University of Glasgow

College of Medical, Veterinary & Life Sciences

GLASGOW MOLECULAR PATHOLOGY NODE

HIGHLIGHTS AND ACHIEVEMENTS

1st November 2015 - 31st May 2017

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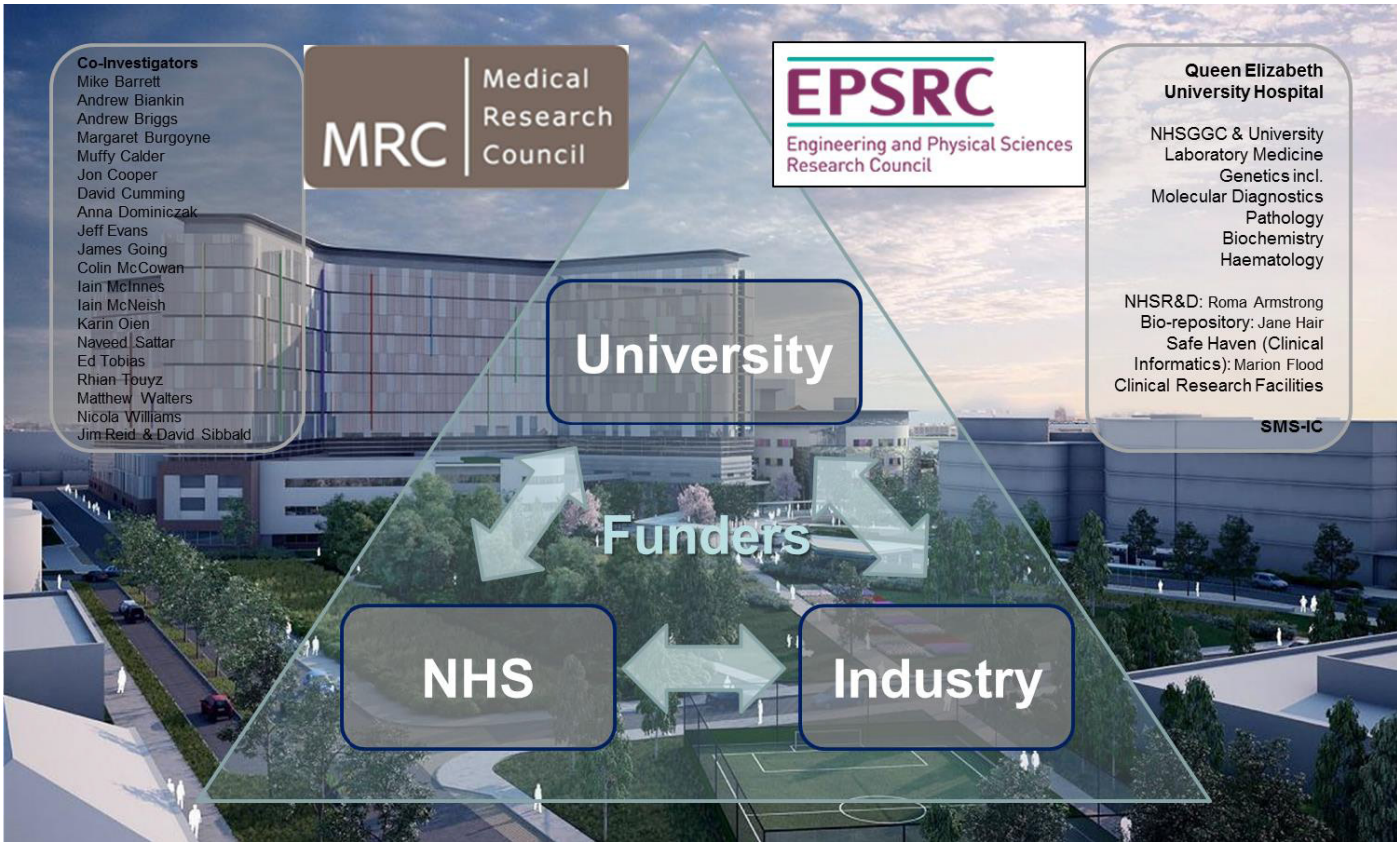
OUR VISION

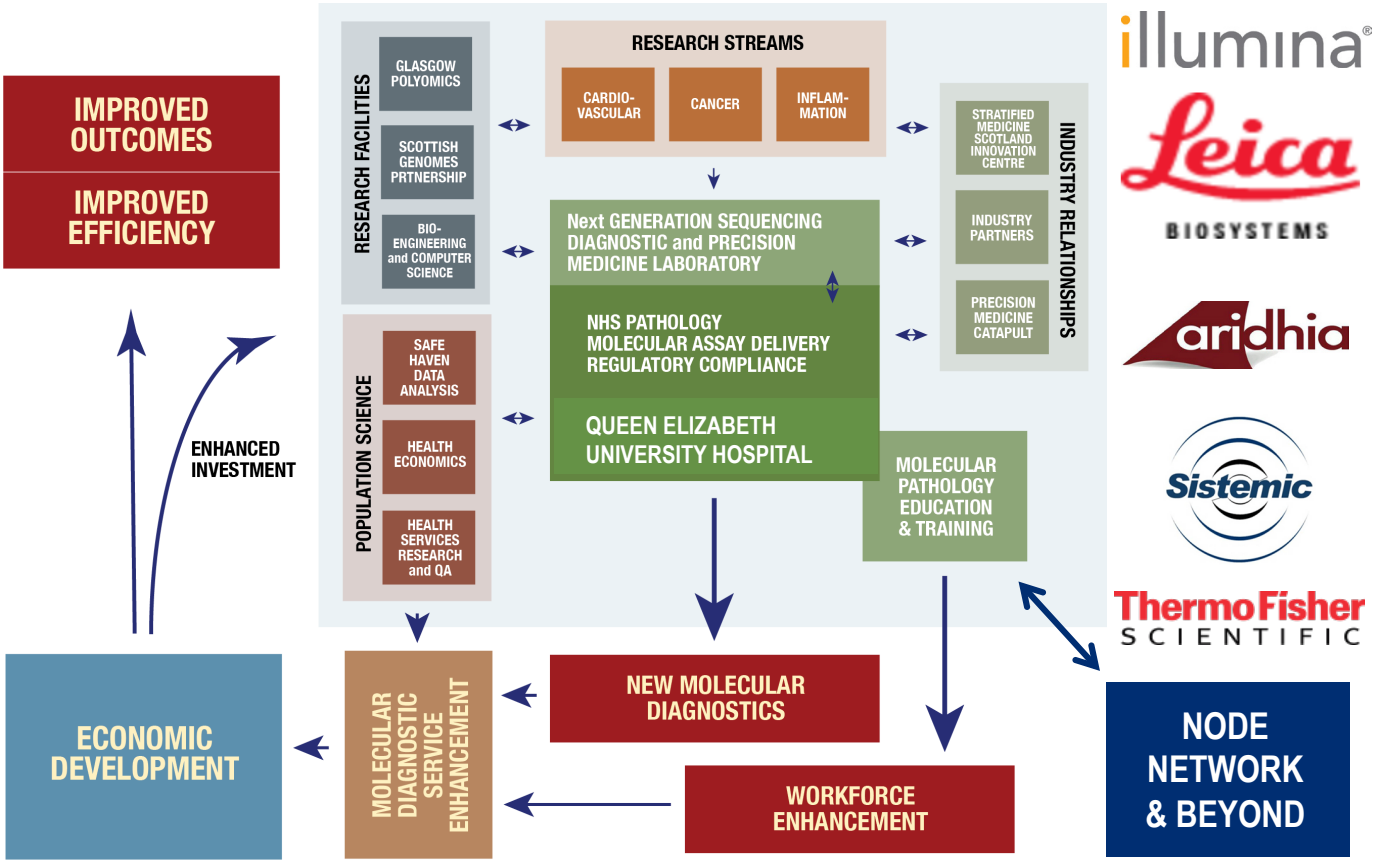
The vision of the Glasgow Molecular Pathology Node is to transform the management of cancer and chronic disease by accelerating biomedical research, high quality healthcare provision and economic growth.

We will achieve this by working in partnership with discovery researchers from the College's Institutes for Cancer Sciences, Infection, Immunity and Inflammation, and Cardiovascular and Medical Sciences 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 enhance our capability in molecular pathology and informatics, through staffing and high quality training to further build capacity and expertise. This will enable enhanced delivery and development of clinical molecular pathology; and will underpin the parallel development of pipelines for molecular diagnostics from discovery through validation and implementation.



Central to the structure of the Node is the NHS Laboratory Medicine Departments at the Queen Elizabeth University Hospital (QEUH) which provides pathology services and molecular assays for the West of Scotland (population >2.8 million). The Node feeds into clinical service areas of significant activity and has invested in broad based research facilities to support specific research streams and industry interactions. A key element is the establishment of the cutting edge next generation genomic sequencing precision medicine laboratory at the Wolfson Wohl Cancer Research Centre, which will be under the regulatory umbrella of the QEUH. It will integrate workflows for preprocessing and for return of results facilitating diagnostic NGS for clinical trial enrolment in the first instances, and subsequently for clinical practice. Research activities will interact with other areas to develop assays that are compliant with regulatory standards. Clinical trial and clinical practice diagnostics will be provided through established networks and direct industry and NHS interactions. Education and training will be coordinated by the Node and exploit opportunities in each specific area.



BUILDING CAPACITY & EXPERTISE

The Glasgow Molecular Pathology Node will build capacity and expertise in molecular pathology through enhanced capacity for clinical development and delivery through staffing; expertise through training and enhanced working for delivery and development. Our training in molecular pathology, genetics, informatics and stratified medicine will address national skill shortages and contribute to a workforce capable of developing, undertaking, interpreting and applying the results of novel molecular molecular diagnostics, across a range of professions and expertise from geneticists, pathologists, clinical and other scientists, informaticians and clinicians across hospital practice and primary care.

This increased capacity and expertise will enable improved clinical practice in molecular pathology in the UK and beyond, through staff and improved working patterns and by underpinning development pipelines. The molecular diagnostics and approaches developed will drive beneficial change in clinical practice for patients worldwide; and their commercial exploitation will benefit the UK economy.

1. Enhanced capacity through staffing: "people"

- Investment in staffing and infrastructure to build capacity in molecular pathology, informatics and health economics
- Across University and NHS - Safe Haven, Biorepository, Pathology, Genetics and -omics
- Multi-disciplinary with industry partnership
- Enabling integrated, collaborative working: "proximity"

2. Expertise through training: "people"

- To develop a workforce with expertise through high-quality, Masters-level training
  - Multi-disciplinary, including pathology, genetics, informatics and stratified medicine
  - Offered flexibly, at different levels, suitable for trainee & consultant scientists, pathologists, and other specialties
  - Linked to appropriate curricula

3. Enhanced working for delivery & development: "paths"

- In Glasgow, pathologists work in specialist teams, which will have consultant leading on molecular pathology, to support clinical delivery, development & research
- Working with an expanded set of clinical scientists specialising in molecular pathology
- And University-funded academic pathologists

4. Pipelines for molecular diagnostic development: "paths"

- In cancer, inflammatory and cardiovascular disease
- With discovery researchers in biomedicine, biostatistics, health economics and bioengineering
- With industrial partners, leading to translation and commercialisation

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TRAINING

Molecular training that enables diagnostic pathology services

- Generation of "Core" courses within MSc Molecular Pathology and delivery to 17 students in session 2016-17, including 12 pathology trainees (stage B-D of training) and 5 clinical scientists/geneticists (from trainees to senior staff)
- Buy-out of time for pathology consultants supporting academic pathology development and innovative molecular pathology teaching
- CPD options generated for pathology and molecular diagnostics staff
- Close collaboration with Molecular Diagnostics department

Building next generation of research leaders in molecular pathology

- Generation of "Advanced" courses within MSc Molecular Pathology for delivery to at least 5 students in the session 2017-18, comprising 2 pathology trainees and 3 clinical scientists/geneticists
- Leadership and support from consultant and trainee pathologists for Node research
- Buy-out of time for pathologists: a proof of principle that if time is made available and funded, pathologists can make a significant research contribution, which has improved understanding and involvement of trainees and researchers in academic pathology.
- Laboratory Medicine Grand Rounds held with an increased emphasis on molecular pathology research. The participants were regularly over 40 in number and included pathologists, clinical scientists and university undergraduate and postgraduate students, from all lab medicine departments (including pathology, molecular diagnostics, genetics, haematology, biochemistry, and microbiology) as well as Node research groups.

Provision of bioinformatics training to enrich molecular pathology diagnosis and research

- A scholarship was awarded to a candidate to start an MSc in Bioinformatics in 2017

Provision of doctoral level training supporting the development of molecular diagnostics

- "Cardiochip" PhD studentship
- Health Economics PhD
- Presentation on Liquid Biopsy for bladder cancer (PhD studentship funded by Pathological Society) at Node-related Glasgow Liquid Biopsy Interest Group meeting.

Investing in next generation of pathologists through undergraduate opportunities

- Presentations on tissue-based and molecular pathology research to Level 2/3 medical, clinical and life sciences students in Head of College Scholars' scheme
- Molecular Pathology project awards for BScMedSci Clinical Medicine students
- Generation of student-selected component (SSC) for level 3 Medical students in pathology case-based e-learning tutorials for delivery in early 2018

Involving public and consumers

- Series of public engagement activities including European Researchers Night, Pathology Week and British Science Week
- CM-Path Consumer training was provided in Lab Medicine Building, QEUH

Networking with Nodes and external bodies to influence training nationally

- Glasgow Molecular Pathology Node has established regular (quarterly) teleconferences
- Peer learning across Nodes on course development, organisation and delivery for molecular pathology enables sharing of best practice
- National perspective enhanced by Node network working together with CM-Path, especially its co-Lead for the Training & Capacity workstream
- Node director and training workstrand team act as external examiners/advisers and reviewers as part of Node network
- A brochure showcasing Molecular Pathology training opportunities across the UK is being compiled
- Harmonization of Masters curricula across the Node network has been proposed
- A workshop to support and enhance the Masters level training in Molecular Pathology provided by the Nodes is being planned for November 2017

Case Study: 1

MSc Molecular Pathology

The MSc Molecular Pathology has been designed with the vision of creating the next generation of leaders in molecular pathology. The course provides state of the art training for pathologists, clinical scientists and related health professionals.

The courses are delivered in a blended online format that allows participation of trainees and staff in the courses without interrupting their on-going NHS service delivery and training. It has also been designed to maximise opportunities for face-to-face interaction facilitating the new highly-collaborative environment of the molecular pathology multidisciplinary team.

The main areas of focus include diagnostic molecular pathology, stratified medicine clinical trials and translational research, bioinformatics and digital pathology. The courses have been developed and are delivered by genetics staff, pathologists and other scientific and academic colleagues.

Case Study: 2

Increased opportunities for pathologists at Queen Elizabeth University Hospital

One colleague who has been undertaking the Masters-level training in Molecular Pathology was until recently a trainee with special interests including cardiovascular and head and neck pathology. She has just been appointed consultant pathologist and is already applying the teachings to her clinical and academic practice.

'One of my particular interests is HPV in oropharyngeal squamous cell carcinoma and I used assessment tasks to learn more about testing strategies for HPV in this tumour type. My knowledge has directly contributed to clinical care in our department as we begin to implement TNM8. As a result, I have been asked to lecture on this subject to surgical trainees on the Head and Neck Surgery course in October 2017'.

With the support of the Node, our colleague has been instrumental in establishing the Scottish cardiovascular tissue biobank which supports the Node cardiovascular research workstrand, and is contributing to translational studies, including as co-investigator on the T-TIME trial, CorMICA pilot study and STRAT-MED-C MRC stratified medicine application.

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RESEARCH

Established pipeline of potential molecular diagnostics

- PRECISIONPanc/ovarian cancer – genomic panel for pancreatic and ovarian cancer
- ORBIT – transcriptomic panel for predicting therapeutic response in RA
- Drugomics – clinical test for determining adherence to drugs in hypertension
- CardioChip – point of care test to measure cardiovascular biomarkers

Evaluating potential molecular diagnostics and associated technologies for use in clinical practice

- Genomic panel for cancer - evaluation for clinical practice
- Myeloid neoplasm panel – health economic evaluation for adoption into clinical practice
- Optimal biospecimens – optimisation of tissue processing parameters for NGS

Discovery research projects to identify potential molecular biomarkers

- Neuroimmunology of mood and Alzheimers (NIMA) – transcriptomic panel to guide treatment stratification in clinical depression
- Cardiovascular biomarkers for prediction of sudden cardiac death; risk of sudden death in patients with heart failure and for prediction of cardiovascular risk.

Health economic assessment to prioritise promising biomarkers/diagnostics and provide a framework for commercial development

- Initial assessment of potential value of Node research pipeline via the Industry Scientific Advisory Board
- Qualitative input to research teams across workstrands to help determine value proposition and pathway to clinic
- Early health technology assessment to inform development of molecular diagnostics

Engaging pathologists with research

- Consultant and trainee pathologists supporting Node pipeline projects
- Grant applications with pathologists as co-investigators (STRAT-MED-C)

Publications and additional funding secured for Node research

- 30 high impact publications related to developments within Glasgow Molecular Pathology Node
- £4.4 million in research income underpinned by the Node
- ~£1.1 million in direct and in-kind contributions from industry partners

Highlighted publications

- Porter, D. et al.(2016) Tumour necrosis factor inhibition versus rituximab for patients with rheumatoid arthritis who require biological treatment (ORBIT): an open-label, randomised controlled, non-inferiority, trial. Lancet, 388(10041),pp.239-247.
- Bailey, P. et al.(2016) Genomic analyses identify molecular subtypes of pancreatic cancer. Nature, 531(7592),pp.47-52.
- Swerdlow, D.I. et al.(2015) HMG-coenzyme A reductase inhibition, type 2 diabetes, and bodyweight: evidence from genetic analysis and randomised trials. Lancet, 385(9965),pp.351-361.
- Rahbari, R. et al.(2016) Timing, rates and spectra of human germline mutation. Nature Genetics, 48(2),pp.126-133.
- MacIsaac, R., et al.(2016) Allopurinol and cardiovascular outcomes in adults with hypertension. Hypertension, 67(3),pp.535-540.

Case study 1

Precision Panc: linking molecular pathology, therapeutic development and routine clinical practice to improve pancreatic cancer outcomes

Precision Panc is an ambitious program of discovery, pre-clinical and clinical work that aims to accelerate the evolution of pancreatic cancer treatment in the clinic. Its first three clinical trials will launch later this year and recruit around 650 patients from hospitals across the UK.

The PRIMUS (Pancreatic cancer Individualised Multi-arm Umbrella Study) trials focus on the therapeutic opportunities that arise through defective DNA damage response in tumours and through the immunogenicity of tumours.

The ultimate aim of Precision Panc is to expand the portfolio of clinical trials, such that the right trial can be found for every pancreatic cancer patient. In order to achieve this we are establishing streamlined patient recruitment, tissue collection, sequencing, analysis and reporting workflows, integrating routine clinical practice with rapid-turnaround research.

Case study 2

Development of 'supply side' economic model to inform decisions around diagnostic research and design

The Glasgow Molecular Pathology Node health economists are working closely with the inflammation workstrand who are developing transcriptomic signatures to predict response to biologic drugs in Rheumatoid Arthritis.

A 'supply-side' model is being developed (that is a model designed from the developers' perspective) to inform decisions around product and research design. Supply-side health economic modelling is characterized by difficulties in obtaining evidence of likely performance (as the technology is still under development) and the need to model many options (as it is not clear where in the disease pathway the signatures may be used). Models need to be simple in order to be effective tools for communication and flexible as they are adapted many times during the technology development process. Key aspects that our model will explore are test position in the disease pathway and necessary test performance.

Alongside the next stage of validation we are undertaking some qualitative research work in the form of a simple questionnaire to clinicians. We will explore attitudes to the potential use of a response prediction test and aspects of test design. Our findings will include the clinicians' preferred form of prediction (e.g. good response/no response or response/no response or continuous score) and the most useful time to predict response (3 month, 6 month or 12 month).

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INDUSTRY PARTNERSHIPS

Multi-disciplinary partnerships supporting research and development of molecular diagnostic tests

- Molecular pathology diagnostic systems (Leica Biosystems)
- Medical informatics and data analysis (Aridhia)
- Next generation sequencing (Illumina)
- Novel diagnostic systems and biomarkers (Sistemic)
- Genetic testing and precision medicine instruments (ThermoFisher)

Facilitating access to world leading academic researchers and facilities and end user environments

- Collaborative research to optimise platforms for application into a healthcare setting and fast track the adoption of new products/services into practice
    - Optimisation of tissue processing parameters for NGS (Leica collaboration)
    - Evaluation of genomic panel for clinical use (Illumina collaboration)
    - Validation and feasibility testing of software development for a data platform that can process data from clinical, genomic and social courses (Aridhia collaboration)

Increasing engagement between academics and clinicians with industry and opportunities for translational research

- Industry Scientific Advisory Board (ISAB)
    - Provides oversight of the longer lasting potential commercial, economic and societal impact of academic research to ensure prospects are effectively translated or quickly re-directed or dropped.
- Industry supported pipeline projects
    - Development of transcriptomic panel for predicting therapeutic response in rheumatoid arthritis
    - Identification of biomarkers for: prediction of sudden cardiac death, risk of sudden death in patients with heart failure and for prediction of cardiovascular risk.
- Annual Node research symposium featuring technology presentations, industry partner area and networking opportunities

- ‘Promoting partnerships’ (PRecision diagnOstics: MOlecular paThology and imagING) series of events planned to identify opportunities for collaboration which will include
    - Horizon scanning/landscape presentations from academia, industry, NHS and Innovate UK
    - Facilitated group work to agree opportunities, actions and strategies.
    - Industry showcase presentations to highlight technologies available to support the development of molecular diagnostics
    - Industry needs presentations to outline the support required from academics and clinicians/pathologists to accelerate technology development implementation.
    - Partnering meetings
- Capital equipment, consumables/materials, access to products at a preferential rate, R&D support, further training, education, seminars and workshops.

Collaborations are currently in development with the following companies:

- Multidisciplinary collaborations in development with industry to accelerate development and implementation of molecular diagnostics and associated technologies

‘As part of BioClavis’ extensive diligence process to find these conditions necessary for our success, we evaluated several possible locations in North America, Europe and Asia as a new base to facilitate our growth plans. As a result of this evaluation process we have identified an excellent opportunity for developing our business based at the University of Glasgow/QEUH Clinical Innovation Zone. Specifically, this location rose to the top of our list based on our critical need for access: to clinical samples, to clinical expertise, to world-class collaborative academic researchers, and to a centralized healthcare system. We were very impressed with the connectivity that exists in Scotland: between research clinicians, NHS Scotland, the biorepository, SMS-IC, University of Glasgow, the wider SME community and Scottish Enterprise support mechanisms to assist with our growth plans. The Molecular Pathology Node is central to the substantial task of fostering the partnerships between all these stakeholders, critical to success (and hence, our success) in translating academic discoveries to development of new diagnostics that impact patient care’ **Dr Harper VanSteenHouse, General Manager, BioClavis**

Case Study: 1

Optimal biospecimens for NGS

The Leica project is an example of a collaborative research project which is between the NHS and Leica Biosystems and facilitated by the Glasgow Molecular Node. This project aims to optimise and standardise patient sample preparation technologies to improve the outcome of next generation sequencing, for use in a clinical diagnostic pathology setting.

The partnership has been developed by monthly calls with both parties to update and address any issues that arise and frequent emails communication where required. Meetings are held to brainstorm each phase of the project so all decisions are made jointly and agreed before continuing with the project. These meetings occur regularly so both Leica and NHS can contribute to the project.

Equipment used in the project has been provided by Leica Biosystems to optimise their products while expertise and staffing for the project is provided by the NHS and tissue samples have been collected via ethical approval by the NHS Biorepository.

Case Study: 2

The Scottish Ecosystem for Precision Medicine

The University of Glasgow’s investment at the heart of Queen Elizabeth University Hospital (QEUH) (the largest acute medical facility in Western Europe) has created an environment for Precision Medicine and provided an epicentre for the Scottish Ecosystem for Precision Medicine (supported with funding from Scottish Government, Research Councils, major charities and industry). The University of Glasgow Clinical Innovation Zone (CIZ) provides units designed to foster open innovation and access to world-leading clinical academics, outstanding clinical research facilities, state-of-the-art facilities, and industry partners co-located on site.

Glasgow Molecular Pathology Node is located at the QEUH campus and this proximity has placed the Node at the heart of the ecosystem and is ensuring close working relationships, sharing of staff and expertise and strategic alignment with initiatives such as Stratified Medicine Scotland-Innovation Centre (SMS-IC), Imaging Centre of Excellence (ICE) and CIZ.

The Scottish Ecosystem for precision medicine offers precision medicine, imaging, and diagnostic companies an outstanding opportunity to collaboratively accelerate their research towards impacts on patient care, society, and the economy.

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WORKING WITH THE NHS

Creating capacity within NHSGG&C to support molecular research

- Research nurse – identification, consent, collection of biological samples
- Senior biomedical scientist – processing and preparation of biological samples
- IT developer – access to data and integration of data into SafeHaven
- Buy out of 0.5 WTE equivalent consultant pathologists time to support development and delivery of MSc Molecular Pathology and provide support for research projects
- Opportunity for existing staff - senior biomedical scientist – to engage with industry led Node research

Establishment of workflows and processes to support molecular research

- Processes for acquisition of biological samples for molecular research established
- Comprehensive data sets and screens developed for clinical annotation of samples
- Linkage with biorepository to enable tissue processing/handling to support research requirements
- Linkage with molecular diagnostics to enable DNA/RNA extraction and pre-analytics for molecular analysis
- Linkage with existing pathology and other research infrastructure to support tissue research

Building expertise for the delivery, analysis and interpretation of molecular diagnostics

- 12 trainee pathologists and 5 biomedical scientists undertaking first year of Masters level education in molecular pathology
- Buy-out of consultant pathologists' time to develop and deliver MSc Molecular Pathology
- Two Node funded clinical scientists to expand the set of clinical scientists specialising in molecular pathology
- Award of scholarship for NHS Senior Biomedical Scientist to undertake MSc in Bioinformatics, Polyomics and Systems Biology starting session 2017-2018

Increased engagement of pathologists with research

- Consultant and trainee pathologists supporting Node pipeline projects
- Grant applications with pathologists as co-investigators (STRAT-MED-C)

Support for MDT working

- Time allocated for discussion of treatment issues related to complex and novel mutations identified in EGFR testing in lung cancer.
- Development of p16 deletion testing through the mesothelioma MDT group
- Development of MDT IT platform to enable access to the information needed to make informed treatment decisions in oncology

Generation of models to assess value of potential new molecular diagnostics or cost of extending diagnostic testing for cancer

- Health economic evaluation of potential new myeloid neoplasm panel (linking with NHSGGC Joint Working Project)
- Heath economic evaluation to assess economic impact and patient outcomes associated with a potential change in KRAS/BRAF testing

Development of infrastructure and resources to support molecular research

- Establishment of the Scottish cardiovascular tissue bank
- Development of a 'tool kit' to assess cardiovascular and renal fibrosis
- Automated sample data transfer - XML file containing anonymised data can be automatically generated, validated and sent to project collaborators.
- Expansion and improvement of IT Hardware and Software to cover new projects and sample types
- Automated linkage with clinical data providing enhanced sample tracking, reporting and data transfer functionality

Case Study: 1

MDT Information Technology Platform

Requirement: There is currently no single GG&C IT system which allows oncology multi-disciplinary teams (MDTs) access to the information needed to make informed treatment decisions. Currently forms must be used to transcribe data from other systems.

Solution: Following the tracking model exemplified by Stratified Medicine, we coordinate with eHealth and Orion to develop an integrated system to be used initially for the PrecisionPanc study but easily extended to encompass all patients. Acquisition of a sample marks the start of a pathway involving sample processing, pathology and whole gene sequencing; at each stage information relevant to an MDT both from these data and from other clinical systems will be drawn together into an 'MDT view' presented by the proposed system.

Impact & Outcomes:

- Standard MDT dataset available across all of GG&C Health Board.
- Data will be current and accurate, sourced in 'real time' from electronic patient records.
- Data are already available, saving time currently spent transcribing from other systems.
- Security of data will be maintained by having a central point of control for granting access to the system.
- Information can be tailored to the specific requirements of an MDT to aid in the patient management and decision making process.
- The ability to also clearly show the current status of the tissue sample molecular diagnostic status.

Case Study: 2

Scottish Cardiovascular tissue biobank

The Node has supported the formation of the Scottish cardiovascular tissue biobank which is the first and only one of its kind in Scotland. The resource is based at the Queen Elizabeth University Hospital and is an invaluable resource for both the molecular pathology Node cardiovascular workstrand and external researchers. The new systems and process we have developed relates to the acquisition of surplus tissue from ex-planted hearts which will support a wide range of research end users.

NHSGGC biorepository worked closely with the Clinical and nursing staff at the Golden Jubilee (Scotland's heart transplant centre) in order to implement a generic patient consent / authorisation process regarding the use of any surplus tissue in research. This collaborative work also included the development of additional procedures with the organ transplant team as well as with the theatre staff in order to collect and transfer of the "fresh" ex-planted hearts in order to maintain its viability for downstream research studies.

The tissue acquisition aspects is one of our most complex and detailed retrieval exercise, providing tissue from all regions of the heart which are also tailored to the specific pathology or disease type. This includes: fresh tissue, snap frozen samples as well as FFPBs. Our specialist cardiac pathologist has been critical to this success.

We have worked closely with our ICAMS researchers during this development stage who have helped validate the sample quality and viability for a wide range of research technologies and the biobank is already collaborating with groups across Glasgow and Dundee. It is anticipated that this research will lead to publications in peer reviewed journals but more importantly, will seek improve patient care by providing useful information to clinicians, particularly with regard to cardiac arrhythmias.

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INFORMATICS

Development/optimization of new informatics methods and techniques for molecular diagnostics

- **New genomic panel for pancreatic cancer** developed using integrated data analysis of whole genome data and literature curation by selecting pancreatic cancer-specific genomic features and all events that are potentially clinically actionable relevant, including those linked to immunotherapy response/resistance.
- **Multiplex assay for fixed tumour material** to capture a broad range of genomic features including point mutations, indels, copy number changes, gene fusions, structural variations and non-coding driver events from tumour material that is formalin-fixed, paraffin-embedded and may be of low cellularity.
- **HOLMES, a bespoke validation pipeline for clinical trial support** combining best of-breed third-party software with custom algorithms to deliver panel based sequencing analytics in accordance with GCLP guidelines and software-development best practices.
- **Methods/workflows for predicting therapeutic responses to drugs** developed for RNA sequencing analysis, patient stratification, feature selection and supervised learning based predictive modelling for Optimal Management of Rheumatoid Arthritis Patients Requiring Biologic Therapy (ORBIT) project and Neuroimmunology of Mood Disorders and Alzheimer's Disease (NIMA) project.
- **Liquid Chromatography-Mass Spectrometry method to predict cardiovascular disease** through identification and quantification of carboxymethyl-lysine (CML) and carboxyethyl-lysine (CEL).

Development/optimization of new computational tools/platform for clinical research

- BATMAN - Bayesian Automated Metabolite Analyser for NMR spectra software has been optimized to quantify metabolites in serum samples.
- An internal cloud-based virtual machine computational platform for reproducible high-throughput computational analysis.
- tranSMART/eTRIKS platform-based database to integrate clinical and omics data under construction.
- New IT/Database infrastructure with improved security and disaster recover strategy created at the Glasgow NHS Safe Haven.

- Expansion of data collection systems to encompass new projects and sample types.
- Enhanced sample tracking with automated reports to allow monitoring samples sent to next generation sequencing facility.
- Automated linking of routine clinical reporting of blood tests with patients in each study.
- Automated sample data transfer - XML file containing anonymised data can be automatically generated, validated and sent to project collaborators.

Publications/outputs

- Manuscript under peer review: NMR metabolomics identifies phenylalanine as a novel predictor of incident heart failure hospitalisation: results from PROSPER and FINRISK 1997.

National & International networking led by Glasgow Molecular Pathology Node

- Led and organized regular teleconferences with all Nodes.
- Organizing a bioinformatics workshop for all Nodes (September).
- Working with NHS Greater Glasgow and Clyde to enhance bioinformatics capability within NHSGGC.
- GMP Node staff provided NMR workflow from data processing to metabolite identification training at the European Molecular Biology Organization (EMBO) Practical Course on Metabolomics Bioinformatics for Life Scientists at European Bioinformatics Institute (EMBL-EBI), Cambridge.
- GMP Node staff provided metabolomics training at Pretoria and Cape Town, South Africa.
- GMP Node staff provided SNP calling and variant annotation training at the Glasgow NGS workshop in May 2017.
- GMP Node staff organizing a Scottish Metabolomics Network Symposium in November 2017.

Case study 1

Conversion of Project-Specific Data Entry and reporting Web Application into a Multi-Project System

Requirements: PrecisionPanc study requires a means of recording sample data for tracking and analysis, and a way to link these sample data with clinical records to produce complete research datasets. The same will be required for future studies.

Solution: Convert existing secure 'Safe Haven' web-based system to allow recording of sample data from any study.

Impact & Outcomes:

- Minimal software development required for sample recording in new studies.
- Staff already familiar with current system so minimal training required.
- Samples currently stored on system can be assigned to other studies with minimal further data entry.
- All data entered into system are instantly linked with collated clinical datasets held by Safe Haven: patient demographics, medical procedures, co-morbidities, and prescribing data are all available for inclusion in a study dataset.

Without having this system adapted for use all data would be collected using Excel spreadsheets, prone to error and inconsistent recording of data, which would then be periodically manually uploaded to the Safe Haven in order to be checked and linked with clinical data: potentially a very time-consuming process.

Case study 2

Predictive test development to direct biologic therapy in rheumatoid arthritis

The ORBIT project aims to identify the right treatment to the right patient at the right time in patients with Rheumatoid Arthritis (RA), as only about 50-70% of the RA patients respond to their first biologic treatment, and it takes about 6 months to evaluate the response.

From a previous clinical trial that recruited over 1000 patients and whole transcriptome profiling using RNA-Sequencing, this project has identified biomarkers that predict treatment response. In order to translate the laboratory results into clinical practice, development of a suitable clinical laboratory test is underway, and in the first-phase, which will be completed before the end of this year, this test will be evaluated using the exiting samples. Then the test will be validated in a clinical trial that will recruit 320 patients.

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NODE NETWORK ACTIVITIES

Networking nationally with the nodes and external bodies to influence national training

- Glasgow Molecular Pathology Node has established regular (4 times a year) teleconferences which include CM-Path
- Node director and training workstrand team acting as external examiners/advisers and reviewers for node network
- The network has established a relationship with the Royal College of Pathologists (RCPath) training lead
- Node representatives participating in RCPath workshop in July 2017 to discuss provision of molecular pathology training
- Harmonization of masters curricula across the Node network has been proposed and is in progress
- A workshop which focusses on the Masters level training in Molecular Pathology provided by the Nodes is being held in November 2017
- A Molecular Pathology training brochure is being compiled

Networking nationally with the nodes and external bodies to enhance health economic and technology assessment for molecular diagnostics

- Glasgow Molecular Pathology Node initiated Node network discussions to explore opportunities for alignment, complementarity and shared learning across the Node network.
- Node network discussions identified four common themes which represented opportunities or challenges for health economics to support precision medicine approaches (diagnostics or devices)
    - Appropriate methods for early HTA (led by Glasgow)
    - Trial Design (led by Edinburgh and Leicester)
    - Reimbursement policy and informational requirements (led by Manchester)
    - Whole disease modelling (led by Newcastle)

- Cross Node workshop which included representatives from the Diagnostic Evidence Cooperatives (DECs) took place in May 2017
- Node network outputs anticipated from the workshop include:
    - Preparation of a series of linked papers
    - Submission to International Society For Pharmacoeconomics and Outcomes Research (ISPOR) in Glasgow in November 2017
    - Production of a formal guidance document which outlines a novel approach to HE around precision medicine/diagnostic test development pathway.

Networking nationally with the nodes to enhance bioinformatics capabilities to support the development of molecular diagnostics

- Teleconferences organised by Glasgow Molecular Pathology Node to identify potential opportunities for collaboration
- Four themes have been identified as opportunities for joint working and knowledge exchange
    - Training and development of Node informaticians
    - Image analysis
    - Clinical data collection and integration
    - Data integration of multiomics
- Shared resources have been created which provide the following information
    - Skills and expertise of Node informaticians
    - Matrix of particular interests of each Node to identify possible research collaboration opportunities
    - Successful and unsuccessful bioinformatics approaches used across projects and research questions
    - High level descriptions of the datasets held by each Node
- Cross Node workshop will be held on the 1st September in Glasgow November 2017.

Case Study: 1

Cross node health economics workshop - 10 May 2017

Our cross node workshop brought together a group of 20 individuals for a day of face to face discussions. Teams from Edinburgh, Newcastle, Manchester and Glasgow nodes were joined by colleagues from the MRC and Newcastle, London and Oxford DECs.

Health economics in the context of stratified medicine is challenging and methods are developing alongside the scientific field. The opportunity to meet personally, share experience and set an agenda for our collaboration was invaluable. Presentations on each of the four themes (Appropriate methods for early HTA, Trial Design, Reimbursement policy and informational requirements, Whole disease modelling) stimulated wide-ranging discussions and thought for future collaborative work.

Following from the workshop two of the themes have put in abstracts to the International Society For Pharmacoeconomics and Outcomes Research (ISPOR) European meeting in Glasgow in November 2017. This is a high profile health economics conference with anticipated attendance of 5,000 from industry, academia, government and third-sector.

Case Study: 2

Influencing provision of molecular pathology training

- The Nodes are making a major contribution to the delivery of new training in molecular pathology in the UK
- For implementation, changes in training need to fit with the post-graduate pathology training curriculum and career structure
- The Node network has established a relationship with the Chair of the Training Committee of the Royal College of Pathologists which has responsibility for the curriculum
- Working together with CM-Path, the Network has contributed to discussions on enhanced molecular pathology within curriculum including support for core lab experience and optional modules
- Node representatives participating in CMPath/RCPath strategic workshop in July 2017 to discuss molecular pathology training provision.
- We envision our role as key Nodes for training delivery and implementation for the future of molecular pathology.

EPSRC Engineering and Physical Sciences Research Council
NHS Greater Glasgow and Clyde
MRC Medical Research Council

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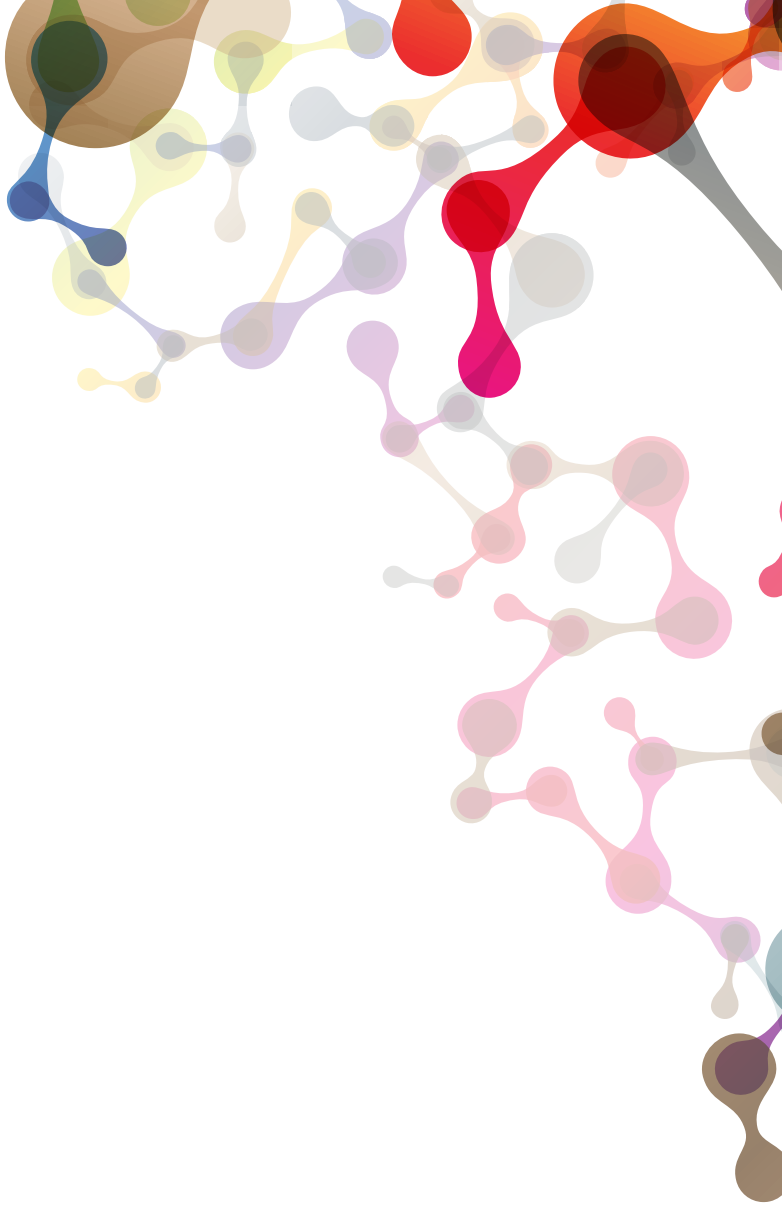

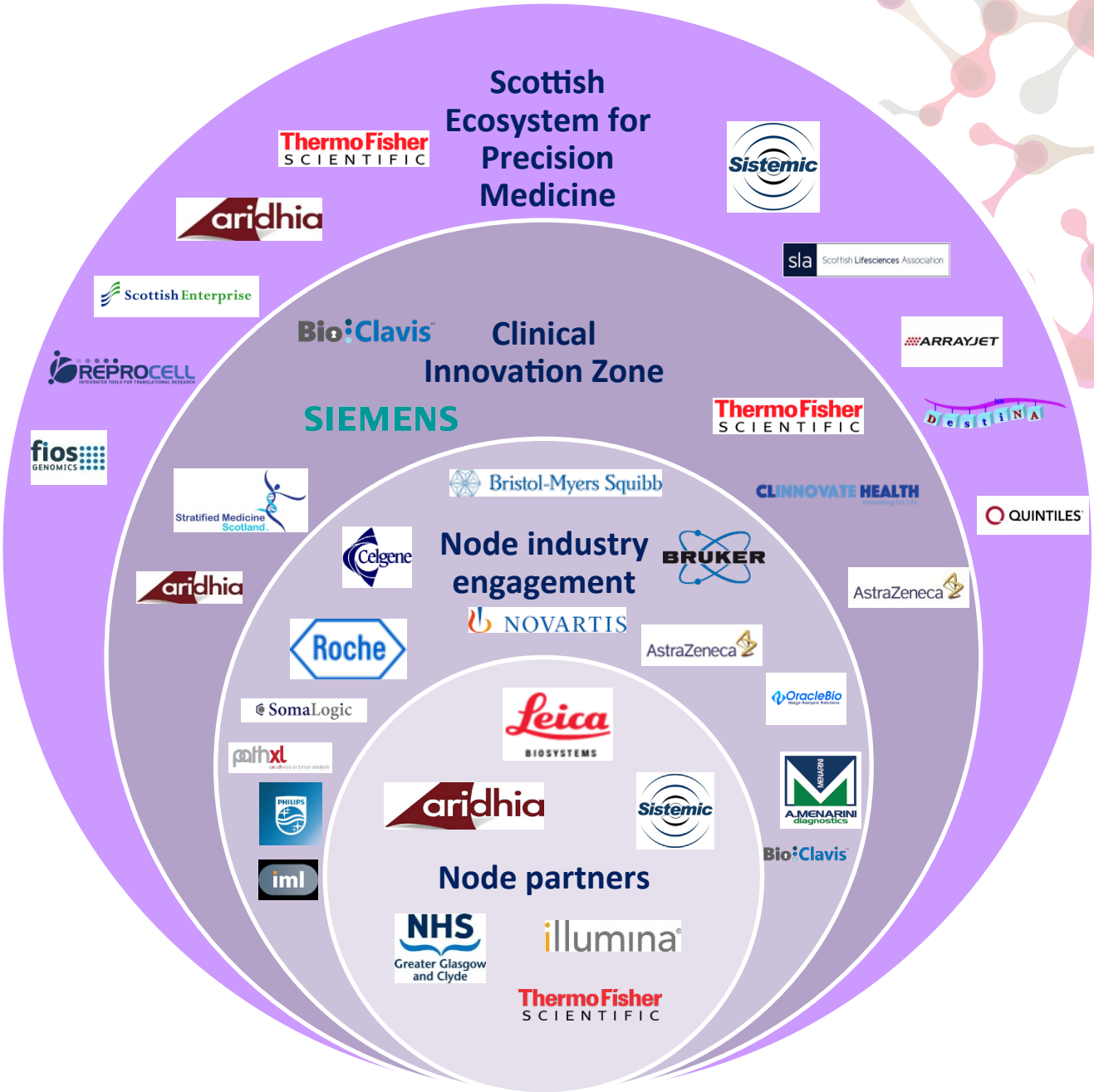
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