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The opportunities today for advancing patient care and improving cancer outcomes are unprecedented. The Cancer Research UK Manchester Centre, and the partnership that it represents, provides the ideal environment to realise these opportunities by bringing together doctors and biologists, physicists and chemists, statisticians and computer scientists, nurses and technicians, thereby creating the multidisciplinary approach that is essential for delivering progress in cancer research.

Our vision is to implement personalised medicine for cancer patients through understanding how and why patients respond differently to various treatments and through using the individual patient’s clinical, genomic and epidemiological characteristics to deliver the most effective first-line and subsequent treatments to achieve sustained responses. We will not only focus on molecularly-targeted drug based therapies but also implement personalised medicine at diagnosis and all the way through treatment with surgery, radiotherapy and drug therapy.

Through the generous support of Cancer Research UK to the Centre we can now invest in the advanced infrastructure that will help us to achieve our ambition. This support is focused on the development of research expertise and capability in four key themes: biomarker discovery, validation and qualification in the clinic; tissue acquisition and molecular pathology; radiotherapy and imaging, and experimental cancer medicine supporting scientifically driven and informed early phase clinical trials. These cross-cutting themes support research in a number of tumour specific areas with particular emphasis on lung, melanoma, prostate, breast and haematological cancers. Within the following pages, we highlight the opportunities and goals in these four crucial themes.

Together with colleagues across the Cancer Research UK network of Centres, and collaborators from within the UK and further afield, we can work to achieve personalised medicine not just for cancer patients in the North West but for all cancer patients worldwide.

Professor Nic Jones
Director
Cancer Research UK Manchester Centre
Only by mapping the genomic landscape of all cancers and identifying the key driver mutations can we hope to develop more novel therapies and test them in the right patients.

Only by following the evolution of individual tumours can we understand the problem of acquired treatment resistance.

Only by linking a patient’s cancer ‘signature’ – be that based on genetics, imaging or other biomarkers - to the potential success or failure of a particular therapeutic approach can we truly personalise their treatment.
Currently, personalised medicine is largely focused on late stage patients and based on invasive tumour biopsies. Importantly, we will go beyond this to implement personalised medicine at diagnosis and throughout the patient journey by molecularly profiling serially-sampled liquid biopsies, and matching with not only drug based therapies but also treatment with radiotherapy and surgery.

Delivery of such a vision requires comprehensive integration of basic and clinical research, a culture and strategy that has patient benefit at its heart, a broad and comprehensive platform of enabling infrastructure and technologies and people with the optimum balance of skills, interests and experience. This philosophy has guided our development over the last few years, resulting in a proven track-record of working and investing together as a successful partnership, and a globally-competitive platform for further development.

Our vision is to transform the clinical care of cancer patients by developing and implementing an integrated personalised medicine approach.
RESEARCH

Our powerful partnership unites those working in basic, translational and clinical research.

Building on our expertise across a range of disciplines and a variety of disease areas, research within the Centre is focused on four key themes:

- **Biomarkers** - discovery, validation and qualification in the clinic
- **Experimental Cancer Medicine** - early phase clinical trials that are scientifically and biomarker driven
- **Molecular Pathology** - acquisition of high quality tissue samples for genomic analysis
- **Innovations in radiotherapy** delivery and imaging

Each theme brings together those working across the full spectrum of cancer research and links fundamental laboratory discoveries to improvements in patient care.

**BASIC SCIENCE**
- Understanding how cancer starts, grows, spreads and returns
- Identifying key cancer-causing genes
- Exploring similarities and differences between cancers

**TRANSLATIONAL RESEARCH**
- Developing new anti-cancer treatments
- Learning how to choose the right therapy option
- Predicting patient benefit and outcome

**CLINICAL TRIALS**
- Bringing the latest therapies to the clinic

**ROUTINE PATIENT CARE**
- Ensuring each patient receives the most appropriate treatment
- Learning how individual patients respond
In Manchester, we have a large biomarker laboratory run to Good Clinical Practice (GCP) standards, with the necessary quality assurance processes required by EU regulations for clinical trials. Our strength is therefore in biomarker validation and standardisation according to GCP, leading to routine use in the clinic. Building on success that is unsurpassed nationally and at the forefront internationally, we are creating a new Centre for Cancer Biomarker Sciences, which will become a major hub for biomarker research and development within the Cancer Research UK network.

Particularly, our work focuses on the potential of tissue and circulating biomarker assays, and we have so far developed an extensive portfolio, including:

- Enumeration and characterisation of circulating tumour cells (CTCs)
- Multiplex ELISA panels for angiogenesis and cell death biomarkers
- CTC-derived mouse models – termed CDX – to study small cell lung cancer (SCLC) and other diseases
- A toolkit of approaches to assess tumour genetics via circulating nucleic acids (cfDNA and miRNA)

We are bringing together multidisciplinary teams within a series of integrated, specialised laboratories:

- Preclinical pharmacology laboratory, using CDX, PDX and cell line models, for therapy testing and biomarker development
- Genome biomarker laboratory for the analysis of tissue and circulating nucleic acids

Biomarkers are essential to our vision of personalised medicine, allowing us to diagnose cancer sub-types, to select appropriate treatments and to predict and monitor response and resistance.
• Cell and protein laboratory for the analysis of circulating tumour cells and circulating protein biomarkers
• Molecular pathology laboratory aligned to tissue biomarkers
• Bioinformatics and biomarker statistics hubs
• Pharmacometrics modelling hub
• Integration centre for clinical and biomarker data

Clinical qualification of biomarkers is hugely challenging, requiring a range of dedicated facilities and specialised skill sets, integration of different disciplines, access to large patient cohorts and extensive early phase clinical trial activities and access to highly sensitive and innovative technology platforms. Much of this is already in place in Manchester, but the Centre is now investing in further recruitment and expansion.

We have established partnerships with pharmaceutical companies, we are working with several comprehensive cancer centres in the USA and in Europe on biomarker studies and we also collaborate with manufacturers to drive forward development of advanced technological approaches. Indeed, we have joined the international CANCER-ID consortium, which focuses on the optimisation and standardisation of circulating biomarker assays for multi-centre trial use. Looking ahead, exciting projects with various partners are underway or in the pipeline, including studies in collaboration with AstraZeneca, Novartis, Roche, Abbvie, Boehringer and GSK, and Dana-Farber and Memorial Sloan Kettering.
Our Experimental Cancer Medicine Unit, located within The Christie’s Clinical Trials Unit, conducts early phase clinical trials in a dedicated 2,000m$^2$ state-of-the-art development with extensive inpatient and outpatient facilities and a large research sample collection laboratory. It is ideally located next to the cancer discovery and translation laboratories within the Cancer Research UK Manchester Institute, the Wolfson Molecular Imaging Centre and the new Manchester Cancer Research Centre building. Moreover, The Christie is the largest single-site cancer hospital in Europe, treating 14,000 new patients every year, and we currently have around 400 trials taking place at any one time.

The Unit is becoming a major international centre for experimental therapeutics providing access to novel therapies for a significant proportion of patients and acting as a ‘go-to’ centre for scientifically driven and biomarker informed trials. Our overall ambition is to reach the scale and scope of early phase clinical trials achieved by the leading cancer centres in Europe and the USA.

In particular, we aim to be a leader in the use of liquid biopsy for personalised medicine and real-time clinical trial data acquisition to enable adaptive decision-making in phase I, and work in partnership with other centres to conduct basket/bucket trials. Recent steps include the initiation of the TARGET study, optimising the pathway to molecularly characterise all patients entering early phase trials in order to allow routine patient stratification. We are basing our approach not on tissue characterisation, but blood-borne or ‘virtual’ biopsy using both circulating tumour DNA (ctDNA) and circulating tumour cells (CTCs).

Key to our vision of personalised medicine is being able to offer novel experimental therapies to cancer patients at all stages of treatment, if that is the most appropriate and likely most effective option. This shifts early phase clinical trials from being an end-of-life experience to one that is considered for patients from the day of diagnosis.

We are delivering a major goal of Cancer Research UK’s strategy – the development of an early phase trials centre that has the size and capacity, innovative culture and expertise to be at the forefront nationally and to compete internationally – driving advances in stratified, biomarker-led trials.

Early phase clinical trials underpin the introduction of innovative new treatments to the clinic, allowing us to develop the arsenal of therapies necessary to achieve personalised medicine for all cancer patients.
TARGET
Tumour characterisation to guide experimental targeted therapy

1. Actionable Results?
2. Incidental Results?

Sequencing
Tumour Board

1. Actionable Results?
2. Incidental Results?

Genetic Counselor

Disclosure of Results

Sequencing
Analysis
Blood
Tumour Biopsy
Informed Consent
Treatment
MOLECULAR PATHOLOGY

Acquisition of tumour tissue is key to translational research and we have developed an extensive biobanking infrastructure that exploits the huge patient base in Manchester.

Our Biobank was established in 2007 and currently supports tissue collectors in five NHS Trusts across Greater Manchester, collecting high quality tumour and matched samples with linked clinical data from at least 12 tumour types. From initially focusing on a sample ‘six pack’ of blood, urine and frozen and fixed tissue, the biobank has evolved to collect other samples of interest including plucked hair and ascites. It has been an invaluable resource, transforming the way tissue is collected for translational research locally and proving its worth through successful delivery of internal and external projects such as the Cancer Research UK Stratified Medicine Programme, Genomics England 100K Genomes Project and TRACERx.

A personalised medicine strategy requires routine molecular analysis of tumour samples and circulating biomarkers from the very beginning of the patient journey to determine the optimal combination of therapies for treatment. A key challenge is the acquisition of repeat tumour biopsies for most cancer types, particularly in the early phase clinical trial setting. We are meeting this challenge through the development of a Research Biopsy Suite at The Christie, which is unique in the UK and allows repeat tumour biopsies to be part of standard patient care and to fit alongside research activity.

We are building on our strong biobanking platform to readily acquire samples from each stage of the patient pathway and meet increasing demand for bespoke tissue collections. We are developing more extensive capabilities in the establishment of in vivo models, including PDX and CDX, and novel cell lines. In addition, we are implementing robust informatics that can deliver routine dataset collection from all patients and more detailed data collection for specific projects.

Facilitating high quality translational research by implementing a flexible and innovative approach to ethical sample collection and analysis.
Radiotherapy and Imaging

Radiotherapy plays a vital role in the treatment of cancer and is used in around 40% of patients who are cured of their disease. Our radiotherapy related research covers a diverse range of focus areas, including sensitivity and toxicity biomarkers, image-guided therapy and combined modality approaches that encompass both targeted agents and immunotherapy. Ultimately, we are looking to personalise radiotherapy through the integration of patient-specific and tumour-specific information, increasingly in real-time.

The Christie is home to the largest radiotherapy facility in Europe, treating 8,500 patients each year, and we have a proven track record in pioneering advanced techniques. Over the last fifteen years we have supported major developments in image-guided radiotherapy, and we are now part of a worldwide research consortium with a mission to develop an integrated magnetic resonance imaging (MRI) guided system. The MR Linac will greatly enhance the real-time visualisation and tracking of cancer targets during the delivery of therapeutic radiation, and our world-leading expertise in this area will drive forward progress.

Our personalised medicine focus recognises the potential for the personalisation of radiotherapy - including changes in field, dose and fractionation and the use of chemotherapy – through the integration of tumour, patient and treatment information. We are developing a theragnostics programme, which will develop and validate predictive models for survival, radiation response and toxicity of such a high accuracy that they can be used in clinical practice. By implementing such an approach, we can optimise radiotherapy delivery for individual patients and improve outcomes over conventional standardised treatments. We have a potential goldmine of information stored in databases and information systems, with new data being generated every day in clinics at The Christie. Data mining can assess the benefit of new interventions and technologies in all patients, notably those patients generally excluded from clinical trials.

In 2010 we were selected, alongside University College London Hospitals NHS Foundation Trust, to host one of the UK’s first high-energy proton therapy centres. To realise the full potential in proton therapy, significant clinical, radiobiological and technical research is required. Within the clinical facility, The Christie is building a fourth gantry room, dedicated to research, with a direct proton beam feed from the accelerator to facilitate studies focused on improving proton beam therapy techniques and clinical indications. We have strong relationships with the Manchester Accelerator Group at the Cockcroft Institute of Accelerator Science and Technology and with the Ion Beam Centre in Surrey and the National Physical Laboratory. This is an area of significant potential and our goal is to become an internationally recognised centre for proton therapy research.
PARTNERS

The Cancer Research UK Manchester Centre benefits from a long-established and strong partnership between University, NHS Trust and Cancer Research UK.

The University of Manchester
The University of Manchester is one of the largest universities in the UK. It has 20 academic schools and hundreds of specialist research groups undertaking pioneering multi-disciplinary teaching and research of worldwide significance. It has an exceptional record of generating and sharing new ideas and innovations. Many of the advances of the 20th century began at the University, such as the work by Rutherford leading to the splitting of the atom and the developments of the world’s first programmable computer in 1948. The University has a rich academic heritage and can lay claim to 25 Nobel laureates amongst its current and former staff and students.

The Christie NHS Foundation Trust
The Christie specialises in cancer treatment, research and education, and is the largest cancer centre in Europe. As well as treating 40,000 patients a year from across the UK, its experts have been pioneering cancer research breakthroughs for more than 100 years. The Christie serves a population of 3.2 million people across Greater Manchester and Cheshire, while 26% of its patients are referred from across the UK. Based in Manchester with radiotherapy centres in Oldham and Salford, The Christie is known for many world-firsts, which have impacted cancer treatment on a global scale.

Cancer Research UK
Cancer Research UK is the world’s leading cancer charity dedicated to saving lives through research. Their groundbreaking work into the prevention, diagnosis and treatment of cancer has helped save millions of lives and is entirely funded by the public. Cancer Research UK has been at the heart of the progress that has already seen survival rates in the UK double in the last forty years. Cancer Research UK supports research into all aspects of cancer through the work of over 4,000 scientists, doctors and nurses. Together with its partners and supporters, Cancer Research UK’s vision is to beat cancer sooner.

Manchester Cancer Research Centre
The Manchester Cancer Research Centre was formed in 2006 as a partnership between The University of Manchester, Cancer Research UK and The Christie NHS Foundation Trust. It acted as a model for Cancer Research UK’s pioneering chain of Centres across the UK that link laboratory and clinic, and has since been established as the cancer research arm of the Manchester Academic Health Science Centre (MAHSC).
Manchester has a wealth of facilities and infrastructure that enables world-leading cancer research.

**Scientific Computing**
Providing a UK-leading High Performance Computing and data management service for genomic analysis.

**Research Biopsy Suite**
Enabling routine biopsy for patients at every stage of their treatment.

**Clinical Trials Unit**
Housing one of the largest early-phase clinical trials units in the world.

**Advanced Imaging and Flow Cytometry**
Cutting-edge tools for the study of cancer, from molecular interactions in primary cells through to tissue-wide responses: super resolution microscopy – using a state of the art gSTED system – as well as cell sorting and analysing, spectroscopy and both confocal and widefield microscopy.

**Molecular Biology**
High throughput exome sequencing, RNA sequencing, ChiP-based sequencing, qPCR, SNP detection and targeted sequencing.

**Proton Beam Therapy Centre**
One of two national high energy proton therapy centres in the UK.

**Wolfson Molecular Imaging Centre**
Preclinical and clinical PET and MRI, plus an on-site cyclotron, radiochemistry production facilities and analytical and biochemistry laboratories for the development of novel radiolabelled compounds.

**Biobank**
Coordinating centralised and standardised collection of high-quality biological samples.

**Radiotherapy**
Offering a dedicated space for research alongside 11 clinical linear accelerators.

**Centre for Cancer Biomarker Sciences**
Good Clinical Practice (GCP)-accredited biomarker laboratories.

**Histology**
Various platforms to enable sectioning, staining and mounting of tissue samples for immunohistochemical analysis, in situ hybridisation, laser capture microdissection, or morphological examination.

**World Leading Cancer Research**
In order to build expertise in early phase clinical trials within Manchester and across the UK we have established an MRes in Experimental Cancer Therapeutics. The course is aimed at medical, nursing and clinical research students who are considering a career in Phase I clinical studies, and alongside taught elements, participants will be allocated to one or more clinical trials that are being conducted by the Experimental Cancer Medicine team at The Christie.

In Molecular Pathology, we are creating a Clinical Research Training Fellowship, which would lead to the award of a PhD. The Fellows will receive training in University laboratories and in an NHS Trust, thus giving access to all aspects of the diagnostic pathway from discovery to adoption. Industry partnerships will also provide unique training opportunities within the commercial sector.

Within laboratory-based research, we offer PhD studentships for those with clinical and non-clinical backgrounds. Our projects are chosen to fit within our overall strategy to translate research into patient benefit in order to drive the adoption of more personalised treatment approaches.
ENGAGEMENT

We are committed to increasing knowledge and understanding of our research amongst our supporters and the general public.

Our committed Research Engagement Manager and the wider Cancer Research UK Research Engagement team are responsible for running inspiring laboratory tours and open days, as well as using a variety of other events to increase awareness of cancer research progress in Manchester.

Biannual open days and regular laboratory tours allow Cancer Research UK ambassadors, supporters and fundraisers to meet our scientists and get first-hand experience of our cutting-edge research. Guests can learn about our recent successes and our ambitious plans for the future, and by seeing real research in action are able to appreciate the impact of Cancer Research UK funding.

Away from the lab, we engage the public with our research in creative and collaborative ways. Through involvement in local science festivals, we offer hands-on activities to children and families, often as part of larger science fairs. We have also held public debates - aimed at adults - that give members of the public a chance to meet our researchers and engage in discussion about current issues around cancer research. Other recent highlights include a performance of ‘The Immortal Woman’, based on the story of Henrietta Lacks, and Pint of Science – an informal lecture by Professor Caroline Dive in a nearby pub.

Online and through social media we are exploring new avenues to spread the word about our progress in cancer research. In addition, virtual engagement activities enable us to reach a wider audience in exciting and innovative ways.
CONTACT US

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