MANCHESTER CANCER RESEARCH CENTRE

Annual Report

2020/2021

Contents

	page
Executive Summary	4
At a Glance	6
Developing a World-Leading Collaboration between Manchester and Kenya	8
Practice-Influencing Research: Lynch Syndrome and Womb cancer	10
The Lung Cancer Town Hall Initiative: Combining Precision Medicine and Team Science	12
Spotlight on Strategic Developments	14
Fifteen Years of World-Leading Cancer Research	16
Paterson Redevelopment Project: Laying the foundations for synergy and Team Science	18
The MCRC Strategic Operations Team	20
Team Science at the MCRC	21
The Christie	22
Developing the Next-Generation of Cancer Researchers	24

	page
International Partnerships	26
A Nexus of Research Excellence	28
The Digital Cancer Centre	30
Equality, Diversity, Inclusivity and Engagement	32
STEM Engagement: An interview with Dr Heather Williams	33
Cancer Research and COVID-19	34
Industry Engagement and Commercialisation	36
News	38
Selected Awards	40
Spotlighted Publications	42
MCRC Events 2020-2021	44
Spotlight on the Health Inequalities in Early Detection ACED Workshop	47
Q&A with Christine Mullen and Caroline Stone	48
The MCRC Strategic Operations Team	49

MANCHESTER CANCER RESEARCH CENTRE





A partnership founded by



MCRC Vision

Cancer Precision For All: Uniting translational science and driving clinical excellence to create a future free from the burden of cancer

Mission

To enable us to achieve our vision, we need to ensure precision treatments and medicines are equitable and embrace the diversity of our entire population. The MCRC will lead in the development of cancer precision research that enables cancer to be identified earlier and curative treatments to be delivered to everyone.

Our aim is to unite the best science with world-leading clinical care by leveraging our synergistic Team Science approach, to break down research silos and enable interdisciplinary and inter-organisational collaboration.

By encouraging innovative thinking and creating opportunities for collaboration, we can unite and translate the basic and discovery scientific work performed in state-of-the-art laboratories with novel patient treatments. These will influence clinical practice and ultimately change patient outcomes.

It will take a One Manchester approach to align the best research across the University, trusts, and funders directed towards improved outcomes in Greater Manchester and beyond.



Values



Openness and Transparency



Championing Innovation



Creating Opportunities to Excel



Interdisciplinary Scientific Excellence and **Research Co-creation**



Scientific Integrity



Equality, Diversity, and Inclusivity

Executive Summary

2020 will be recognised as a landmark year that has had a lasting impact on the research landscape. We have seen research put at considerable risk, the NHS placed under substantial strain and progress on the latest cancer research activities paused as a result of the pandemic.

As a unique partnership between The University of Manchester, Cancer Research UK and The Christie NHS Foundation Trust, the Manchester Cancer Research Centre (MCRC) has and will continue to see the significant challenges caused by COVID-19 across the clinical, academic and funding environments.

Despite these complications, we have seen scientists, healthcare professionals and patients assemble together to transform these challenges into a range of exciting opportunities. I hope that this report will highlight some of the exemplars in digital data, equality, diversity and inclusivity, strategic partnerships and many more.

Precision medicine for all

Patients are at the heart of a comprehensive cancer research centre and in order to have international impact, we must ensure that our research represents all types of cancer in all populations around the world. This is the concept of precision medicine and cancer precision for all. At a local level, by aligning research with the Greater Manchester Cancer Plan, we can better understand the impact of a range of factors on cancer research and outcomes and we have been able to utilise a number of digital assets at The Christie to improve patient outcomes.

At a national level, we are focused on the NHS long term plan and goals and through prevention and early treatment programmes we aim to see a significant increase in the detection of early stage cancer. At a global level, our UK-Kenya High Commission project is driving a bespoke model to link counties to early detection and treatment.

Research Strengths

The MCRC prides itself on its approach to novel science. This year has been no different in delivering new discoveries and initiatives that are continuing to push the boundaries of our collective understanding.

Through proton beam therapy, Prof. Karen Kirkby and a number of key collaborators, including Prof. Kaye Williams, will ascertain how protons can have new indications for the treatment of a number of different tumours. In addition, the TORPEdO trial, led by Prof. Catharine West and Dr David Thompson is one of the first translational studies that compares the activity of proton beam therapy with photon therapies in head and neck cancers.

Another exciting case study is in hypoxia, where research leads Prof. Ananya Choudhury and Prof. Catherine West have derived a number of tumourtype specific hypoxia signatures, which are focusing on biomarker validation, building cohorts and progressing for clinical application.

On a national level, the DETERMINE trial aims to change the treatment of patients based on a number of mutations identified. In addition, the iMATCH consortium, led by Prof. Fiona Thistlethwaite, is looking to scale up and improve access to ATMPs for patients while ensuring their efficient and safe delivery.

We have been able to uplift our ambitions in paediatric oncology, with the advent of protons to treat paediatric patients. This was showcased by receiving research grants from the children's cancer research charity Friends of Rosie, and a Stand Up to Cancer grant. For the latter, the BRAINatomy team, led by Dr Martin McCabe in collaboration with colleagues at St Jude's hospital in Tennessee and Groningen in the Netherlands will look at interactions between photons and brain radiation.

Work on prevention and early detection research continues to be driven by the International Alliance for Cancer Early Detection (ACED) and NIHR Manchester Biomedical Research Centre (BRC). As mentioned on pages ?? in this report, exemplar work led by Prof. Emma Crosbie has also been integral in driving NICE guidelines for offering testing for Lynch Syndrome in those diagnosed with endometrial cancer.



Challenges and Opportunities

In spite of an adverse climate surrounding the COVID-19 pandemic, we have continued to do research and provide the best care for our patients. We have been able to keep trials going and take advantage of the environment that we found ourselves in and Manchester researchers have been investigating the effect COVID-19 has had on cancer patients. Examples include the RECOVERY (Randomised Evaluation of COVID-19 Therapy), RECAP (Remote Monitoring of Cancer Patients) and COSMIC-19 (Continuous Signs Monitoring in COVID-19 patients) trials as well as tools like CORONET

(COVID-19 Risk in Oncology Evaluation Tool). A special mention should also be made to the over 30 researchers and scientists from across the CRUK Manchester Institute and Division of Cancer Sciences who early on supported the national effort to rapidly increase national testing capacity offering their laboratory skills and volunteering to work in the Lighthouse laboratory at Alderley Park.

I want to thank everyone for their continued commitment and drive. While we will no doubt feel the impact of the COVID-19 pandemic for many years to come, there are still many opportunities on the horizon. With renewals of our CRUK Manchester Centre, Experimental Cancer Medicine Centre and NIHR Manchester BRC, there is a real opportunity to integrate more novel science and impactful cancer research into our activities.

As the Director of the MCRC, I feel proud that we have turned many challenges into opportunities and we will continue to drive and lead cancer research in Manchester. I hope you all enjoy this year's Annual Report.

Professor Robert Bristow, Director, MCRC and Cancer Research UK Manchester Centre

At a Glance



I R R M C R C	MANCHESTER 1824 The University of Manchester World-Leading Internationally Recognised University	CANCER RESEARCH UK World's Largest Funder of Cancer Research
889 Jinical studies currently open at The Christie		MANCHESTER CANCER RESEARCH CENTRE
ate who		
since 020	GM Cancer Plan: NHS Strategic Goals	AHSC and HInM
	Meet long term NHS strategic goals in early detection and novel treatments	Multi-domain projects deploying research into population health



Exceptional Clinical Trials: Translational Research Delivered Through NHS Trusts



Novel Multi-Disciplinary Team Science and Training

Increased partnerships and interdisciplinary research ACED, RadNet, CAT (MB-PhD programme), PCUK Movember Centre of Excellence, Lung Cancer Centre of Excellence, NIHR Manchester BRC and CRF

Developing a World-Leading **Collaboration between** Manchester and Kenya

At the MCRC we pride ourselves on striving for global health equity. That's why, in addition to strengthening our existing national and international collaborations, we are always seeking new opportunities to share our collective laboratory and clinical expertise.

In 2020, we made significant progress by forming a new strategic partnership with colleagues in Kenya, to target unmet clinical needs and to change the bias around genomics.

The Christie, The University of Manchester and KUTRRH partnership

In September 2020, The Christie and University of Manchester co-developed a memorandum of understanding with Kenyatta University Teaching, Referral and Research Hospital (KUTRRH). alongside a detailed first-year plan to initiate the collaboration's initiative of developing a long-term relationship. This demonstrated a collaborative commitment in helping to deliver better cancer outcomes in not only Kenya, but the whole of the East

African region through improvement of cancer services. KUTRRH indicated their desire of developing a comprehensive cancer centre and joint funding is being sourced to support our research ambitions.

The partnership is an exemplar of scientific co-creation and hypothesis generation. We have developed a hub and spoke model in which The Christie and KUTRRH act as a "Hub" aligned with "Spokes" that represent health care workers and patient engagement groups to offset geographic barriers. This will bring early detection and systematic therapies to outlying locations using a combination of mobile units and online education programmes.

The similarity in needs between Kenya and Manchester allows for an instance of reciprocal learning and research co-creation, thereby seeing skills and knowledge transfer in areas such as telemedicine.

Tackling a deadly cancer, together

Our focus on oesophageal cancer is invested in uplifting cancer care on a national and international basis. Cancer of the oesophagus remains at a case fatality rate of 99.3% (source: Globocan 2018) in Kenya which is thought to be as a result of late onset and recognition of symptoms by the patient and general practitioner which results in a delay in diagnosis.

The training provided from The University of Manchester to doctors and nurses in Kenya will raise awareness of diagnostic endoscopy and provide training to ensure cancer is identified at earlier stages in patients, pioneering early detection, accurate staging and systemic therapies.

Cancer precision for all

When looking at specialised research in genetics, African populations are underrepresented in a lot of genetic databases. Biopsy collection and our genome sequencing programme will help to identify risk factors of oesophageal cancer in this East

African population. In turn, this could give rise to precision medicine programming in which clinicians will understand tumour drivers and appropriate treatments for cancers of particular genetic trajectories.

Under the umbrella of 'cancer precision for all' we are exploring ways to support this strategic partnership through specific research support grants, such as our NIHR research

The UK-Africa strategic partnership between The University of Manchester. The Christie NHS Foundation Trust and the Ministry of Health in Kenya, demonstrates our commitment to working collaboratively to overcome cancer care challenges, health inequalities, and implement a joint precision medicine and early detection.

Professor Robert Bristow, MCRC Director

group application. We aim for this to provide long-term financial stability to this collaboration and support the continual goal of delivering novel treatments for squamous cell carcinoma of the oesophagus (OSCC).

The importance of the partnership is to bring better health to Kenya but also to lay some good

ground for the future of healthcare internationally, incorporating a lot of learnings from Manchester and the research being performed.

Dr George Njoroge, **Chief Scientific Advisor at** Kenyatta University Teaching, **Referral & Research Hospital**

Practice-Influencing Research: Lynch Syndrome and Womb cancer

As a pioneering cancer research organisation, the ultimate goal of our researchers is to see laboratory research implemented in the clinic and thus improve the lives of patients across the world. The MCRC and our partners share a heritage of achieving this through the development of new treatments, and changing national healthcare guidance.

Lynch syndrome

Lynch syndrome is an inherited genetic condition caused by a faulty gene that can significantly increase the risk of developing cancer, in particular womb and bowel cancers. This faulty gene runs in families with around one in 300 people thought to carry it, although most do not know.

Womb cancer is often the first cancer that people with Lynch syndrome develop, providing a diagnostic opportunity. If Lynch syndrome is diagnosed, people can protect themselves and their family members from future cancers by engaging in bowel cancer screening and aspirin chemoprevention.

Recommendations from NICE

Research led by Professor Emma Crosbie with Professor Gareth Evans and Dr Neil Ryan from The University of Manchester and Manchester University NHS Foundation Trust has shown that almost 3% of womb cancers are linked to Lynch syndrome.

These results have meant the National Institute for Health and Care Excellence (NICE) has adopted a new guideline stating that women diagnosed with womb cancer should now be routinely offered screening for the genetic condition.

Background image shows malignant cells in urine sample of womb cancer patient, demonstrating the potential of simple urine test for womb cancer detection (O'Flynn H, Ryan NAJ, Narine N, Shelton D, Rana D, Crosbie EJ, doi: 10.1038/s41467-021-21257-6). Image courtesy of Ms Nadira Narine, Dr Durgesh Rana and Dr David Shelton (Manchester University NHS Foundation Trust)

Previous guidance meant routine testing was only recommended for patients with bowel cancer, and their atrisk family members. This new guidance for Lynch syndrome screening in womb cancer could identify an estimated 1,000 people per year with the condition in the UK alone, providing an opportunity for cancer early detection and improved patient outcomes.

Impact for women moving forward

There are a range of benefits that come from knowing someone has Lynch syndrome. Screening for Lynch syndrome helps categorise the patient's tumour into one of four molecular subgroups, thereby enabling clinicians

to predict whether the cancer will respond to adjuvant therapy or could benefit from immunotherapy at relapse.

In addition, for every index case of Lynch syndrome there are on average three family members who also test positive. Identifying these cases creates an avenue for risk reducing surgery or surveillance for gynaecological cancer in those who have not yet completed their families.

Next steps for this research area

These new NICE guidelines will mean that thousands more cases of Lynch syndrome are identified. Research efforts will now focus on managing and

The Pathway for NICE **Guideline Changes**

Observation

Womb cancer identified in people with Lynch syndrome. Noticed a policy gap between screening for Lynch syndrome in people with womb cancer and those with bowel cancer.

Hypothesis

Screening for Lynch syndrome in patients with womb cancer is beneficial to reduce the risk of future cancers and identify Lynch syndrome in family members.

Evidence gathering Literature review was carried out that involved consultation with patients and clinicians involved in their care that identified a research gap.

PETALS study

Tested 500 consecutive womb cancer patients at St Mary's hospital for Lynch syndrome.

benefit analysis A micro-costing study identified the NHS costs of Lynch syndrome screening and a health economics analysis showed that Lynch syndrome screening all womb cancer patients is cost-effective

for the NHS.

Cost/

Results interpretation Found 3% of womb cancers were linked to Lynch syndrome.

reducing gynaecological cancer risks in healthy Lynch syndrome carriers. This involves raising awareness about the red flag symptoms of gynaecological cancer, to encourage early presentation, and developing non-invasive tests that could screen for gynaecological cancers before symptoms develop.

Emma is currently working on developing a non-invasive urine-based test for womb cancer. Her preliminary findings were published in Nature Communications earlier in 2021, with plans to see if this test could be rolled out for womb cancer screening in Lynch syndrome carriers.

NICE consultation

Brought the evidence gathered to NICE and consulted on potential guidance change.

NICE guidance

NICE agreed that all women diagnosed with womb cancer should be offered screening for Lynch syndrome.

The Lung Cancer Town Hall Initiative: Combining Precision Medicine and Team Science

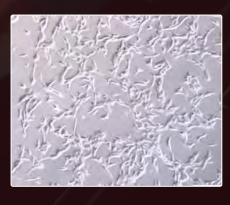
Team Science lies at the heart of our research strategy. We bring individuals and teams together to collaborate and solve problems, and our aim is to work collaboratively to drive high-impact research projects.

To exemplify this collaborative ethos, between 2017 and 2019 we held a series of town halls focused on specific disease sites that each led to a highimpact research project. We caught up with Dr Colin Lindsay to discuss the Town Hall Lung Cancer project and highlight key developments so far.

Lung cancer in Manchester

As part of the MCRC Town Hall events, healthcare workers, researchers and patients were invited to collaborate and develop novel strategies for specific research themes that could only be achieved in Manchester. For Dr Lindsay and his team, this presented an opportunity to collaborate through the MCRC to study smoking associated mutations in lung cancer at both a local and national level.

In the North West, the incidence of lung cancer is higher than the national average, in part due to higher rates of tobacco smoking. In Manchester,



we consequently see a higher incidence of smoking associated mutations, including KRAS G12C – a mutation associated with lung cancer.

One key focus for the Town Hall Initiative has been research into KRAS mutations including G12C, with Dr Lindsay leading as national co-ordinating investigator for several clinical trials of G12C inhibitors in Manchester. "Although we have known about it since 1983 and it is the most common driver mutation in cancer, KRAS mutation has only become directly targetable in the clinic for the past two years. Supported by the MCRC, the lung cancer team have the molecular, translational and clinical infrastructure to characterise these patients, and we have several G12C inhibitor trials that are either running now or are opening in the next year," said Dr Lindsay.

Building strong collaborations

Research into RAS mutations has led to a series of national and international collaborations. In the Trans-Atlantic RAS precision medicine partnership between Manchester, Stanford and the Gustave Roussy Cancer Centre, data from hundreds of patients with either KRAS mutation or NF1 mutation (part of the RAS pathway in lung cancer) has been shared between these research centres. This has enabled researchers to study patient outcomes and treatment vulnerability based on the KRAS or NF1 mutation affecting their cancer.

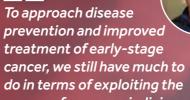
The MCRC also hosted a two-day international RAS workshop to explore developments in precision medicine of the RAS mutation. Over 300 delegates registered for the event, with speakers including Principal Investigators from the Francis Crick Institute, Cologne, Torino and the NCI RAS Institute in Maryland. The workshop has paved the way to more collaborations and workshops similar to this in the future.

Team science

Along with Professors Fiona Blackhall and David Wedge, the team in Manchester have also helped lead analysis from the Genomics England <u>100,000 Genomes Project</u>, which has sequenced >15,000 genomes from NHS patients affected by cancer. "There are over 1500 national lung cancers recruited with full genome information, and through this data we are able to see smoking patterns or even chemotherapy-induced patterns that may influence carcinogenesis", said Dr Lindsay.

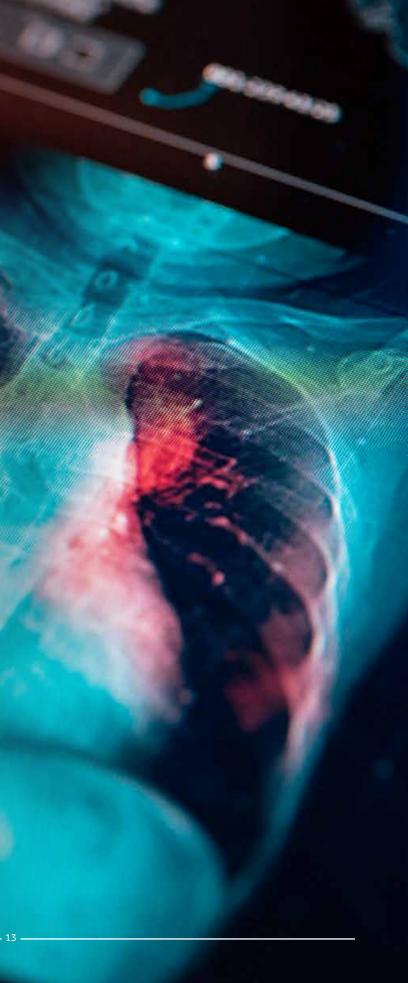
By combining these rich data sets with clinical information, Dr Lindsay and his team will be able to explore correlations between smoking and lung cancer at an unparalleled level of granularity. "We are starting to see thresholds for when smoking a certain amount for a certain length of time may lead to more damaging and persistent types of cancer", said Dr Lindsay.

"



do in terms of exploiting the genome for a more judicious approach to prevention and screening programmes.

Dr Colin Lindsay, Clinical Senior Lecturer



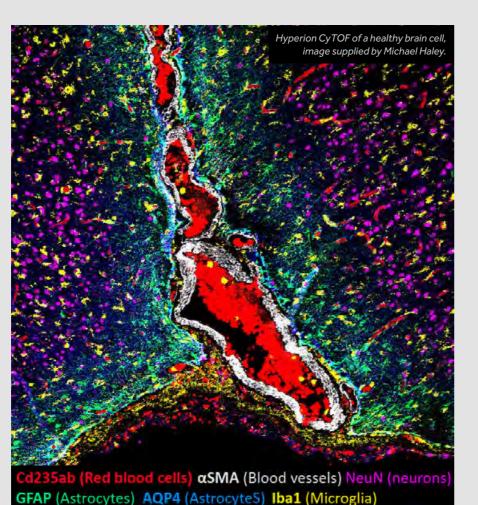
Spotlight on Strategic Developments

Neuro-Oncology

The MCRC Neuro-Oncology research stream includes preclinical studies, advanced imaging studies, and early clinical trials within the new Geoffrey Jefferson Brain Research Centre (GJBRC).

The focus of our increasing portfolio of brain tumour research is to understand and exploit the heterogeneity of the brain tumour microenvironment that occurs de novo or following treatment. We have been designated as one of nine UK Tessa Jowell Brain Tumour Centres of Excellence that recognises the excellence of neuro-oncology patient care within the programme that spans the Salford Royal and Christie NHS Foundation Trusts.

Current multidisciplinary translational research strengths include deep phenotyping of intratumoural heterogeneity using spatial genomics, transcriptomics and proteomics, exploring the role of neuro-matrix, neuro-immunology and glioma stem cell transitions during tumour progression and the role of proton radiotherapy in combination with molecular targeted drugs to improve outcomes. Novel imaging projects are exploring the role of inflammation in low to high grade glioma transitions and inventing new technologies into the operating theatre for cortical mapping during brain tumour



resection with colleagues in the National world lead in cancer genomics which

resection with colleagues in the National Graphene Institute.

The central nervous system research team has grown with the recruitment of Dr Gerben Borst, a clinician-scientist from the NKI-Amsterdam to lead glioma research in clinical oncology and the arrival of Professor David Wedge recruited from Oxford as a world lead in cancer genomics which are being integrated into studies of low to high grade glioma transitions and microenvironmental parameters. Further step-change will occur with the appointment of the £1.35M Brain Tumour Charity funded Chair in Translational Neuro-Oncology.



Paediatric Oncology

Paediatric oncology research is an emerging area of focus within the MCRC with recent success in three grants from Friends of Rosie (FoR), a children's cancer charity, and a new CRUK-Stand up to Cancer (SU2C) team grant; altogether worth more than £1.2M.

Clinical care takes place in the Royal Manchester Children's Trust (part of Manchester University NHS Foundation Trust [MFT] and one of the UK's largest paediatric hospitals) and Manchester is the lead centre for the national **Paediatric Network ECMC**, which is funded by the National Institute for Health Research. This consists of 9 UK centres running early phase clinical trials in children's cancer. It is also one of five designated phase I trial centres for children's cancer in the UK and one of five UK Innovative Therapies for Childhood Cancer (ITCC) First-in-Child centres (one of only 19 in Europe).

There is a large research portfolio from phase I to phase III studies covering the full range of childhood cancers, both haematological (relating to the blood) and solid tumours, from the most common to the rarest. Our patient population is mostly acute leukaemia and brain tumours (as is usual in childhood cancer), and we have particular expertise in neuroblastoma (nerve cell), leukaemia (blood), sarcomas (connective tissue), and brain tumours. The Christie, in partnership with MFT-Children's, is providing highenergy proton beam therapy to children and young people from the whole of the North of the UK.

The FoR grants were awarded on projects exploring the role of proton beam radiobiology (Dr Amy Chadwick, Dr Martin McCabe and Prof. Karen Kirkby), developing liquid biopsies for personalising Ewing's sarcoma treatments (Prof. Caroline Dive and Dr Martin McCabe) and preventing facial disfigurement following radiotherapy (Dr Marianne Aznar). The team grant called "BRAINAnatomy" is led by Dr Martin McCabe was one of only three international awards by the CRUK-SU2C committee and brings together the MCRC, St Jude's Hospital, USA, and University of Groningen, NL, to map the effects of proton beam therapy on neurocognitive changes in treated children using pre-clinical models and machine learning around brain imaging and clinical outcomes data.

Fifteen Years of World-Leading Cancer Research

Collaboration and innovation are at the heart of the Manchester Cancer Research Centre and its partnerships.

Since its inception in 2006, Manchester-based researchers have continuously pushed the boundaries of innovation and discovery to influence clinical practice across the world and ultimately change the lives of patients with cancer. Here are some of the key highlights over the past fifteen years at the MCRC.

2



The first patient is treated using a new MR-guided linear accelerator (MR-Linac) radiotherapy machine at The Christie and makes Manchester one of only two sites worldwide to offer both MR-Linac and proton beam therapy treatments and research. Manchester is named as a member of the International Alliance for Cancer Early Detection (ACED) joining Cancer Research UK, The Canary Center at Stanford, the University of Cambridge the Knight Cancer Institute at OHSU

Building on the strengths in radiotherapy-related research, Manchester is named as a Radiation Research Unit as part of the CRUK Radiation Network, in collaboration with The Christie.

and UCL to develop novel solutions in

cancer early detection.

2018

2019

A CONTRACTOR OF THE OWNER OW

The first patient is treated at the newly opened Proton Beam Therapy Centre, making The Christie in Withington the first hospital to offer high energy proton beam therapy on the NHS.

The Christie and The University of Manchester enter a strategic partnership with Kenyatta University aiming to develop new collaborative research projects in early detection and oesophageal cancer. Despite the COVID-19 pandemic, construction continues to build a £150M cancer research facility to replace the Paterson Building. which was severely damaged in a fire in 2017, and due to be completed in 2022.

2020

Paterson Redevelopment Project: Laying the foundations for synergy and Team Science



Completion December 2022

Home to 7000 scientists, clinicians and administrative staff

In 2017, a fire caused serious damage to the Paterson research building, leading to the displacement of over 300 scientists and research staff.

Whilst causing setbacks in worldleading research activities, the fire gave rise to a new opportunity to create a brand new globally leading cancer research facility. As construction continues, the new facility lends promise to scientific collaboration and a transformation in cancer patient outcomes. In July 2019, we outlined our ambition for the new £150 million flagship purpose-built biomedical research centre that will replace the Paterson Building. It is a critical development in our journey to become one of the top five preclinical, translational and clinical cancer centres in the world. Realising this ambition will ensure that the impact of our research and on patient benefit will not only be delivered locally and nationally but also internationally.

This new facility is designed to support our translational approach to cancer research and care, by promoting

Current progress on Paterson Redevelopment Project (Summer 2021)

d. Realisingwith its state-of-the-art facilities andmat the impactwith the research it supports will alsotient benefitact as an important tool in attractingbocally andnew talent from all over the world.tionally.The building will be twice the size ofact os supportits predecessor, bringing together thelargest concentration of scientists,doctors and nurses in Europe. A further

400 staff will be supported by the facility, alongside the over 300 research scientists and support staff who are currently displaced.

the interaction, integration and

collaboration between research and

clinical staff through co-location. As a

result, joint research programmes will

be stimulated that tackle some of the

most important challenges in cancer

detection and care. The new building.

Building Development Progress

Building work has continued throughout the pandemic. Whilst facing challenges over the past year, construction has now reached the fourth floor, with another five to go. The building is scheduled to reach its apex on the in autumn 2021, with final completion due by December 2022. Discussions are ongoing to determine the exact distribution of groups across the four floors of research space and our multiple laboratory blocks. The economic hit to research funding organisations and academic organisations as a result of the pandemic has been immense but the commitment of the partnership between The University of Manchester, Cancer Research UK, and The Christie NHS Foundation Trust has remained incredibly strong. It is a clear illustration of the confidence the partners have in the strength and direction of cancer research in Manchester.

In the end, the building is simply a conduit for great science; what really matters is the research that will go on in the building because that is what's really going to gain recognition. The exciting bit is the way the building is designed, the way the philosophy works the whole essence of team science. We believe this will result in more translational research and therefore a bigger impact on cancer patients going forward.

We'll continue to update our researchers, clinicians and staff from across Manchester in order to draw more attention to this impressive new build and effectively showcase that in Manchester, we can re-write the future of cancer.



Double

the number of patients offered a clinical trial by 2030

Artist's impression of the Paterson Redevelopment Project

The MCRC Strategic **Operations** Team

At the MCRC, the concept of Team Science instructs and influences all of our research activities, encouraging researchers, patients, clinicians and project managers to collaborate on projects.

This concept is also reflected in the MCRC Strategic Operations Team. Our team comprises a small group of individuals, focused on optimising and expanding the delivery of Manchester's cancer research portfolio. Our role is to ensure our scientists, academics and clinicians have the best support to collaborate and progress their research. We focus on uniting researchers, breaking down silos and enabling collaboration across the city. Additionally, we optimise existing synergies and education as well as facilitating professional development within the research space.

Following Claire Trinder joining in April 2020, the team has grown significantly. The past year has entailed significant challenges, working under different conditions and within an altered funding landscape. Despite these challenges, our team has worked diligently with the MCRC strategic partners on activities around the new Paterson Building development, outlined on page 18-19, Moreover, we are now looking to the many research projects and activities that form the foundation of upcoming funding renewals, including the CRUK Manchester Centre and Experimental Cancer Medicine Centre.

In addition, as detailed on page 26-27, we have continued to grow and establish strong national and international partnerships in key research areas. We look to continue to grow our connections with Kenya, Toronto and Melbourne over the coming years.

We have four main pillars within the team, namely 'Professional Services', 'Communications', 'Training and Education' and 'Strategic Research and Partnerships'.

Professional Services

Caroline Stone and Christine Mullen are experienced executive assistants who ensure cohesion within the MCRC. They manage many aspects of the team's activities, including planning the activities and diaries of our directors. They also play an integral role supporting the wider Strategic Operations Team in order to maximise the efficiency and effectiveness of strategic projects.

Communications

The communications team is headed up by Joe Mowll-Clarke and supported by Elizabeth Openshaw and Sally Best. They work to coordinate and collaborate on communications content with our partners to ensure we have accurate and professional information on research activities, an engaging presence across our website and social media channels, and deliver interactive and high-quality virtual events including seminars, lectures and workshops.

Training and Education

Rachel Chown manages our training and education initiatives by working closely with The University of Manchester and The Christie School of Oncology to drive cancer education and professional development. This means not only delivering to the next generation of cancer researchers but also developing the skills of our current and established researchers and medical professionals.

Georgina Binnie-Wright works alongside Rachel and has a focus on postgraduate education, coordinating a number of programmes including our MB-PhD and clinical academic training awards.

Strategic Research and Partnerships

Sinéad Savage leads on all of our strategic research initiatives and works with colleagues from The University of Manchester and The Christie to ensure we are optimising our reach into different funding options. This enables collaborative and crosscutting research across our range of partnerships. This includes both academic and industry partners as well as developing our international links.

Team Science at the MCRC

The MCRC's approach to Team Science underpins all of our activities. It is an integral component of our most successful projects, from our Town Hall approach, involving academics, professional services, and patients - as highlighted on page 12-13-to the Paterson Redevelopment Project, as highlighted on page 18-19.

recognition of everyone's contribution role of professional support services and

> Project **Managers**

Partnerships

Team



The Christie



The Christie is a world leading specialist cancer treatment centre and is the largest single site cancer centre in Europe.

3.2m Serves the population of

3.2 million people across **Greater Manchester and** Cheshire while more than a quarter of our patients are referred to us from

across the UK.

10. 889

Over 889 studies active during 2020/21, including open and follow-up studies and clinical trials.

4,400 4,400 patients involved in Christie research

projects in 2020/21.

sililiiii ••• Every year, over 44,000 patients treated • at The Christie and its affiliated sites • including 19,000 new patients.

97,000

Over 97,000 chemotherapy treatments delivered to patients.

One of nine UK Centres to offer advanced CAR-T therapies. Mobile chemotherapy unit provides treatment options at locations across Manchester closer to patients' homes.

87,000

Extensive radiotherapy facilities providing over 87,000 treatments in fields including: MR-Linac, Proton Beam Therapy, FLASH radiotherapy, SABR, Adaptive Radiotherapy.

The Christie was the first UK member audited and accredited as a Comprehensive Cancer Centre by the Organisation of European Cancer Institutes; meeting quality standards in care, education and research.

SI

The Christie was the first specialist hospital to be ranked OUTSTANDING by the Care Quality Commission twice in successive inspections describing the hospital as a 'leader in cancer care'.

Top 100

The Christie has been named one of the 100 best specialist hospitals in the world by Newsweek magazine one of the highest profile publications in the USA, sharing this accolade with a small group of the world's elite specialist hospitals.

The Christie has been named as the most Technologically advanced hospital outside

The Christie works with national and international industry organisations including: Roche, AstraZeneca, Bristol-Myers Squibb, Novartis, GlaxoSmithKline and Celgene.

We also work with clinical research organisations Pharmaceutical Product Development (PPD), IQVIA and Paraxel.

of North America.



Developing the Next-Generation of Cancer Researchers

Empowering the future generation of cancer researchers and scientists is core to the successful delivery of our vision. By providing individuals with the opportunities to grow and succeed, they will go on to become future leaders of cancer research.

Rachel Chown manages our training and
education initiatives by working closely
with The University of Manchester
and The Christie School of Oncology.Trust awarded funding for MB-PhD
places to existing institutions with
CRUK MB-PhD funding, including
The University of Manchester, than
to the success of the CRUK model.Binnie-Wright who focuses on the
postgraduate research programmes.In addition, we have recruited three
Clinical Research Training Fellows

Clinical Academic Training programme

We are approaching the halfway mark of our successful Cancer Research UK (CRUK) Clinical Academic Training Programme and we are delighted with our achievements to date. Now, in the third year of the programme, we have been effectively recruiting to build the cohort and to date we have six MB-PhDs students across a range of disease sites. The MB-PhD scheme provides aspiring clinician scientists with experience of research and the opportunity to obtain an MBChB and PhD in Cancer Sciences.

As part of the Clinical Academic Training (CAT) programme, the MCRC hosted a virtual joint lecture and panel session with Baylor College of Medicine (Texas, USA) and The Kennedy Trust IMPACT Inflammation MB-PhD with an international keynote from Professor Sharon Plon, Director of the Baylor Medical Scientist Training Program (MD/PhD Program). The Kennedy places to existing institutions with CRUK MB-PhD funding, including The University of Manchester, thanks to the success of the CRUK model. In addition, we have recruited three Clinical Research Training Fellows (CTRFs) to our CAT Leeds-Manchester strategic partnership in clinical trials and academic pathology.

Non-clinical training programme

We have taken on basic and translational postgraduate researchers to Non-Clinical Studentships funded by the CRUK Manchester Centre, International Alliance for Cancer Early Detection, RadNet Manchester and CRUK Accelerator Awards. Researcher successes include publications in *Frontiers in Oncology* and *The British* Journal of Radiobiology, amongst other journal features. Our Non-Clinical researchers delivered invited, international talks and won prizes including the British Institute of Radiobiology Nic McNally Radiobiology Travel Award (awarded to Conrado Guerrero Quiles, Translational Radiobiology group).

Team science

In line with our multidisciplinary approach and team science ethos, we have been recruiting for a range of PhDs from different disciplines, including nurses and Allied Health Professionals. Funding applications are in process to expand these cohorts even further.

The RadNet AHP Doctoral Academy has been set up and is the first of its kind in the UK. We have recruited two cohorts of Radiographer PhDs and have three Radiographer Researchers on this PhD programme.

As part of our ambition to ensure interactions between basic and clinical science are maximised at every opportunity, we continue to partner closely with The Christie International Fellowship scheme to provide links between our scientific trainees and Clinical Fellows within the hospital.

Spotlight on Nadin Hawwash

First-year MB-PhD student

Diabesity and Cancer Research Group, Professor Andrew Renehan

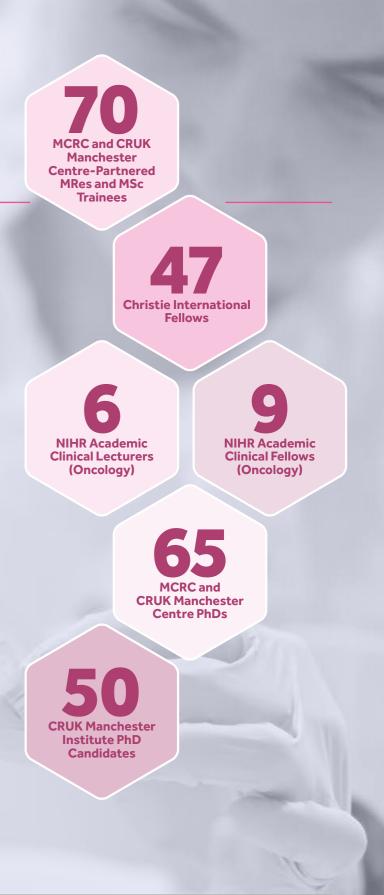
PhD Title:



Adolescent and adulthood BMI and Cancer risk using obese-year metrics (ABACus 2)

The MB-PhD and pathway to become a clinical scientist stood out for me especially given the statistic that 70% of women who take on an MD-PhD in the US stay in research after graduation. This aspect of continuity was important to me.

With obesity affecting around 1 in 4 adults in the UK and being the second commonest cause of cancer, understanding the effect excess adiposity has during an individual's life-course is undoubtably crucial and at the forefront of research. As this project focuses on using 'dry data' as opposed to lab work, I am looking forward to learning more about advanced statistics and applying this to my research. background image is UoM stock shot



International Partnerships

MCRC strategic research and partnerships

In December 2020, Dr Sinéad Savage joined the MCRC as Strategic Research and Partnership Manager. This role ensures the oversight of work across The University of Manchester, The Christie, and the portfolio of CRUK work within Manchester, to foster collaborations at a local, national and international level.

Sinéad works closely with business development and engagement teams at The University of Manchester, the research and innovation division at The Christie, and the Regional Translation Lead at CRUK to maximise the translation and commercialisation of research across the partnership. She also works closely with the strategic funding team at The University of Manchester and the R&I division of The Christie to coordinate academic research collaborations and grant opportunities to broaden our funding portfolio.

Strategic International Partnerships

With the overall aim of delivering precision medicine for all, the team have been developing and expanding national and international partnerships in multiple key priority areas. Alongside our strategic partnership with Kenyatta University and transatlantic ACED partnership that began in 2019, this year has seen our continued collaboration with our key partners in Melbourne, Toronto, Sri Lanka, and India. In early 2020, representatives from The University of Manchester and the Christie visited the Peter McCallum Cancer Centre (PMCC) in Melbourne to discuss exciting opportunities to collaborate and learn from each other. As a result, the MCRC will be working with PMCC to drive workshops and knowledge exchange in areas of key expertise, such as Electronic Patient Records at the Christie, and strategies for patient data use.

The University of Manchester also has a strategic partnership with the University of Melbourne. There will be joint funding opportunities in the coming months to facilitate partnerships which the MCRC will help to drive with its Manchester based partners.

Strategic collaboration between Manchester and University of Toronto

The Joint Research Fund between The University of Manchester and The University of Toronto, awarded in 2020, has enabled ongoing collaborative projects between the two institutions. The partnership is at the forefront of establishing successful Adoptive Cell Therapy programmes in both paediatric and adult settings. The Joint Research Fund also enabled a remote participant (based in Toronto) to join an iMATCH taught module of the ATMP MSc.

The partnership was developed further through a two-day virtual meeting: "Trans-Atlantic Journeys in Cell and Gene Therapy". The virtual meeting covered topics such as Tumour Infiltrating Lymphocyte (TIL) therapy, locoregional delivery of CAR-T in paediatric malignancies, haematopoietic stem cell therapy approaches for lysosomal disorders and TCR gene modified cells in solid malignancies.

Industrial partners

The Partnerships team also coordinate with industrial partners to understand their needs and act to introduce suitable academic partners for collaboration. By setting up showcase meetings with appropriate academic researchers and venture capital companies, the aim is to develop mutually beneficial projects with industrial partners.

In addition, by understanding the wide range of ongoing research across The University of Manchester, The Christie and Cancer Research UK Manchester Institute, the team also work to ensure opportunities for commercialisation are fully supported and realised. This includes opportunities like the Alderley Park Oncology Development Programme, initiated in late 2020.

How do we support collaborations?

The MCRC supports collaborations through facilitating a host of workshops between partners on key strategic research priorities. Using the expertise of the combined MCRC Strategic Operations Team, these workshops aim to find mutually compatible areas for collaborative working.

Canada

Joint Research Partnerships fund to develop joint projects in multiple areas, including immuno-oncology and tumour microenvironment.

USA

International Alliance for Cancer Early Detection seeking to identify develop innovations in early detection.

Examples of successful activities include: a Liverpool-Manchester workshop on immune-oncology and adverse drug reactions which has led to the formation of a working group and preparation of a programme grant; two Real-World Evidence workshops to build internal collaboration between the MCRC partners resulting in the creation of a patient data statement which will advance to a focus group for public engagement.

One of many ways we have worked with Christie clinicians is supporting content submitted to the Goldacre review, a national document which has illustrated Manchester's strengths and experience in digital health.

India

Implementing Manchester-based healthcare strategies to improve the lives of children with acute lymphoblastic leukaemia.

Australia

Joint learning and projects with Peter MacCallum Cancer Centre on electronic patient records and data use.

Kenya

Strategic collaboration with KUTRRH to develop collaborative early detection and oesophageal cancer research.

> It is through high-quality content creation on behalf of our partners that we can showcase their strengths and collaborative potential.

A Nexus of Research Excellence

Cancer research in Manchester exists as a nexus. Research is interconnected, collaborative, world-leading, and impactful. Discover more about the various Centres of Excellence, Institutes, and Teams all driving excellence in cancer research across Manchester with research strategies aligned to the MCRC.



The Digital Cancer Centre **Delivering Precision Medicine for All**

Underpinning our vision of creating a future free from the burden of cancer are our strategies around integrating digital technologies with cancer research and treatment. Our ambition is to establish a Digital Cancer Centre in Manchester within the next two years, that will result in the seamless integration of targeted clinical trials driven by patients' data and novel, precision treatments.

An exciting ecosystem

Our Digital Cancer Centre is only possible here in Manchester, bringing together all digital assets within The Christie, the MCRC, The University of Manchester, and the Pankhurst Institute into one rich ecosystem. All data will connect to patient medical records at The Christie, and by bringing digital assets under one umbrella, it becomes possible to ask questions about individual patients at an extraordinarily granular level.

A rich database

Data will be collected from various sources, including the MCRC Biobank, which has close to 150,000 specimens of tissue, blood and other sample collection across four NHS Trusts; the

Digital Pathology & Radiology Picture Archiving and Communication System (PACS) at St Mary's hospital, which has a genomics summary of all mutations found; and the North West Genomic Laboratory Hub.

Data will also be collected in real time from the patient themselves, through electronic patient-reported experience measures (ePREMs) and electronic patient-reported outcome measures (ePROMs), where the patient reports their experiences through a digital device. Currently, over 10,000 ePROMs have been completed by patients at The Christie. The database will also be linked to the Greater Manchester integrated care record, which means further data can be captured around co-morbidities, polypharmacy and ethnicity.

Precision medicine for all

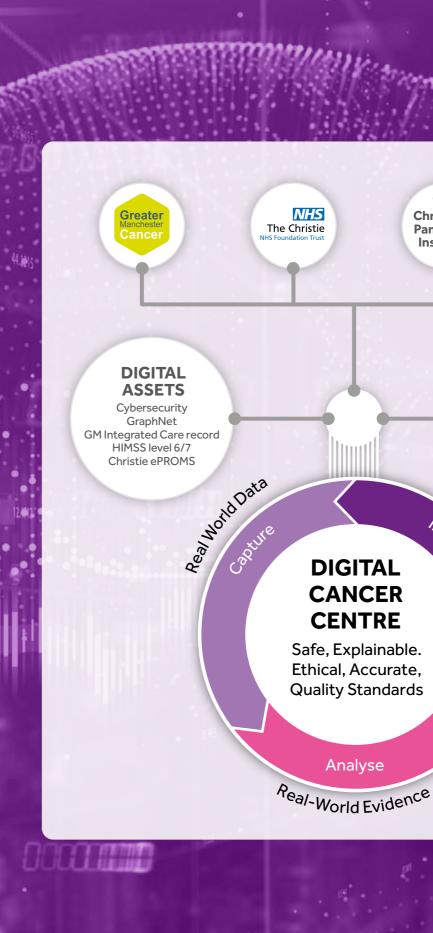
Having such a rich database means scientists can ask specific questions about a patient based on their pathology, genomics and ethnicity. Accessing such data can give extremely rich granularity around factors that may influence a patient's fragility and treatment outcomes. Essentially, we can begin to set up new clinical trials and ask complex questions about complex patients.

We aim to make the Digital Cancer Centre a place where investigators from other institutions nationally and internationally can come and study in collaboration, ask questions and

carry out modelling based on their own populations. We are aiming to set up a similar system in Kenya with the Kenyatta University Teaching, Referral & Research Hospital (KUTRRH), where we will develop an exemplar model that other cancer centres can integrate into their own infrastructure.

Co-creation with our patients

The ultimate stakeholders of the Digital Cancer Centre are the patients themselves. We are engaging patients earlier on to co-create the science through accessing data from their GP or other health providers. This is exciting because it really brings them into how their data is being used, and also how they are allowing us to use their data. The data use promise, in line with current strict data guidelines, will allow patients at The Christie to fully understand what happens with their data, and work with us to co-create our ambition in Manchester to be a worldleading comprehensive cancer centre.



The Christabel Pankhurst Institute The University of Manchester

The Alan Turing Institute

FUNDING

The Christie Charity dECMT CRUK Accelerator CRUK RadNet Manchester **CRUK Manchester Centre** Al Turing Fellows

Improve Care

110 ement

Equality, Diversity, Inclusivity and Engagement

The MCRC has a vision to deliver a cancer free future and provide Precision Medicine for All. This means providing tailored treatments to people within all demographics of the population regardless of age, ethnicity, or gender identity.

We adopt our inclusive strategy to our research activities too. We aim to engage with as many voices as possible from research concept to project delivery, and give every contribution to a project the recognition it deserves, from PhD student, and project manager to chief investigator and patient representative.

Equality diversity and inclusivity

At the MCRC, we believe our approach to cancer research needs to be uniform. equitable and inclusive. Therefore, we see it as our responsibility to engage with communities and individuals as much as possible throughout the lifecycle of a project.

In late 2019, the MCRC and Social Responsibility team at The Division of Cancer Sciences within The University of Manchester began working with the community representation group BRAG. This enabled us to begin devising a mutually beneficial research strategy that puts community engagement at the heart of research.

This ongoing collaboration has resulted in several efforts towards this shared objective, including co-hosting events at World Cancer Day 2020 and 2021, alongside other research specific workshops. Our end goal is to continue working with communities and organisations that help us to engage and reach individuals to tackle any health inequalities that may exist.

Virtual engagement

The COVID-19 pandemic has had a major impact on many aspects of research, but it has also resulted in a shift to virtual events. This shift means we have been able to connect with more individuals, capturing new experiences and voices that we otherwise may not have been aware of.

Throughout 2020, the MCRC has been involved in several public-facing virtual events, including the Manchester Breast Centre public engagement session run by Dr Ahmet Ucar and Prof. Rob Clarke, to mark Wear it Pink day in October 2020. We were also involved in a virtual World To develop a Cancer Day in collaborative research 2021 to update strategy with on the challenges representatives of faced during **BAME** communities the COVID-19 pandemic.

Our virtual engagement affords researchers the opportunity to get involved and spread their knowledge. Whether supporting events such as Greater Manchester Cancer. Cancer Research UK. or external organisations like British Science Week and ScienceGrll, there are plenty of opportunities to get involved.

MCRC Commitments

To work with our

partners and diverse

communities in seeking

the best ways to address

societal inequalities

equality, diversity and inclusion

> To listen and respond to all our communities

To ensure equity in the recruitment and retention of postgraduate researchers from underrepresented groups on the cancer sciences trainee pipeline

STEM Engagement: An interview with Dr Heather Williams

At the MCRC, Patient Public Involvement and Engagement (PPIE) represents an important and active partnership between researchers, patients and members of the public.

Dr Heather Williams, Consultant Medical Physicist, Group Leader for nuclear medicine at The Christie, and co-founder of ScienceGrrl, explains why she takes an active role in STEM engagement.

How did you get involved in STEM engagement?

I joined the Women in Physics group at the Institute of Physics when I was still a PhD student, and alongside working with them I noticed there was an opportunity to 'get things done' outside of a professional organisation, so I set up a network called ScienceGrrl. We initially started as a reaction on Twitter to the European project 'Science: It's a Girl Thing!', where I thought it would be really good if we could run a project that showed people what women actually get up to in science.

What kind of outreach activities have you taken part in?

We take part in various outreach events at festivals, schools and community centres, to show who 'women in

science' really are. We have also used professional photographers to create a calendar that showcased the work of female scientists from a diverse range of backgrounds. We have pulled together a report for Parliament called 'Through Both Eyes', which talks about many of the cultural factors which influence girls' choices regarding STEM.

Why take part in engagement and outreach activities?

Part of the reason is to make things better for the people who are coming after us, and part of that is to say: this is what you can do in science. Quite a lot of what we do has this playful creative edge because we're not doing it for a living - we do it in our own time, and finding new ways of expressing ourselves and communicating what we do is really important. If what you're doing is above and beyond your job, you won't want to take part if it's dull and boring!

You were also awarded an MBE in the 2021 New Years' Honours, for services to diversity and inclusion in science...

That was a complete surprise! I was really touched that somebody somewhere thought that whatever I'd done was worthy of that honour, and that is really quite something.



How can researchers and staff play a greater role in **STEM engagement?**

There are a lot of volunteer opportunities for science communication through The University of Manchester and British Science Association. In addition, social media can be a brilliant tool for connecting with people outside your own circle of influence, and Twitter is brilliant for professional networking. Social media can also be used directly as an outreach platform: Facebook is really good for speaking with parents and families, and Instagram is useful for speaking with a younger audience who are thinking about going into a STEM career.



Cancer Research and COVID-19

The ongoing COVID-19 pandemic has posed numerous challenges to the healthcare sector and to wider society, with many research organisations, including those in Manchester, needing to rapidly reallocate resources and expertise to tackle the public health crisis.

Despite these challenges, Manchester researchers have remained at the forefront of research during the COVID-19 pandemic. Their efforts span from the set-up of novel trials to investigate ways to treat COVID patients through the RECOVERY trial, to the reallocation of clinical personnel and reorganisation of research activities to enable research to continue in a safe and effective manner.

An Emerging Research Theme

In the early phase of the pandemic, researchers and clinicians were presented with a unique question: What was the impact of COVID-19 on patients with cancer? With so many unknowns and rapidly evolving information, our scientists stepped up to the challenge. They explored a variety of basic translational and clinical research questions to answer key questions of how COVID-19 affects patients with cancer, including:

- Does the COVID-19 virus increase side effects from cancer treatment?
- How does the virus interact with cancer cells to affect cancer cell biology?
- How are clinical trials affected by the COVID-19 pandemic?
- Can we leverage our research expertise to aid in building testing capacity?
- How does the virus impact persons with other health conditions as well as cancer?
- Does COVID-19 have unique effects on cancer patients from different populations within Greater Manchester?

Global Challenges, Manchester Solutions

In adapting to this new landscape, Manchester scientists have leveraged their skills and expertise to find solutions to the many challenges we face.

Through programmes like the COVID-RT Lung project led by The Christie and supported by the NIHR Manchester BRC, researchers aim to assess the impact of the pandemic on radiotherapy delivery and assess the clinical evidence of reduced fractionation in radiotherapy treatment.

From a clinical research perspective, clinical studies paused their recruitment and much activity during the first national lockdown in spring 2020 leading to a large drop in new trials and new patients brought onto those trials. However, a quick recovery in summer 2020 and continued activity following has led to a substantial recovery in clinical research activities at The Christie and also to the development of more life-saving research.

Maintaining laboratory operations

Laboratories were among the buildings that closed during late March 2020. This resulted in researchers working from home and transitioning to creating virtual connections and non-labbased research activities. This led to many virtual workshops and seminars, bringing international speakers into the homes of research students and helping to build community engagement at a challenging time.

Laboratory activities recommenced in early summer 2020 and our laboratories have since maintained research activities safely throughout the second and third national lockdown. While still operating at reduced capacity for the safety of staff and researchers, the next year will see an increase in activities and a return to pre-pandemic capacity as soon as is feasible.

The pandemic has been a large hindrance for our activities. Like the Paterson Building fire in 2017, it has served as another event that has interrupted, disrupted and paused our life saving research. But this pause is only temporary and the recovery and recommencement of activities is firmly on its way.

Please send the hyperlink for the Cancer and Covid booklet (

The Christie

remained open at



Industry Engagement and Commercialisation

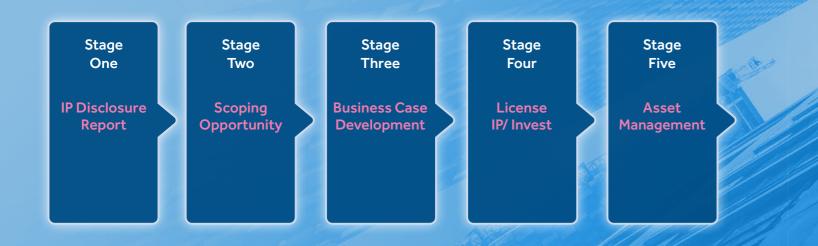
Our ambition is to accelerate the delivery of research from the bench to the bedside. One way to achieve this is by working together with industry to develop and commercialise novel discoveries or to engage with existing companies. This work will ensure our life saving research reaches patients as quickly as possible.

The MCRC is ideally placed between partners to leverage access to expertise from the <u>Business</u> <u>Engagement</u> team at The University of Manchester, the <u>Innovation Factory</u> for business development, and CRUK's Regional Translation Lead to ensure our ground-breaking scientific advancements leave the lab and have real impact to patients.

The COVID-19 pandemic has resulted in a more challenging and competitive research landscape. While our lifechanging and world-leading science will continue, it has never been more important to forge new collaborations and partnerships.

Whether through sponsorship of clinical trials, collaborating to develop intellectual property, accelerating production, knowledge exchange, or developing spin-out organisations, business engagement is critical for the continued development of research activities. An example organisation that demonstrates the power of continued partnerships is iMATCH, a consortium of 12 academic and industrial organisations that has helped deliver new advanced therapies to patients.

Alongside engagement, it is also vital to develop grassroots businesses. Focusing on commercialisation, 2020 was notable with having opportunities for researchers to develop their own spin outs. The MCRC was one of several partner organisations as part of the Alderley Park Oncology Development Programme, aiming to help set-up new start-up businesses. In addition, as shown by spin-outs like ManTra DX, the first step to commercialising research is nurturing and supporting a great idea.





iMATCH is a 12-partner consortium consisting of clinical, academic and commercial partners. It was established in 2018 with a £6.8M grant from Innovate UK to scale up activity across a broad range of clinical indications for cell and gene therapies including adult and paediatric conditions in the cancer and non-cancer setting.

Originally scheduled to finish in March 2021, iMATCH has since secured additional costed extension of deliverables and £1.75m for 'runway' projects.

This increased funding recognises the significant impact of the programme on advanced therapy medicinal products (ATMPs) within Manchester. Since the start of the programme, there has been a four-fold increase in the number of trial patients treated with ATMPs (excluding current COVID-19 based trials) and over 80 patients treated with commercial CAR-T products.

During the past year, Innovate UK facilitated the redirection of many iMATCH activities to combat the pandemic. One such concept was the trial COSMIC-19: Continuous Signs Monitoring In COVID-19 patients, which used technology to identify inpatients who may need escalation of their care. Now the team is looking to repurpose learnings from this trial to identify patients who may be at increased risk of developing significant toxicity from CAR-T therapy.

Alderley Park Oncology Development Programme

The Alderley Park Oncology Development Programme is funded by both Cancer Research UK and Innovate UK and supported by a unique collaboration between AstraZeneca, Johnson & Johnson Innovation, GlaxoSmithKline, Roche, The Christie NHS Foundation Trust, the MCRC and Medicines Discovery Catapult representing global big Pharma and research institutions.

ManTRa DX will be a diagnostics development company originating from Department of Translational Radiobiology, led by Professor Catharine West and based within the Manchester Cancer Research Centre (MCRC) part of The University of Manchester. ManTRa DX will be led by three co-founders: Catharine West, Joely Irlam and Darren Roberts.

ManTRa DX will deliver a major advance in personalised cancer medicine, focused on tumour hypoxia. Solid tumours have different amounts of oxygen and low levels (hypoxia) are associated with resistance to treatment and a poor prognosis. There is currently no way to measure the level of hypoxia in tumours in routine clinical practice.



From an initial pool of applications, 30 projects were selected for a predevelopment workshop with eight projects being selected to proceed to a development phase. Two projects, led by Professor Caroline Springer, and Professor Richard Marais from the CRUK Manchester Institute, have been selected to proceed to this stage, with further development taking place during the summer of 2021, before the final six projects are selected.

ManTRa DX

ManTRa DX provides tumour-sitespecific gene expression signatures to assess hypoxia. Our initial offering will be a pan-cancer NGS panel (ManTRa DX test -bladder, sarcoma, head and neck and prostate) delivered as a laboratory derived test (LDT) from a regulated laboratory. While specific genetic alterations provide a route to personalisation, tumour hypoxia provides a global picture of resistance. Around a half of solid tumours will be hypoxic, which reduces the efficacy of surgery, radiotherapy and many chemotherapeutic agents. Conversely, there is likely to be an enriched population with low tumour hypoxia with increased efficacy. ManTRa DX will focus on hypoxia suppression of immune and DNA damage responses because developing inhibitors of these processes are fast-growing markets.

News



Manchester Researchers develop new European partnerships to accelerate cancer research

In March 2020, an investment of £4m across three separate Cancer Research UK Accelerator Awards aimed to develop new research projects with partners across the UK and Europe. The UpSMART Accelerator is being led by Prof. Caroline Dive, while Prof. Tim Illidge will collaborate on testing immunotherapy-radiotherapy combinations, and Omer Aziz will collaborate on a project to create a tissue bank to collect data of Pseudomyxoma peritonei, a very rare type of cancer.

Alongside these new accelerator awards, the CRUK Lung Cancer Centre of Excellence, in partnership with UCL, has also been renewed for a further five years.

READ MORE

First ever patient in the world to be entirely treated for cervical cancer using MR-Linac at The Christie

As part of the MOMENTUM trial, which is a worldwide radiotherapy trial using the MR-linac, this will be the first time a full course of this type of radiotherapy is being used to treat cervical cancer.

The trial aims to target a wide range of cancers to find out which cancers react best to the treatment before it is hopefully rolled out across the globe. The trial is being overseen by Dr Cynthia Eccles and the MR-linac team at The Christie and supported by the NIHR Manchester Biomedical Research Centre.

MAHSC extended for a further five years

In April 2020, Manchester Academic Health Science Centre (MAHSC), part of Health Innovation Manchester, had its world leading health research partnership extended by five years.

Major investment in new paediatric cancer research

The combination of two grants from Friends of Rosie to investigate the use of proton beam therapy to treat sarcomas in children, and prevent facial disfigurement with head and neck cancers, along with a Stand Up to Cancer grant help to fund novel research in paediatric cancers across Manchester. First proton beam therapy clinical trial in the UK taking place at The Christie The TORPEdO trial is co-led by The Christie and ICR and aims to determine whether the use of proton beam therapy reduces long-term side effects and improves quality of life for patients treated with radiotherapy for throat cancer.



INTERNATIONAL ALLIANCE FOR CANCER EARLY DETECTION

Funding boost to develop new initiatives in Early Detection science

Since its inception in October 2019, ACED Manchester has now been awarded almost a further £1m to further accelerate our programme in early detection research and build upon the original £3.2m for an initial three work packages.

Specific new areas of research that are now active include: nanoparticle analysis of blood to detect cancer sooner; identifying the risk factors from hereditary breast and ovarian cancers; setting up and delivering new trials to detect prostate cancer; and community engagement strategies to reach individuals at risk of cancers.

First of its kind CONCORDE trial begins recruitment across UK

The trial will use explore a number of new drugs alongside standard radiotherapy with the aim of improving survival in people with non-small cell lung cancer. The trial is co-led by Professor Corinne Faivre-Finn alongside colleagues at Newcastle University and The University of Leeds.

Shorter radiotherapy courses reducing risk of side effects

Research from The University of Manchester and The Institute of Cancer Research, London, funded by Cancer Research UK, found shorter radiotherapy courses reduce the risk of bladder cancer returning after comparison of radiotherapy schedules currently used to treat muscleinvasive bladder cancer. The results were subsequently published in The Lancet Oncology.



Alderley Park Oncology Development Programme launched

ALDERLEY PARK

ONCOLOGY

DEVELOPMENT

PROGRAMME

Launched in November 2020, the Programme aimed to provide researchers with opportunities to commercialise research and was funded by Cancer Research UK and Innovate UK and supported by a unique collaboration between AstraZeneca, Johnson & Johnson Innovation, Roche, the MCRC, The Christie and the Medicine's Discovery Catapult.

Selected Awards

Professor Fiona Blackhall has been awarded the Heine H Hansen award 2020 by the European Society for Medical Oncology (ESMO) and the International Association for the Study of Lung Cancer (IASLC) in recognition of her outstanding contribution to lung cancer research.

Alice Lallo from the Cancer Biomarker Centre and Dr Mark Williams from the Leukaemia Biology Group at the Cancer Research UK Manchester Institute were jointly awarded the Dexter Award for the Best Young Scientist of 2019. READ MORE

Wendy Trotter from the Cell Division group was awarded the *Dexter Award* for 2020. <u>READ MORE</u>

Dan White was awarded the **Best Poster Prize of 2020** by ECMC for his poster on the 'Development of liquid biopsy assays for translational research and clinical use'. Karoliina Tuomel, from Professor Dan Davies group at the Lydia Becker Institute of Inflammation and Immunity, won the *silver poster prize* for her work on radiotherapy research at STEM for Britain event in March 2020.

Dr Neil Ryan was awarded the

Faculty Academy Postgraduate Student of the year as well as receiving a Distinguished Achievement Medal from Dame Nancy Rothwell, recognising him as The University of Manchester Student of the Year 2020.

Dr Rachel Eyre was awarded the *Sir Anthony Driver Prize* for the Breast Cancer Now Researcher of the Year 2019.

Professor Vaskar Saha wins award for Outstanding benefit to society through research for 2020 for his efforts in Improving outcomes for children with leukaemia internationally. <u>READ MORE</u>

Professor Caroline Dive receives

Distinguished Service Award of 2020 by the International Association for the Study of Lung Cancer (IASLC). In addition, Caroline was also awarded the **Johann Anton Merck award** recognising her outstanding research in the field of oncology. **READ MORE**

Professor Gareth Evans was appointed as a fellow of the Learned Society of Wales. READ MORE

Professor Emma Crosbie was awarded an *NIHR Advanced Fellowship* to study urine HPV testing for cervical screening.

Dr Heather Williams, consultant Medical Physicist at The Christie NHS FT. was awarded an *MBE* in the latest round of New Year's Honours by HM the Queen.

Dr Lana Lei from the Cancer Prevention and Early Detection group was awarded an *outstanding research award at NCRI 2020*.

Professor Marcel van Herk received an Honorary Fellowship of the Royal College of Radiologists, in recognition of his exceptional contribution to radiotherapy physics.

Professor Peter Hoskin has been awarded NIHR Senior Investigator status. The highly prestigious award reflects his standing in the national and international research community.

Dr Angélica Santiago-Gómez was

awarded the **Best Selected Oral Presentation** at the British Association for Cancer Research (BACR) Special Conference on Breast Cancer, Newcastle 2019 for her presentation titled 'NOTCH signalling regulates bone metastatic stem cell dormancy in ER+ breast cancer.'



Spotlighted Publications

In the period from 1 January 2020 to 31 March 2021, Manchester researchers published over 950 publications related to cancer research. This year, we're spotlighting publications from two areas: gynaecological cancer and prostate cancer.

A focus on gynaecological cancers

Professor Stephen Taylor

A living biobank of ovarian cancer ex vivo models reveal profound mitotic heterogeneity

Louisa Nelson, Anthony Tighe, Anya Golder, Samantha Littler, Bjorn Bakker, Daniela Moralli, Syed Murtuza Baker, Ian J. Donaldson, Diana C. J. Spierings, René Wardenaar, Bethanie Neale, George J. Burghel, Brett Winter-Roach, Richard Edmondson, Andrew R. Clamp, Gordon C. Jayson, Sudha Desai, Catherine M. Green, Andy Hayes, Floris Foijer, Robert D. Morgan & Stephen S. Taylor.

Nature Communications, 11, 822, (2020), doi: 10.1038/s41467-020-14551-2

A multidisciplinary team led by Professor Stephen Taylor created a "Living Biobank" for ovarian cancer studies with clinical input and tissues generated within the Christie and Central Manchester Foundation NHS Trusts. The work used RNA sequencing and single-cell genome sequencing to predict drug sensitivity in ovarian cancer cells growing outside the patient's bodies in short term cultures. The approach has the potential to generate personalized "avatars" for

ovarian cancer patients in which their tissue samples can be used to guide personalised therapy and clinical decision making.



Neil A. J. Ryan, Raymond McMahon, Simon Tobi, Tristan Snowsill, Shona Esquibel, Andrew J. Wallace, Sancha Bunstone, Naomi Bowers, Ioana E. Mosneag, Sarah J. Kitson,Helena O'Flynn, Neal C. Ramchander, Vanitha N. Sivalingam , Ian M. Frayling, James Bolton, Rhona J. McVey, D. Gareth Evans, Emma J. Crosbie.

PLOS Medicine 17(9): e1003263. doi: 10.1371/journal.pmed.1003263

Professor Emma Crosbie and colleagues completed studies in ovarian and endometrial cancers associated with Lynch syndrome; a syndrome of defective DNA mismatch repair. They reported that 3% of unselected endometrial cancers, which are very common in the developed world, have an association with Lynch Syndrome. Ovarian cancers were also found to have mismatch repair defects. The team suggests that using an

immunohistochemistry test for mismatch repair proteins, they can place screened women on defined surveillance programmes for other Lynch cancers, such as colorectal cancer. The test for Lynch endometrial cancers has been adopted by NICE as a new standard of care for the NHS.

The International **Pan-Prostate Cancer Group**

Pan-cancer analysis of whole genomes

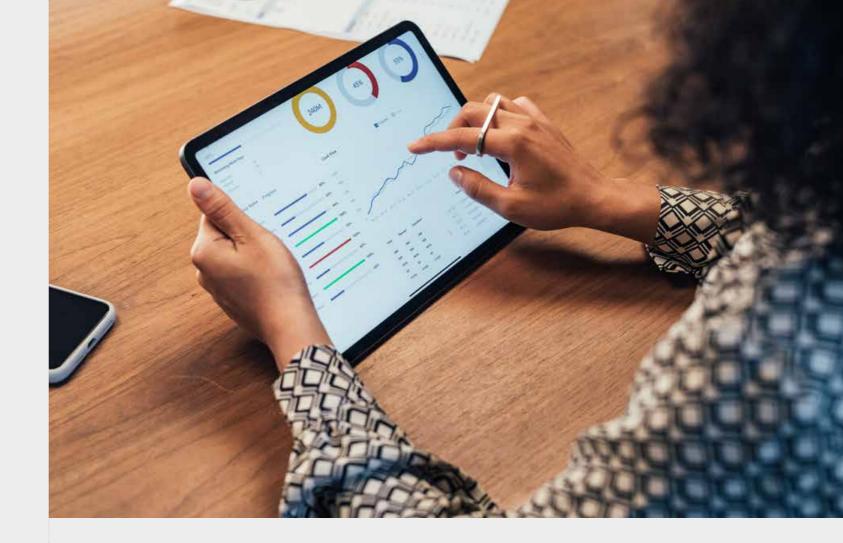
The ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium. Pancancer analysis of whole genomes.

Nature 578, 82-93 (2020). doi: 10.1038/s41586-020-1969-6

Prostate cancer evolution from multilineage primary to single lineage metastases with implications for liquid biopsy

Woodcock, D.J., Riabchenko, E., Taavitsainen, S. et al. Prostate cancer evolution from multilineage primary to single lineage metastases with implications for liquid biopsy.

Nature Communications 11, 5070 (2020). doi: 10.1038/s41467-020-18843-5



Divergent mutational processes distinguish hypoxic and normoxic tumours



of the tumour microenvironment (e.g. hypoxia) in cancer evolution and progression.1

In collaboration with colleagues at Tampere University (Finland), Professor Wedge re-constructed primary and secondary tumour genomic profiles in ten prostate cancer patients with fatal disease in conjunction with their histopathology and tumour DNA extracted from blood and cerebrospinal fluid. They observed that tumour cell selection, frequently acting at the genetic level, enables cells from a

¹ Nature **578**, 82–93 (2020). <u>doi: 10.1038/s41586-020-1969-6</u> ² Nature Communications **11**, 5070 (2020). doi: 10.1038/s41467-020-18843-5 ³ Nature Communications **11**, 737 (2020). doi: 10.1038/s41467-019-14052-x

Bhandari, V., Li, C.H., Bristow,

R.G. et al. Divergent mutational processes distinguish hypoxic and normoxic tumours.

Nature Communications 11, 737 (2020). doi: 10.1038/s41467-019-14052-x

Professors David Wedge and Robert Bristow lead members of the international Pan-Prostate Cancer Group (PPCG) and Pan-Cancer Analysis of Whole Genomes Consortium (PCAWG-ICGC), published important work in cancer genomics and the role

single lineage to escape the prostate and colonize distant sites with further re-emergence of heterogeneity in the metastases.²

Professor Bristow, with colleagues from UCLA (California, USA) observed that elevated hypoxia associates with increased mutational load across many cancer types. Driver mutations in TP53, MYC and PTEN were enriched in hypoxic tumours and interacted with hypoxia to direct distinct tumour evolutionary trajectories.³ These papers set the stage for new treatments that target both the genomics and microenvironments of cancer cells to improve outcomes for our patients.

MCRC Events 2020-2021

All events organised by the MCRC Strategic Operations Team between January 2020 and March 2021

Lectures and Seminars

Professor Sean Lawlor MCRC Director's lecture

23/04/2020 "Overcoming barriers to

glioblastoma therapy"

Managing Director, Harvey Cushing Neuro-oncology Laboratory Assistant Professor, Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School

Professor Mark Rubin

MCRC Director's lecture 07/05/2020

"Towards Understanding Lineage Plasticity Prostate Cancer Resistance" Director of the Department for BioMedical Research (DBMR), University of Bern, Switzerland

Professor Eric Deutsch

MCRC Director's Lecture 25/06/2020

"The importance of the myeloid component into tumour and normal tissue response to radiotherapy" Professor of Radiotherapy, Institut

Gustave Roussy

Dr Lara Barazzuol

MCRC Seminar 02/07/2020

"Mechanisms of radiotherapy-induced neurocognitive dysfunction" Principal Investigator, University Medical Center Groningen (UMCG)

Dr Claire Vanpouille-Box

CRUK RadNet Manchester Seminar 15/10/2020

"Targeting the immune-metabolic enzyme FASN in irradiated glioblastoma" Assistant Professor. Weill Cornell

Medicine

Dr Chad Brenner 29/10/2020

CRUK RadNet Manchester Seminar "Leveraging molecular adaption to reprogram the immune composition of head and neck cancers."

Assistant Professor, Department of Otolaryngology-Head and Neck Surgery, University of Michigan

Professor Bart Cornelissen MCRC Seminar 12/11/2020

"Nuclear medicine and DNA damage repair" Department of Oncology, University of Oxford

Dr Karl Butterworth

CRUK RadNet Manchester Seminar 30/11/2020

"Optimising spatio-temporal dose

delivery parameters in biologically optimised radiotherapy" Senior Lecturer in Translational

Radiation Biology at the Patrick G. Johnston Centre for Cancer Research, Queen's University Belfast

Dr Phedias Diamandis

MCRC lecture 16/12/2020 "Topographic mapping and targeting of the niche-specific proteomes of human glioblastoma" Neuropathologist at the University Health Network

Scientist at the Princess Margaret Cancer Center, Toronto

Professor Nicola Valeri MCRC Director's lecture

23/02/2021

"Next Generation Biopsies in **Gastrointestinal Cancers**"

The Douglas and Katherine Longden Chair in Oncology, Imperial College London, UK

Professor Sharon Plon

MCRC Training and Education Event 16/03/2021

"Tales of a Physician-Scientist Career: from single genes to exomes on a cell phone" Director of the Medical Scientist Training Program (MD/PhD Program) at Baylor College of Medicine, Texas, USA

More than speakers

Over of research



60 hours and education content

MCRC-Affiliated Workshops

World Cancer Day

04/02/2020 Raising awareness of cancer and encourage its treatment, early detection and prevention through engaging with communities across Manchester.

Launch of the CRUK RadNet **Doctoral Academy** CRUK RadNet Manchester Workshop 12/05/2020

Launch event for the CRUK RadNet Manchester Doctoral Academy and associated opportunities for radiographers.

Ex-vivo modelling workshop ACED Workshop

20/05/2020

Exploring the use of ex-vivo modelling in cancer early detection.

Radiotherapy-Immunotherapy Workshop CRUK RadNet Workshop

15/09/2020

Exploring how to use radiotherapy and immunotherapy combinations can help to overcome the immune suppressive tumour microenvironment.

Health Informatics Workshop

ACED Workshop 13/10/2020

Using routine healthcare data for research on cancer early detection.

MCRC Cancer Trial Science and Methodology Meeting MCRC Workshop 20/10/2020

Discussing the latest clinical trial methodology and science to develop impactful clinical studies.

MBC How to Predict and Prevent Breast Cancer Now?

Manchester Breast Centre Event 23/10/2020

Public engagement session to understand how to predict and prevent breast cancer.

PhD Welcome Event

MCRC Training and Education Event 26/10/2020

Welcoming our new PhD students to Manchester and introducing them to the MCRC and cancer research eco-system.

Meet the Cancer Researchers **MB-PhD Event**

MCRC Training and Education Event 18/11/2020

Meet the cancer researchers and understand more about the MB-PhD programme being offered at Manchester.

Paediatric Oncology Workshop MCRC Workshop 25/11/2020

A workshop to exploring paediatric oncology chaired by Dr Martin McCabe.

Health Inequalities in Early Detection ACED Workshop 01/12/2020

Addressing the guestion: How do we tackle health inequalities in early detection science?

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RAS Workshop MCRC Workshop

08/12/2020 -09/12/2021 A two-day workshop to highlight the latest developments in RAS research.

Meet the Cancer Researchers MB-PhD Event MCRC Training and Education Event

09/12/2020

Meet the cancer researchers and understand more about the MB-PhD programme being offered at Manchester.

CRUK Manchester Centre Scientific Showcase

CRUK Manchester Centre Workshop 27/01/2021

Showcasing the achievements of the CRUK Manchester Centre over the past five years.

Virtual World Cancer Day

04/02/2021

A look back and reflection on the challenges and opportunities the past year has presented.

Al for optimising radiotherapy outcomes workshop

CRUK RadNet Manchester Workshop 10/02/2021

A workshop exploring how AI and machine learning can be used to improve the efficiency of radiotherapy.

MB-PhD – Training the Next **Generation of International Clinician Scientists**

MCRC Training and Education Event 16/03/2021

An event to raise awareness of the MB-PhD programmes available in Manchester funded by Cancer Research UK and The Kennedy Trust.

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Spotlight on the **Health Inequalities** in Early Detection ACED Workshop

2nd December 2020, 4pm – 6pm

This ACED-MCRC Workshop aimed to explore the issues of healthcare inequalities from a range of perspectives all connected to the central theme of cancer early detection.

Postgraduate researchers, academic scientists, and healthcare professionals who attended the workshop left being able to:

- Understand more about the complexities of health inequalities within early detection.
- Meet people who research and are interested in healthcare inequalities within cancer early detection.
- Think about and discuss how healthcare inequalities could be tackled to ensure early detection research is more inclusive in the future.

Speakers at the event included:

- Chair: Dr Suzanne Johnson, The University of Manchester
- Keynote speaker: Professor Nalin Thakkar, The University of Manchester
- Dr Christian Von Wagner, University College London
- Dr Kelly Fagan Robinson, University of Cambridge





INTERNATIONAL ALLIANCE FOR CANCER EARLY DETECTION

- Professor Robert Bristow, The University of Manchester
- Professor David Wedge, The University of Manchester
- Dr Jo Waller, Kings College London
- Dr Jessica Currier, **Oregon Health Science University** (OHSU)



Q&A

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Christine Mullen Executive Assistant to the MCRC Directors

Tell us about your role at the MCRC?

As Executive Assistant to the MCRC Directors, my role is to provide highquality personal and professional administrative support to the Director of Strategic Initiatives, Prof. Nic Jones, and the MCRC Director of Research Operations and Strategy, Dr Claire Trinder. I provide additional support to the MCRC Director, Prof. Rob Bristow whilst also functioning as a part of the wider MCRC Operations team.

I also give professional administrative oversight related to the Paterson Redevelopment Project. This includes coordinating relevant processes and procedures, governance and acting as a liaison for the partners and groups that will be cohabiting in the space and the OCRB.

What is your day-to-day work like?

No one day is the same. My role is extremely multifaceted, but in essence it is about proactively maximising my principles' time. I work to enable the team and individuals within the team to succeed, staying one step ahead and keeping myself and everyone else sane in the process. Easier said than done!

How does it feel being part of a cancer research organisation?

It feels great! A lot of the tasks you undertake as an EA are similar anywhere you work but working for the MCRC I get to see the big picture and understand my part in the team in the context of 'Team Science'. That's what makes all the more routine day to day pieces of the role really worth it.

I also enjoy working with a wide variety of colleagues and like the relationship building and learning that comes along with it. I feel very fortunate to work in partnership with three amazing organisations in CRUK, The Christie and University of Manchester.

Read the full interview on our website

Caroline Stone Executive Assistant to the MCRC Director

Can you tell us about your role and what you do at the MCRC?

My primary role is to provide professional executive administrative support to the MCRC Director, Prof. Rob Bristow. I also provide support to the Director of Strategic Initiatives Prof. Nic Jones and Director of Research Operations and Strategy, Dr Claire Trinder.

Working with the MCRC Operations Team, I also strive to ensure maximum office efficiency wherever possible and to provide support for projects on an ad hoc basis.

What is your day-to-day work like?

Working across all three partnerships, my work day is very varied. My work is predominantly diary management driven and I ensure that time is utilised in the best ways possible. It is necessary for me to be proactive as well as reactive in adapting to last minute changes. My role certainly keeps me on my toes!

How does it feel being part of a cancer research organisation?

Rewarding is how I would sum it up. I'm not a scientist and I am permanently in awe of what the researchers do but the way I see it is that my little pieces of input into helping organise Rob's life around his diary is my contribution into cancer research.

Read the full interview on our website



The MCRC Strategic Operations Team



Professor Robert Bristow Centre Director



Professor Nic Jones Director of Strategic Initiatives



Dr Claire Trinder Director of Research Operations and Strategy



Rachel Chown Education and Development Lead



Dr Georgina Binnie-Wright Postgraduate Programme Manager



Dr Sinéad Savage Strategic Research and Partnership Manager



Dr Joe Mowll-Clarke Communications Manager



Elizabeth Openshaw NCITA Education and Communication Manager



Sally Best MCRC Science Writer and Communications Assistant



Rebecca Elliott Senior Programme Manager



Dr Martin Bone ACED Programme Manager



Dr Ellena Badrick ACED Project Manager



Stephanie Ng ACED Project Coordinator



Christine Mullen EA to MCRC Directors



Caroline Stone EA to MCRC Director



Dr Amanda Rees Head of Research Operations, ECMC and ECMT

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