying patients with schizophrenia and related disorders;
2. develop multiplex tests for biomarkers that allow diagnosis and stratification of autoimmune and inflammatory diseases including neurodegeneration and the early detection and characterization of infections.

These directly address key "futures" areas for stratified medicine highlighted in the MRC Molecular Pathology Review namely, psychoses and autoimmunity. We intend to establish a comprehensive translational pathway for delivery of diagnostic assay development and validation, including quality control/quality assurance, CE marking, training packages for laboratory/clinical teams and, most importantly, economic evaluation for the development of commissioning packages. This will be a key development and build on existing proximity of University/NHS staff and facilities to enhance collaboration and meet the remit of the initiative.
**Principal Investigator:** Professor Terence Cook  

**Institution:** Imperial College London  

**Title:** Imperial College Molecular Pathology  

**Summary:**

We will develop a joint research/clinical service node that will integrate data from conventional histopathology and cytopathology with data from metabolomics, genomics and transcriptomics to build comprehensive signatures of disease processes for stratification. We will focus on studying how imaging mass spectrometry and transcriptomics can add value to the range of tests already established in our clinical molecular pathology laboratories. Imaging mass spectrometry allows the spatial integration of metabolomics data with histology and opens the door to examiner-independent identification of tissues. We will develop metabolic signature-based tissue classification systems which will be able to deliver full diagnostic and prognostic information in a single step for the proper stratification of patients. For transcriptome analysis we will use RNA sequencing to generate clinically relevant gene panels that can be interrogated using NanoString nCounter technology. Use of this technology will also allow us to extend transcriptome analysis to large numbers of stored specimens of formalin fixed paraffin embedded tissue, thus allowing analysis of the transcriptome in large cohorts of patient with defined clinical outcomes.

The node will be led by academic pathologists ensuring that it is clearly focused on developing clinically relevant and translational diagnostic tests linking research developments and the clinical service. It will bring together researchers from different areas including engineering, biochemistry and analytical chemistry.

We will run a comprehensive training programme in molecular pathology for trainee clinical pathologists and a Masters course in molecular pathology for healthcare personnel.
Principal Investigator: Professor Jo Spencer

Institution: King's College London

Title: Molecular Pathology of Body Surface Inflammation (MoPBSI)

Summary:

The Node at King's will provide a structural pathway by which to greatly accelerate molecular diagnostics development. Ongoing outstanding research germane to key clinical priorities will be captured and wholly new initiatives proposed and nurtured. Progress from concept to implementation will be tracked by an highly inter-disciplinary team including researchers, technologists, clinicians, mathematicians and industry. The goal will be to develop “nextgeneration patient reports” whereby the clinician is guided by reliable, highly incisive datasets, processed and communicated via novel, clearly informative algorithms, coupled with new means of patient engagement. The clinical focus will be body surface inflammation that underpins severe illnesses, that are on the rise, that often require life-long monitoring and care, and in which arena there is intensive development of new, disparate, and sometimes very costly therapeutics.

The diagnostics development pipeline will include disparate approaches, requiring advances in tissue processing and analysis across many platforms; heterogeneous data integration; and new means of archiving and communicating the integrated results. Progress in each area will be made via industrial partnerships, many of which are in place. Product validation and stringent quality assurance will be accelerated by our large, diverse patient groups, and progressive changes in the technological and regulatory environments for tissue and blood analysis.

Our Academic Health Sciences Centre, BRC, and our current activities provide supporting frameworks for accelerating our Node's development. Within it, we shall provide workforce re-training and MSc and MBBS educational modules so that the culture of the molecular pathologist that is central to patient assessment becomes prevalent within today’s and tomorrow’s medicine.
Principal Investigator: Professor Andrew Hall

Institution: Newcastle University

Title: The Newcastle Proximity Laboratory

Summary:

Based in the city’s Royal Victoria Infirmary, the Newcastle Proximity Laboratory (NPL) will bring basic research undertaken in Newcastle University into the heart of clinical practice undertaken by the Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH). The bid brings together a large Cellular Pathology Department with more than 30 consultants, a research intensive Medical School with a focus on healthy ageing, chronic disease, rare diseases and precision medicine and University departments with established expertise in nanotechnology and computing.

Newcastle hosts the NIHR Biomedical Research Centre in Ageing and Age-Related Chronic Disease (1), the NIHR Biomedical Research Unit in Lewy Body Dementia (2), the MRC Centre for Ageing and Vitality (3), the Wellcome Trust Centre for Mitochondrial Research (4), the MRC Centre for Neuromuscular Disease (5) and a NIHR Bioresource in Rare Diseases. Building on this strength in discovery science there will be an emphasis on the development of in vitro diagnostics for disease stratification in chronic and rare diseases, focussing on the multiparameter analysis of small biopsy samples, the integration of results into clinically useful formats and the provision of high quality samples for academic and commercial partners. Promising new in vitro diagnostics will be validated by the Newcastle NIHR Diagnostic Evidence Cooperative (6) (DEC). Initial projects will focus on mitochondrial, liver and bowel disease and childhood cancer. Activity will be linked to the development of a Master’s degree, intercalated degrees for medical students and a fellowship scheme to promote capacity building in Molecular Pathology.
Principal Investigator: Professor Tim Aitman

Institution: NHS Lothian and University of Edinburgh

Title: Edinburgh-St Andrews Consortium for Molecular Pathology, Informatics and Genome Sciences

Summary:

The Edinburgh-St Andrews Molecular Pathology node will build on our key strengths in molecular pathology, informatics and genome sciences, integrating these with conventional histopathology and digital imaging to build capacity, expertise and quality assurance in 21st century diagnostics. Drawing on strengths in the MRC Human Genetics Unit, MRC Farr Institute and EPSRC-funded supercomputer facilities, on existing collaborations between academia, NHS and industry, and through a new Masters course in Molecular Pathology, we will develop new algorithms and standards for genome and epigenome analysis and interpretation of variation in genome sequence and epigenetic state. We will implement state-of-the-art genome technologies to "mainstream" molecular diagnosis of Mendelian diseases in adult medicine and establish rapid genetic diagnosis of acutely ill children and neonates. We will develop "liquid biopsies" for managing cancer via genetic and epigenetic analyses of tumour and cell-free circulating DNA. These techniques will be implemented in the NHS during the award by close collaboration between our clinical and academic pathologists and geneticists, and by defining diagnostic standards in collaboration with the National External Quality Assurance Scheme in Molecular Genetics, which is based in Edinburgh and includes Molecular Pathology. These activities will be dovetailed with industry at every stage: technology development, assay design and implementation, data interpretation and clinical validation. Crucially, through the new Molecular Pathology MSc programme, we will train and sustain a generation of clinical pathologists and scientists and create a virtual Centre for Molecular Pathology that will provide the basis for a substantive MRC Centre in the longer term.
Principal Investigator: Professor Nick Lemoine

Institution: Queen Mary’s University, London

Title: An Integrated Molecular Pathology Training Programme

Summary:

The aim of this proposal is to form a national training programme in Molecular Pathology, building on our existing strengths, to provide:

(i) A cadre of future leaders in molecular pathology providing the link between academia, industry and health provision,
(ii) Knowledge and skills in molecular pathology and molecular diagnostics for pathology training and services,
(iii) A mechanism to up-skill the existing pathology workforce.

We have aligned with the Royal College of Pathologists Specialist Training Committee to ensure the training provided is relevant and in keeping with the national pathology curriculum. The Programme will deliver an MSc in Molecular Pathology and Genomics and a series of basic and advanced Short Courses to cover basic molecular biology, bioinformatics and data analysis, an understanding of health economics and service delivery and diseasespecific molecular pathology, which will conform to RCPath training requirements whilst allowing flexibility to up-skill existing consultants. MRes and Lectureship positions will be available for the future leaders in Molecular Pathology, with the MRes providing a springboard to PhD fellowships and Lectureships providing advanced support to more established talented trainees. These training programmes will tap into the national network of Stratified Medicine Programmes and NIHR BRCs, so adding further value to existing initiatives. We also are in the unique position of co-localising with the Genomics England Headquarters, and access to the GE 100,000 genome project for further research opportunities. With proposed links to Industrial partners and NICE, we aim to provide unique training to create the leadership for Molecular Pathology and Diagnostics.
**Principal Investigator:** Professor Manuel Salto-Tellez

**Institution:** Queens University Belfast

**Title:** Belfast MRC Molecular Pathology Node: A UK National Reference Centre for Molecular Pathology Clinical Trial Testing for Diagnostics and Discovery

**Summary:**

The Belfast MRC Molecular Pathology (MP) Node will be an MRC reference lab for biomarker-led clinical trials in the UK and internationally.

The existing NI MP Node is a reality: a fully integrated model already structured along the MRC MP Node vision. It is centered around a hybrid laboratory, the Northern Ireland – Molecular Pathology Laboratory. NI-MPL is co-sponsored by healthcare and academia. It provides molecular testing for the whole of NI and, at the same time, is instrumental in providing MP support for the science at the Centre for Cancer Research and Cell Biology (CCRCB). It has strong ties with regional and national industry in molecular diagnostics and biomarker analysis. This Node has already transformed the landscape of NI cancer diagnostics and science over the last 3 years: more than 6,000 clinical and research tests per year, instrumental in the success in competitive funding by CCRCB, essential in each of 40 high IF cancer publications in NI, already supporting industry in biomarker validation and molecular testing design, and pioneering the training of molecular pathology in the UK.

We now propose to improve on this model by creating a unique UK resource, the Belfast MRC MP Node, aiming to be the UK reference centre for clinical trial biomarkers, for both patient stratification and discovery. This activity requires the synergy of diagnostic rigour and scientific breath proposed here. This will be complemented by an MSc in MP to attend to the shortage of skills in this area, building on the pioneer activity of our group in MP training.

The resources provided by MRC in our proposal will complement the existing commitment by our institutions (£5.79M) and partners (£1.4M) to bring our laboratory to full CLIA accreditation standards, increase its capacity and capability, and build a comprehensive MP graduate programme.
Principal Investigator: Professor Anthony Freemont

Institution: The University of Manchester

Title: Manchester Molecular Pathology Innovation Centre (MMPathIC): bridging the gap between biomarker discovery and the clinic

Summary:

MMPathIC will combine the strengths of the Manchester Academic Health Science Centre (MAHSC), to take university-led technology innovation and informatics, and translate this into new biomarker-based clinical tests. It will build on opportunities provided in the MAHSC £3bn healthcare economy, and MRC and CRUK investment in translational programme grant funding. MMPathIC will co-locate with the MRC-funded Clinical Proteomics Centre (CPC, Lead- Whetton), in close proximity to discovery scientists, engineers, clinical service and medical education and work on the same MRC/CRUK programmes as CPC, offering instant added value.

MMPathIC will be a multidirectional pipeline linking and enabling cross-talk between Manchester’s:

- molecular pathology laboratories, biomedical/ physical scientists, clinicians
- existing training programmes;
- external partners (industry, NICE, NIHR infrastructure).

We will deliver novel tests and devices of clinical utility, by:

- turning promising pre-clinical assays into GCLP standard and clinical tests;
- examining whether predictive, prognostic or disease markers warrant further development into diagnostics and theranostics;
- translating and evaluating novel patient-focused biomarkers in the key MRC and CRUK stratified medicine areas in Manchester (e.g. connective tissue disease, psoriasis, prostate/lung cancer) by building on existing protocols in oncology;
- using our well-established MIMIT (Manchester: Integrating Medicine and Innovative Technology) site miner model to inform clinically important biomarker development based on clinical pull and involvement of biomedical scientists.

MMPathIC will be led by practising clinical molecular pathologists with proven track records of securing RCUK/ charitable funding for basic and translational research, and taking novel technologies into the clinic.
**Principal Investigator:** Dr Keith Hunter

**Institution:** The University of Sheffield / Sheffield Teaching Hospitals NHSFT

**Title:** STANDARD2025: Sheffield TrAining Network in molecular Diagnostics And Resource Development

**Summary:**

To realise the potential of stratified medicine to revolutionise healthcare, molecular pathology services must reach beyond their current remit and lead clinical medicine forward in development of infrastructure and expertise in application of biomarkers of disease. In Sheffield we will consolidate existing expertise and facilities to develop new capacity in application of biomarkers and analytes which have promise to be developed for point-of-care testing. We will initially exploit Sheffield’s expertise in two cancers of unmet need to drive innovative solutions to the clinical problems these cancers present: namely Head and Neck cancer (HNC) and Bladder cancer (BC) by developing multi-omic testing capacity in analysis of saliva and urine. The clinical problems and expense in managing in these cancers arise from their late diagnosis, lack of screening tests and the long clinical course, with surveillance for subsequent recurrence or disease progression. Expertise in the multi-omic analyses of analytes which can be easily, non-invasively collected in many clinical settings has, in conjunction with the development of large cohorts of appropriate patients, the potential to make breakthroughs in a number of diseases, beyond the initial focus. This Node will support projects to assess existing candidate biomarkers and provide infrastructure and support for biomarker discovery, based round themed work packages which will direct the use of resources, standardisation of approach and capacity development. The Node will also facilitate the entry of pathology trainees into translational research in molecular diagnostics, in order to address the acute skill and personnel shortages in academic pathology.
Principal Investigator: Professor Adrienne Flanagan

Institution: University College London

Title: UCL Molecular Pathology Node

Summary:

The UCL Molecular Pathology Node puts pathology in the centre of a cross-disciplinary research structure, enabling novel test development and pathology training. The objectives are to strengthen the research pipeline, to develop and validate new tests, and to increase capacity in pathology expertise. Together with its affiliated hospitals and industry partners, UCL is especially well placed to harness ‘omics data to stratify patients for biomarker-driven clinical trials and personalised care.

The Node will initially focus on oncology and infectious diseases. These areas have well-developed translational research networks across UCL providing a platform for integrating molecular pathology research and training. Longer term, the Node will be extended to include neurodegenerative disease, coagulopathies and metabolic disorders.

The Node benefits from 5*-rated researchers and access to infrastructure funded through the MRC, EPSRC, Wellcome Trust, and CRUK. Basic research is complemented by 3 BRCs (UCLH, GOSH, Moorfields), where research is translated into the clinic, and the CRUK clinical trials unit and the UCL/KCL Comprehensive Cancer Imaging Centre. The Farr Institute and MRC eMedLab for Medical Bioinformatics enable the integration of molecular pathology with patient data. The provision of stratified medicine will be accelerated through our commercial partners for delivery of diagnostic tests: UCL Advanced Diagnostics with the HCA Sarah Cannon Research Institute and Health Services Laboratories.

The node will work with the Academic Careers Office, which hosts Academic Clinical Fellows and NIHR Clinical Lecturers, to develop training in pathology across UCL and its affiliated hospitals.
**Principal Investigator:** Professor Zofia Miedzybrodzka

**Institution:** University of Aberdeen

**Title:** Aberdeen Thoracic Oncology Molecular Integrative Centre: ATOMIC

**Summary:**

Carcinomas of the lung and oesophagus, whose incidence is increasing worldwide, are two of only four malignancies prioritised by Cancer Research UK as "tumours of unmet need". Lung carcinoma (LC) remains nationally and globally the most fatal of malignant diseases but, as a result of molecular profiling, there have been recent improvements in treatment. Oesophageal carcinoma (OC) is the sixth most common cause of cancer mortality worldwide. Aberdeen is internationally recognised for research in both LC & OC, having recently identified the first effective biomarker driven therapy in OC (1).

The vision of ATOMIC – Aberdeen Thoracic Oncology Molecular Integration Centre - is to build upon the existing single campus research expertise and clinical collaborations between pathology, oncology and genetics from University of Aberdeen and NHS Grampian. Working in collaboration with industrial and academic partners we will: 1) discover and develop new biomarkers for thoracic malignancy, by novel work and by mining data available to us from ongoing studies; 2) work with ThermoFisher Scientific to deliver these as clinical grade diagnostics at the international standard of ISO15189 for clinical trials using the tiny fixed tissue samples that are the norm in clinical practice in this setting 3) work with NHS partners, commissioners and industry to take these forward to evaluation, regulation and routine service provision; and 4) provide a bespoke platform for training new staff in molecular oncology and clinical grade diagnostic development by training two new clinical scientists in genetics with a special interest in molecular pathology, and developing an MRes for with taught and supervised research components.
**Principal Investigator:** Professor Paul Murray

**Institution:** University of Birmingham

**Title:** The Birmingham Molecular Pathology Node: establishing a pipeline for new diagnostics in stratified medicine

**Summary:**

Stratified medicine requires the integration of multiple datasets for diagnosis and management of disease to deliver a system of monitoring and treatment tailored to individual patients. To meet the challenge of improving diagnostics within stratified medicine, we propose to create a Molecular Pathology Node based within the Birmingham Life Sciences Campus which will deliver a diagnostic test discovery pipeline integrating existing diagnostic and clinical capabilities with basic research strengths in medicine and engineering/physical sciences.

There is already basic science and clinical synergy with computer scientists, mathematicians and bioinformaticians on the Birmingham campus, underpinned by a £5M University investment in the Centre for Computational Biology. This is integrated with the expansion of ‘omics’ technologies, including the MRC-funded West Midlands Stratified Medicine Innovation & Translation Facility which will encompass deep immunophenotyping and a regional phenomics centre linked to the National Phenomics Centre at Imperial College. We will harness this expertise to drive clinically-relevant diagnostic test discovery.

We will evaluate new tests using UoB expertise in health economics, evidence synthesis, and test evaluation. In addition local, national and international partnerships, particularly with industry, will develop tests which are not only demonstrably robust and valid but also commercially viable, building on our strong track record and infrastructure. The delivery of new tests for ultimate adoption into clinical practice will enable us to provide solutions to current unmet clinical problems, delivering tangible health benefits as well as economic impact.

Importantly, the Node will also lead Molecular Pathology education and training, both locally and nationally.
Principal Investigator: Dr Samar Betmouni

Institution: University of Bradford

Title: Connected Pathology: digital pathology and diagnostic pathways

Summary:

One of the MRC Molecular Pathology Review recommendations focuses on the need for an improved skills base in UK pathology (1). Tomorrow's Doctors (General Medical Council, 1993) shifted the emphasis of medical training away from pathology towards an integrated, systems-based approach resulting in less time spent studying pathology (2-3). Whilst pathology for medical students has been in decline, there has been significant reorganisation of the career pathways of pathology laboratory staff (4). These factors mean that radical solutions for re-connecting pathology services to research and development are needed, as it is unlikely that this is possible solely within the boundaries of medical schools.

We propose a project in which diagnosis, research and service development in histopathology are delivered using the full potential of the Biomedical Scientists (BMS). The Faculty of Life Sciences (FoLS) has been very effective at revising our curricula with input of industry and clinicians to ensure that future healthcare needs are met. BMS at FoLS are educated in molecular pathology research-rich environments: including biomarkers, cancer and skin biology. Our strength in these areas provides an environment for development of novel diagnostics.

Further strong features of this application are our industrial partnership with Philips (Digital Pathology Solution) and our proposed partnership with a local NHS Trust. If successful the project would operate within the University of Bradford’s Digital Health Enterprise Zone: a development comprising a Health & Wellbeing Centre, business incubator to foster development of digital approaches to healthcare, partnership with NHS providers and BT (5).
**Principal Investigator:** Professor Eamonn Maher

**Institution:** University of Cambridge

**Title:** Cambridge Molecular Pathology Node (CMPN)

**Summary:**

The CMPN will build on the world class basic and translational research undertaken at the University of Cambridge, partner institutes and industrial collaborators to (a) accelerate the discovery, development, validation and implementation of novel molecular diagnostics and biomarkers for precision medicine and (b) establish a cadre of academic molecular pathologists. CMPN will offer state-of-the-art biochemical and next generation sequencing facilities, bioinformatic and statistical support for biomarker discovery and validation, access to bioresource samples to produce novel “clinic ready” diagnostic assays and validated biomarkers. The CMPN programme of work will reflect key local research strengths including autoimmunity and infection, cancer, endocrinology and metabolic disorders, epigenomics and genomics, haematology/haemato-oncology, neurosciences and pregnancy research. Projects will be prioritised by the overseeing molecular pathology board to ensure that those projects with the most potential for clinical impact and training are supported. The CMPN will be linked to physical sciences and technology research groups through a partnership with the Cambridge NanoForum Strategic Research Network (comprising >100 nano research groups) and jointly pursue opportunities arising in the field of nanomedicine. The CMPN initiative will be accompanied by educational developments to boost training in academic molecular pathology.
**Principal Investigator:** Professor Sian Ellard

**Institution:** University of Exeter and Royal Devon & Exeter NHS Foundation Trust

**Title:** Exeter Precision Medicine in Diabetes Node

**Summary:**

We propose an Exeter Precision Medicine in Diabetes Node. This node will translate progress in genomic aspects of diabetes research and access to big data resources into improved diagnosis, treatment and care for patients with diabetes. Our vision is to provide advancements in diabetes services similar to those becoming available to cancer patients. Our strategic focus is diabetes - a heterogeneous, costly disease that is increasing in prevalence due to rising obesity. It is becoming increasingly difficult to dissect diabetes aetiology as many young adults and children become obese. The MRC funding will build on outstanding existing infrastructure and expertise. The funding will bring together existing world class expertise and resources in diabetes with next generation DNA sequencing technology, electronic medical records, expertise in statistical and mathematical modelling, technology assessment and health economics. Our node's long term objective is to provide an improved diabetes service. To roll out new tests we will work with industry such as LGC genomics and use local and nationwide infrastructure such as Academic Health Science Networks, our network of NHS scientists and clinicians who work on diabetes, and Prof Ellard’s national role as the provider of the UK diagnostic NHS molecular genetics service. An example of a specific objective is to develop a non invasive prenatal test using next generation sequencing to improve management of diabetic pregnancies when women carry known diabetes mutations.

In summary, the MRC node will facilitate the translation of diabetes research into services by one of the world’s top diabetes institutes.
**Principal Investigator:** Dr Karin Oien

**Institution:** University of Glasgow

**Title:** Glasgow Molecular Pathology (GMP) Node

**Summary:**

Glasgow is ideally positioned to become a Molecular Pathology Node. Our existing clinical strengths in pathology and molecular diagnostics are delivered from the purpose-built Laboratory Medicine Building within our new £1billion South Glasgow University Hospitals campus, which provides services to 52% of the Scottish population. The University of Glasgow’s successful restructure in 2010 created multidisciplinary Research Institutes within the College of Medical, Veterinary and Life Sciences which are perfectly positioned to make use of, and support, the GMP Node proposal.

Our vision is to transform the management of cancer and chronic disease by accelerating biomedical research, high quality healthcare provision and economic growth. We will achieve this by working in partnership with discovery researchers from the College’s Institutes for Cardiovascular and Medical Sciences, Cancer Sciences and Infection, Immunity and Inflammation, and with industry, to create a multidisciplinary centre of excellence in research and development of molecular diagnostic tests.

Our strategic focus and objectives are to build capacity in molecular pathology and informatics, through funding for staffing and high-quality training to develop expertise. This will enable enhanced delivery and development of clinical molecular pathology; and will underpin the parallel development of pipelines for molecular diagnostics validation.

Successful realisation of this vision will: maximise the impact of major recent infrastructure investment; create the next generation of leaders; deliver high impact innovation in molecular pathology and complex informatics for the benefit of NHS care, academic research and UK industry; and contribute a critical Node to this successful new UK network.
**Principal Investigator:** Professor Philip Quirke

**Institution:** University of Leeds

**Title:** Leeds-Liverpool molecular pathology node

**Summary:**

Based on a strong Leeds-Liverpool collaboration, £40M of MRC/EPSRC new infrastructural funding, excellent bioinformatics, extensive EPSRC collaborators and nearly £4M new University/NHS investment in the node we will create a model, integrated world-class facility to promote translational molecular pathology and molecular medicine with its research focussed on its two Universities joint areas of excellence in Pathology, Oncology, Rheumatology and Ophthalmology. We will innovate with undergraduate and postgraduate training, create a seamless University/NHS molecular pathology partnership, add value and break down barriers for our Industrial partners in collaborations with the NIHR Leeds Diagnostic Evidence Cooperative (DEC), Academic Health Services Network's (AHSNs), Northern Health Service Alliance (NHSA) and the other MRC nodes to create downstream economic growth. The joint centre will rejuvenate molecular pathology, adding critical mass and excellence in molecular diagnostics across both Institutions and beyond.
**Principal Investigator:** Professor Chris Brightling

**Institution:** University of Leicester

**Title:** East Midlands Breathomics Pathology Node (EMBER)

**Summary:**

We will establish the East Midlands Breathomics Pathology Node (EMBER) to develop novel breath-based systems for molecular pathology. Exhaled breath contains volatile organic compounds (VOCs) that reflect biological processes occurring within the lung and, via the vena cava, more distant organs. Analysis of VOCs in breath provides rapid, at-patient and in clinic non-invasive approaches for diagnosis, phenotyping and stratifying patients. Importantly the range of clinical conditions is large and includes: bacterial, fungal and viral infections, cancers, respiratory disease such as asthma, and cardiovascular disorders such as heart failure. The East Midlands has a unique and congruent group of clinical and analytical researchers drawn from the University of Leicester, the Leicester University Hospitals NHS Trust and Loughborough University with strengths in clinical research, analytical chemistry, data management and mathematical modelling of complex data. EMBER focusses these combined strengths, and co-ordinates existing collaborations with industry partners to create a nationally-leading centre in “Breathomics” with the critical mass to establish world-class delivery of new technology, applications and training in molecular pathology. EMBER will deliver near-patient and remote sensing technologies to analyse breath and by consolidating the assets and expertise across the consortia build an infrastructure that will result in novel methods to analyse complex “omics” data that will be applicable ultimately to many areas of diagnostic pathology; translated from EMBER’s leadership in the analysis of breath signatures.
**Principal Investigator:** Professor Alan Knox  
**Institution:** University of Nottingham  
**Title:** Nottingham Molecular Pathology Node (NMPN) for Integrated Multi-platform Biomarker Research and Knowledge Transfer  

**Summary:**

NMPN will bring together pathologists, molecular biologists, clinicians, computer scientists and the Nottingham Health Science Biobank. The team will work with Nottingham University Hospitals NHS Trust (NUH), empath and Pharma/biotech companies in the area of infection/inflammation – disease processes with variable outcomes and treatment responses which would benefit from patient stratification. NMPN will focus primarily on upper & lower gastrointestinal and respiratory tracts, and the liver because they are very adversely affected by chronic infection/inflammatory conditions and feature amongst Nottingham’s major research strengths.

Co-localisation of expertise, huge tissue repository with linked real-time patient data and well defined clinical cohorts will allow (i) testing of biomarkers to reveal hidden disease strata (discovery push), (ii) testing of clinically stratified patient cohorts to reveal discriminatory biomarkers (clinical pull) and (iii) robust biomarker validation enabling early clinical translation. NMPN will build mathematical models to integrate multi-platform biomarker data from multiple sources (e.g. DNA/RNA/Proteomic/Metabolomic profiling of tissue samples and bodily fluids, digital image analysis of tissue sections, genomic profiling for germline variants and of infective organisms). The models will have flexibility, allowing integration of data from other sources (e.g. radiological imaging), and although developed for infection/inflammation the models will be trasferable to other diseases.

We are keen to work with Pharma and biotech companies to ensure research is translated from bench-to-bedside. NMPN will also aim to provide in-depth training for PhD students, new Fellowships in Molecular Pathology, rotation of NHS clinical pathology trainees through through the Node, and creation of a new Associate Professor post.
Principal Investigator: Professor Matthew Wood

Institution: University of Oxford

Title: Oxford Molecular Pathology Node (OXMOLPATH)

Summary:

Molecular pathology utilizes macromolecular analysis of patient samples to derive a molecularly derived disease taxonomy that provides precise prognosis and response prediction for use in precision medicine and discovery of novel therapeutic targets. The aim of the OXMOLPATH Node is to use our combined strengths in basic science and molecular diagnostics to develop and implement innovative methods for comprehensive and integrated identification of novel molecular disease classifiers. Oxford has created a Molecular Diagnostics Centre (MDC) in collaboration with the NHS and industry capable of applying multiple tools to tissue from patients in a clinically accredited environment. This builds on the WGS500 programme which has paved the way to clinical implementation of whole genome sequencing of cancer and rare disease in the NHS. As a partner for Genomics England the MDC will now leverage funding from the Chan Soon Shiong Foundation (CSSF) to develop other Omics technologies, in addition to developing digital pathology and tissue preparation tools for use in diagnostics in collaboration with industry, academia and the NHS. Further upstream, OXMOLPATH will establish state-of-the-art methodologies including single cell analysis from liquid and FFPE biopsies to identify new biomarkers that might be applied in future. Validation of new markers will rely on samples from large patient cohorts (e.g. from clinical trials, Genomics England) and mathematical modelling and statistical machine learning tools.

Central to delivering this vision will be a training programme to develop the next generation of pathologists who can work with scientists, industry and clinicians to invigorate UK pathology.
**Principal Investigator:** Dr David Poller

**Institution:** University of Portsmouth

**Title:** The Thyroid Molecular Diagnostics Partnership (TMD)

**Summary:**

This proposal is for a molecular pathology node to develop systems for molecular diagnosis of thyroid nodules and thyroid cancer. Thyroid nodules are common, affecting up to 25% of the population in some ultrasound studies, but thyroid cancer is rare.

This proposal is to establish a pathology node partnership comprising academia (University of Portsmouth, University of Southampton), The National Health Service (Portsmouth Acute Hospitals NHS Trust) and commercial partners (Life Technologies/Thermo Fisher & Boehringer Ingleheim). This partnership will combine their skills to develop and refine new molecular markers for thyroid nodules, and then to pilot these biomarkers into clinical practice. This pilot will firstly occur in the UK NHS initially via a prospective assessment in Portsmouth/Southampton and then subsequently, with a national clinical trial (via a separately funded application).
**Principal Investigator:** Professor Christian Ottensmeier

**Institution:** University of Southampton

**Title:** Molecular Pathology to guide Cancer Immunotherapy (MAP IT)

**Summary:**

Immunotherapy is a major breakthrough in oncology with dramatic clinical benefit across a broad range of cancers [1]. However, this benefit is seen in only a percentage of patients. There is an urgent need to develop standardised tools for routine and trial settings to identify biomarkers of response and non-reponse, to allow pre-therapy stratification [2]. To address this unmet need, we have developed micro-scaled immunometric and next-generation genomics tools to decipher the molecular architecture of immune responses in tumour tissue [3, 4]. We will establish the infrastructure to standardise multi-dimensional analyses of tumour and purified constituent cells types from small-sized diagnostic biopsies. We will use these tools to map the baseline intratumoral immune response in cohorts of head & neck (H&N), lung, oesophageal and colorectal cancer patients.

We have developed and are implementing a diagnostic pipeline in Southampton for comprehensive tissue analysis. This includes clinical annotation, sample processing, immunoprofiling, micro-scaled transcriptomics and bioinformatics to develop standardised assays (resource tools) and generate reference baseline data sets. Complex molecular data will be reduced to immunohistochemical or amplicon based 'theragnostic' tests developed and validated through the Wessex Investigational Sciences Hub laboratory and Department of Cellular and Molecular Pathology for implementation within the NHS. MAP IT will transfer knowledge and technology to other UK Molecular Pathology Nodes for rapid adoption of these assays in mainstream clinical settings, and is collaborating with the Northern Ireland Molecular Pathology Laboratory, in developing a molecular pathology fellowship program for junior cellular pathologists to train in these techniques.
**Principal Investigator:** Professor Gordon Ferns

**Institution:** University of Sussex

**Title:** South-East England Node for Molecular Pathology and Clinical Diagnostics

**Summary:**

We aim to develop a multidisciplinary node that brings together existing expertise from biomedical, clinical, engineering, physical and mathematical sciences, and existing and planned resources within its partner organisations.

- To exploit the stable local population to develop a bio-bank as a regional and national resource
- To use our expertise in the analysis of large data sets and clinical imaging to better define phenotypes.
- To develop appropriate diagnostic algorithms and mathematical modelling for integrating complex clinical information derived from multiple sources.
- To exploit the novel quantum technology ion traps, as mass spectrometers for innovative molecular diagnostic test, permitting unprecedented accuracy, sensitivity and speed.
- To provide new opportunities for training in molecular pathology at several points along the undergraduate-postgraduate continuum for medical and biomedical students.
- To engage with patients and the public working closely with the Kent Surrey & Sussex: Clinical Research Network, the Royal College of Pathologists and partnership NHS Trusts.

We will work to build upon existing strength, to identify, validate and commercialise biomarkers in the following clinical areas:

- Infectious disease and antibiotic resistance (BSUH and Wellcome Trust Centre for Global Health Research, BSMS), with links with the UK-CRC/HICF Microbiology consortium.
- Genetic conditions associated with DNA damage (the latter is already being provided as a limited NHS diagnostic service by the Centre for Genome Damage & Stability, UoS).
- Personalised therapy as applied to paediatrics (Royal Alexandra Hospital), adult health (UoB) and chronic psychiatric conditions including dementia, mood disorders and psychosis.
- Biomarkers of haematological malignancies (Brighton Blood Biobank, BSUH and BSMS).
**Principal Investigator:** Professor Lawrence Young

**Institution:** University of Warwick

**Title:** Warwick Systems Pathology Node: Molecular Cancer Biomarkers for P4 Medicine

**Summary:**

Precision Medicine and integration of medical and science-technology-engineering-mathematics (STEM)-driven innovations are among the top disruptive Innovations in healthcare. In response to the unmet need of Precision Medicine biomarkers in cancer diagnosis and treatment, Warwick University proposes the Systems Pathology (SysPath) Node concept, which is based on three key pillars:

- Systems solutions to provide leading scientific edge to P4 cancer Medicine,
- Partnership with clinical services and industry for rapid uptake,
- Multidiscipline training to deliver future leadership

The Node brings together theoretical and experimental academics, oncologists and pathologists with distinct but complementary expertise, in collaboration with NHS Pathology and Genetics services and Industry. By fostering and integrating exceptional world-class research from diverse academic departments (Medical School, Systems Biology, Statistics, Chemistry, Engineering) and clinical pathology services, the Node aims to lead through bold innovation and provide a novel concept of an outward-facing integrated systems pathology research environment. This will uncover the translational potential of systems modelling approaches and create a discovery pipeline of robust biomarkers, models and platforms for cancer care to enable transition of thinking from a disease-centric reactive, evidence based medicine model to one which is a proactive, individual-centric P4 medicine.

The Node will also take advantage of Warwick’s expertise in multidiscipline training and develop a unique environment that will bring together the next generation of research innovators with clinical/medical pathologists to learn one another’s languages and work together on multidisciplinary teams and equip them with the necessary vision and skills to transfer cutting-edge science to routine pathology.