Newsletter

CANCER RESEARCH UK | MANCHESTER INSTITUTE

Summer 2018

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MANCHESTER 1824
The University of Manchester

Director's Introduction

April marked the one-year anniversary of the fire which caused serious damage to the Paterson Building.

We commemorated the occasion by gathering together for an event at Alderley Park where we have recently completed relocating the majority of the Institute.

It provided us with an opportunity to reflect on the enormous efforts involved in the recovery and relocation operation and a chance to hear about how much we have managed to achieve scientifically despite all of the upheaval and disruption. The event was incredibly uplifting and highlighted the determination and resilience of our staff.

I am delighted that we were joined on that day by a number of colleagues who have played pivotal roles in our recovery over the last year, especially from across The University of Manchester's Directorate of Estates and Facilities and also from various companies who have worked tirelessly to help project manage our move and test and install equipment. It has been a huge team effort, the success of which has been built on the foundations of excellent working relationships across a number of teams and organisations.

Looking to the future, we are enjoying having the Institute together again and making the most of our new location, developing new relationships and opportunities at Alderley Park while working hard to ensure that we retain our close links to the Christie NHS Foundation Trust and University colleagues. Plans were recently announced over the future of the Paterson Building, which is to be replaced by a state of the art cancer research centre representing the Manchester Cancer Research Centre partnership between the Christie, CRUK and The University of Manchester.

The new building will host scientists and clinicians, allowing us to build on the critical partnerships that are pivotal to discovery, translational and clinical cancer research. There is a great deal of work to do in order to progress the plans for the building. We want to incorporate ideas from across the Institute to feed into the vision for the new centre and to inform the design process so we shall be seeking your input in the coming weeks and months.

Earlier on this year, as we were in the middle of the final relocation efforts, we were visited at Alderley Park by Sir Harpal Kumar and Professor Sir Leszek Borysiewicz, Chief Executive and Chairman of Cancer Research UK respectively. They enjoyed a tour around our new base of operations at Alderley Park and provided an opportunity for our staff to hear directly about the continued support for the Institute from CRUK and their appreciation of everyone's efforts over the last year.

As you will know, Sir Harpal is moving on after many years of successfully leading CRUK and I would like to take this opportunity to wish him all the best for the future and thank him for his support for cancer research in Manchester during this time. I would also like to extend my congratulations to Michelle Mitchell on her appointment as the next Chief Executive of the charity and I am sure that all of us are looking forward to meeting and working with her as we progress our plans for developing cancer research in Manchester over the next few years.

Professor Richard Marais
Director, Cancer Research UK Manchester Institute

Tour of the CRUK MI facilities at Alderley Park; from L to R: Professor Sir Leszek Borysiewicz, Institute Deputy Director Professor Caroline Dive, Institute Director Professor Richard Marais, Sir Harpal Kumar

Cover Image: Institute Deputy Director Professor Caroline Dive proudly displays her CBE medal

Institute Director elected Fellow of the Royal Society

The Royal Society has granted its prestigious fellowship to Professor Richard Marais, Director of the Cancer Research UK Manchester Institute.

Professor Richard Marais has spent much of his research career focusing on cell signalling in melanoma, for which he has won numerous awards and accolades. Richard became Director of the CRUK Manchester Institute in February 2012 where he also continues to head his Molecular Oncology group. The world-class research carried out at the Institute drives and facilitates the development of translational and clinical research, leading to practice-changing developments for cancer patients. Fellowships are given to distinguished scientists by the Royal Society in recognition of "contributions to science, both in fundamental research resulting in greater understanding, and also in leading and directing scientific and technological progress in industry and research establishments."

After being elected Fellow of the Royal Society, Richard said "I am humbled to be invited to add my name to the same book as many of the greatest scientists the world has known. I am delighted to have been honoured in this way".

"This honour reflects his tremendous scientific contribution to cancer research over his career and is a truly deserved and wonderful achievement" said Professor Caroline Dive CBE, our Deputy Director.

On behalf of the whole Institute, the Editorial Team would like to offer its congratulations to Richard for becoming a Fellow of the Royal Society, a truly outstanding achievement.

Fundraising and Engagement activities - By Tim Hudson

Fundraising and Engagement activities

Corporate Champions Welcomed to the Manchester Institute Labs

Flybe and Cooperative Legal Services, two of CRUK's main corporate fundraising partners, enjoyed visits to the MCRC Building this winter to celebrate partnership milestones and learn more about the work their support funds.

Cooperative Legal Services, who offer their #AWillToTackleCancer service with 10% of proceeds going to Cancer Research UK, had the privilege of an informal meeting and Q&A with Claus Jørgensen to hear about the work of his group, before heading to the labs to meet Colin Hutton and Steve Bagley.

Claus outlined the challenges of pancreatic cancer research and how his work into the communication between cell types in pancreatic adenocarcinoma tumours is helping us to understand this cancer of unmet need better.

Colin took this discussion into the lab, allowing guests to view histology slides and demonstrating the Leica imaging software, whilst Steve talked about the exciting new CyTOF technology soon to be installed in the Institute.

The visit from Flybe's Charity Champions in the New Year was particularly special, as they celebrated reaching a £750,000 fundraising milestone through their partnership with CRUK. Professor Richard Marais took time out of his busy schedule to meet with the Champions, thank them for their support and to talk about his group's leading work in melanoma.

The visitors then met with Wolfgang Breitwieser to get to grips with a bioanalyser, and ended their tour with Franzi Baenke from Richard's Molecular Oncology group, who explained her own project and showed them the tissue culture room.

A special end to Flybe's visit was organised with the team at Café Vivo, who put together a scrumptious celebratory cake in honour of their £750,000 achievement.

Images left to right: Celebratory cake for Flybe, and Wolfgang impresses the Flybe's Charity Champions in the lab.

Images left to right: Unity Band in action in the lab, Systems Oncolgy together for World Cancer Day, and CEP unite for World Cancer Day

Research Community Unites for World Cancer Day

Manchester's research community came together at the beginning of February to mark World Cancer Day, raising vital funds to help progress Cancer Research UK's life-saving research.

Researchers proudly displayed their CRUK Unity Bands in the lead-up to February 4th, both in and out of the labs, with some great photos shared on social media and picked-up by central CRUK channels.

Director of the Manchester Cancer Research Centre, Professor Rob Bristow invited all of Manchester's cancer research community to a special Unity Social event, which saw scientists, clinicians and technicians, alongside operational and administrative staff, join together in the MCRC Building to celebrate their important work.

Addressing the research team, Professor Bristow praised the partnerships and collaborations between hospital trusts, academia and science, which help to accelerate progress in Manchester.

Across the country, CRUK researchers, volunteers and staff joined the World Cancer Day celebrations, raising over £22,500 through public cash collections, and further funds through the sale of Unity Bands in CRUK shops.

Science and Coffee

The Manchester Cancer Research Centre's Research Café series, hosted by Café Vivo in the MCRC Building, continue to attract engaging experts to share their work with the public.

Scientists, health professionals and members of the wider research community in Manchester have talked about their work, their role in Manchester's cancer research arena and their expectations and goals for the future.

Highlights from events earlier in the year included Dr Phil Crosbie, Consultant in Respiratory Medicine at Wythenshawe Hospital, who spoke to a packed audience about his work in the pioneering Manchester Lung Health Check Pilot, Dr Christine Schmidt, BBSRC David Phillips Fellow and Dean's Prize Early Career Researcher who spoke about her investigations into the role of ubiquitin in cancer, and Charlotte Finchett, Health Promotion Advisor at the Christie who gave a thought-provoking talk around stopping smoking and improving outcomes.

Further talks saw Olivia Joseph and Katharine Cresswell from the Biomedical Research Centre discussing how patients can help improve cancer research, and Steve Jones, Health Professional Engagement Facilitator with Cancer Research UK, explained how he works with local GPs to improve early cancer diagnosis.

If you have any ideas for future Research Café talks, or would like to discuss your own research over a coffee with patients, staff and fellow scientists, please contact Science Communications Officer for the MCRC, Katy Holliday.

Clare Finchett's Research Café talk on stopping smoking

Sci-Art Collaboration with MMU

Researchers from the CRUK Manchester Centre collaborated with an art student at Manchester Metropolitan University to create a piece of 'sci-art' for a public exhibition fundraiser.

Alice Thickett stands by her cancer-inspired artwork for Sci-Art exhibition

The artist, Alice Thickett, currently studying a Masters in Visual Culture, approached Manchester Centre researchers with a view to creating a cancer-themed piece for her Sci-Art module.

Following a visit to the labs in the MCRC Building, where Alice chatted with Steve Bagley and Steve Lyons and looked at some cancer cells with Patricia Muller, Diana Drehmer and Heather Woodhouse, Alice decided to focus her ideas on the ambiguity of language surrounding cancer, the disease, and Cancer, the zodiac sign.

The final piece, exhibited at a public showing in February, juxtaposed a description of cancer cells from the CRUK website against an image of the Cancer constellation, next to a description of people born in the Cancer zodiac sign over an image of cancer cells from Diana Drehmer's project. The narrative next to the art explained her research and the collaboration with CRUK.

Through the collaboration, Alice linked up with one of CRUK's Local Fundraising Managers and arranged for the whole event, attended by around 200 people, to be a fundraiser for the charity.

Maggie's Manchester pilots CRUK Clinical Trials Patient Information Service

A new portable Clinical Trials Information Station has been made available for patients visiting the Maggie's Centre, behind the MCRC Building, as part of a pilot being run by CRUK's Health Campaigns and Marketing team.

The station is a resource on clinical trials, designed for patients in hospitals. It's a portable tablet that patients can use to access information from Cancer Research UK's webpages on clinical trials, along with the Clinical Trials Database, which lists over 2400 clinical trials by name, location and tumour type. The information has been optimised for ease of navigation and includes interactive content and video.

CRUK are partnering with Macmillan and Maggie's to pilot the station in their centres – quiet, relaxed spaces where patients go to seek out information and support.

Emily Whiteside from CRUK's Health Campaigns and Marketing team said: "With the portable tablet, patients will be able to browse in their seats, at their leisure with an engaging product – a different approach to leaflets in hospital waiting rooms. "CRUK's expertise in clinical trials has created a product which complements the information offerings available in Maggie's and Macmillan Centres."

Research shows that 9 in 10 people would be willing to take part in clinical research if they were diagnosed with a medical disease or condition. But several barriers mean that this is not always reflected in trial recruitment numbers.

Health professionals face time constraints in their interactions with patients and Clinical Nurse Specialists (CNS) often feel that they do not have the time or the expert knowledge to discuss research opportunities. Only 29% of patients are asked whether they would like to participate in cancer research, yet only 21% said that they would feel confident asking their doctor about research opportunities.

Misconceptions around clinical trials can also deter patients from participating in research. Patients may believe that clinical trials are only suitable for those with no other treatment options, that they are high risk, or that they can offer no immediate benefits to patients. Being approached at the wrong time can also limit uptake.

Giving patients access to clear, easy-to-understand information in a non-intrusive way can empower them to make informed decisions and have a positive impact on participation in research.

Our move to Alderley Park

The Cancer Research UK Manchester Institute is now based at Alderley Park until our new world-class cancer research facility on the site of the Paterson Building is complete.

Richard opens the event

As we all settle into our new temporary home, on 26 April 2018 we chose to mark the one-year anniversary of the fire by reflecting on the devastating incident whilst focusing on our many successes that have continued despite the disruption, and looking forward to an exciting and positive future. With each research group, core facility and operations team illustrating their recent achievements, the event acknowledged how far we have come in the last 12 months, highlighting the incredible effort, resilience and team-work of our staff to have enabled such impressive development and progression.

That we have managed to successfully navigate simultaneously the enormous logistical challenges of emptying the Paterson Building, recovering critical items, relocating staff to interim laboratories, and then moving the entire Institute to our new temporary site at Alderley Park, and be up and running within 12 months, is a testament to the grit and determination of our staff. Throughout the process of our recovery, transition and relocation we have relied upon the enormous help and support of not only staff at CRUK MI but also from the Division of Cancer Sciences and the wider University as well as several external orgnaisations and AstraZeneca at Alderley Park. We are extremely grateful to all.

Establishing core facilities at Alderley Park

One year on from the fire and setting up the Institute's core facilities at Alderley Park is nearly complete. Immediately after the fire, plans were put in place for the storage, delivery, installation and calibration of our equipment so that they would be fully operational once relocated at our temporary site.

Move statistics

Storage & transport

16,000 ft²
Warehouse Space

600 rolls bubble wrap

2,000 foam sheets

1,440 rolls vinyl tape

Storage & transport. This infogram highlights the effort in emptying the Paterson Building of instruments and furniture and transporting it to temporary storage before installing it at Alderley Park.

Laboratory equipment

3,926
crates packed & unpacked

7,109 items removed

3,228 items installed

Laboratory equipment. This infogram describes how many items were removed from the Paterson Building and installed in our temporary home at Alderley Park.

The heartfelt anniversary culminated in Manchester Cancer Research Centre Director Rob Bristow presenting our Director Richard Marais with an award to recognise his outstanding leadership over the last year.

Richard receives outstanding leadership prize

Biological Resources Unit

The Unit have settled in well now at Alderley Park, being one of the earlier groups to move. At the end of January 2018, work at the interim location at the Stopford facility ceased, allowing the whole team to move over to Alderley Park. There are 750 cages up and running and the Unit is now fully operational. Our new VisualSonics ultrasound imaging machine and the Xstrahl X-ray irradiator have arrived and it is pleasing to get both operational since they are in great demand and their arrival has been much anticipated by several of the research groups.

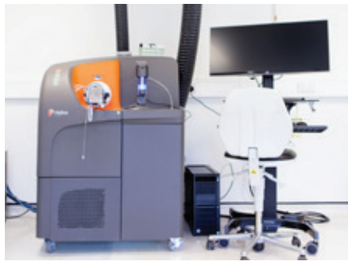
Xstrahl X-ray instrument

Histology

The Histology lab has now been relocated and remains extremely busy with all services experiencing high demand. Over the next month the focus will be on recruitment with one post already being filled and another two posts out to advert. These posts will provide much needed support for our extraction service, routine histology and immunohistochemistry/ in situ hybridisation services. In addition we will be evaluating the Roche Avenio Millisect System, which is an automated, high-performance tissue dissection system enabling precise and consistent recovery of formalin-fixed paraffin-embedded tissue from specific areas for downstream analysis.

Imaging and Cytometry

The majority of the equipment is up and running; confocal and super resolution microscopy is at 80%, flow cytometry is operational, histology imaging is running and so is high



Fluidigm Helios CyTOF

content screening. A new Xstrahl in vitro x-ray irradiator has been installed to replace the system that was in the basement of the Paterson Building and a new Fluidigm Helios CyTOF mass cytometer is currently being installed. It is envisaged that over the next six months there will be a series of training courses and applications talks given by the facility team.

Logistics

The Logistics department offer an equivalent service to that provided at the Paterson Building. The team will continue to receipt and distribute goods and dry ice throughout the site. The onsite store at Alderley Park offers a full range of plastic catalogue, whilst the freezer stores, media and enzymes will be transported from the MCRC Building on a daily basis. The team also support the research groups and core facilities with a twice-daily sample transfer service from the MCRC Building to AP, with a return service daily from AP to the MCRC Building.

Biological Mass Spectrometry

The Mass Spectrometry prep lab is now complete and fully operational. The pre-fire data pipeline has been rebuilt successfully by the Computational Biology Support group thanks to Sam Taylor. After a concerted effort and persistent process, the main lab has suitable environmental conditions to fully install and test the equipment. We have extensively repaired and installed the Orbitrap Fusion and are presently in the final wave of testing to ensure the data quality is equivalent to its pre-fire condition. If the performance of the instrument matches that of 2017, we will have a major component of our service capability back in a few weeks' time.

Computational Biology Support

Great effort has been made to bring our services back to the pre-fire situation and consequently all genomics and proteomics data analysis pipelines are operational. Already the facility is looking into expanding the scope of our service to cover new applications introduced by the Molecular Biology Core Facility, such as those generated by high-throughput single-cell technologies.

Scientific Computing

Reconstructing the storage systems and the High Performance Compute (HPC) cluster gave SciCom the opportunity to update and improve the systems. The rebuilt HPC cluster has been operational since January. All other SciCom computing, storage and virtualisation services for mass spectrometry and the Advanced Imaging core facility were put into production in the middle of February. In the meantime, all our clinical and scientific analysis pipelines have been migrated to the new system (Phoenix) and we are resuming our software and pipeline development.

HPC facility

The Phoenix

Systems Oncology group success

Claus Jørgensen joined the Institute in 2014 as a Junior Group Leader when he established the Systems Oncology group to understand the complex interactions between malignant and normal cells in pancreatic cancer.

Since then his group has gone from strength to strength and culminated last year in Claus' promotion to Senior Group Leader following a highly successful Senior Appointments process. He achieved further success when he was awarded a highly competitive European Research Council Consolidator Award.

These prestigious grants allow the best researchers to ask the most daring and groundbreaking questions in science. Claus, who is considered a leader in the field of tumour-stroma signalling - delineating the reciprocal signalling between cancer cells and the microenvironment - will use the €2million funding from ERC to ask a highly relevant question in tumour biology and specifically in pancreatic cancer biology. He aims to understand the co-evolution between tumours and the stroma and how these two compartments interact and modulate each other's phenotypes and ultimately lead to the selection of the aggressive tumour cells observed in the clinic.

Pancreatic Ductal Adenocarcinoma (PDA) accounts for approximately 95% of all Pancreatic Cancer, and has a dismal prognosis with an average 5-year survival rate below 5%. This is due to the aggressive nature of the cancer, a lack of effective therapy and late diagnosis. While the most frequently occurring genetic mutations have been identified, there are currently no targeted therapies available for PDA in the clinic. Moreover, PDA is characterised by a desmoplastic stroma, which supports tumour growth, metastasis and therapeutic resistance. Delineating the mechanisms whereby the tumour stromal promotes cancer progression may lead to identification of novel therapeutic targets.

Addressing the role of the desmoplastic stroma, a central goal of the Systems Oncology laboratory is to determine how tumour cells exchange information with host stromal cells to support tumour growth and resistance to therapies. Specifically, the group aims to understand how individual stromal cell populations regulate tumour cell response to therapy and to determine how best to combine therapies targeting the stromal cells with drugs currently used in the clinic. Altogether, these efforts aim to improve strategies for personalised therapies in pancreatic cancer.

The team is expanding and currently includes Postdoctoral Fellows Brian Lee, Giulia Veluscek, and Jingshu Xu, Scientific Officer Xiaohong Zhang, Graduate Students Christopher Below, Elizabeth Hogg, Colin Hutton and Amy McCarthy, as well as Clinical Fellow Konstantinos Georgiadis.

Another important success last year for Claus and his group was obtaining funding from CRUK as part of the PRECISION-Panc network, which aims to deliver personalised medicine in Pancreatic Ductal Adenocarcinoma.

Personalised therapy, the application of a therapy that is matched to specific characteristics of individual tumours, has benefitted cancer patients enormously, but is still not available to patients with PDA. In an effort to improve treatment options and patient selection in PDA, Claus and other researchers at the Institute and The University of Manchester are involved in establishing a national infrastructure where individual tumours are subjected to molecular profiling such that patients can be matched with selected treatments.

These clinical trials are underpinned by the development of biomarkers and pre-clinical research to further refine treatment strategies targeting specific dependencies. Understanding the role of the microenvironment in shaping the therapeutic response across selected patient populations is critical to define whether approaches targeting the tumour stroma should be delivered in a personalised manner, or whether a broader non-selected approach can be taken.

Claus and his team

Systems Oncology PhD student goes to MIT

By Amy McCarthy

Amy McCarthy

In November 2017 I was thrilled to have the opportunity to spend two weeks in the lab of Professor Douglas Lauffenburger, in the Biological Engineering department at the Massachusetts Institute of Technology.

Doug's lab has pioneered the use of regression-based modelling approaches to gain insight into biological systems, and my aim was to learn how I might be able to use modelling approaches within my own project, which looks at how different tumour sub-clones might interact with fibroblasts in their microenvironment. Therefore, armed with several RNAseq datasets I had generated here in Manchester, I worked on integrating datasets relating to both tumour cells and fibroblasts to generate a model for how ligands from different sub-clones might mediate the reprogramming of fibroblasts to different phenotypes. Doug's lab was a fantastic environment in which to do this work, with lots of expertise on hand and a truly collaborative atmosphere. I learned a great deal and would like to thank all the members of Doug's lab for their help and for welcoming me into the lab, and of course Doug for the opportunity. I'd also like to thank the EACR for supporting my trip financially, through an EACR travel fellowship award.

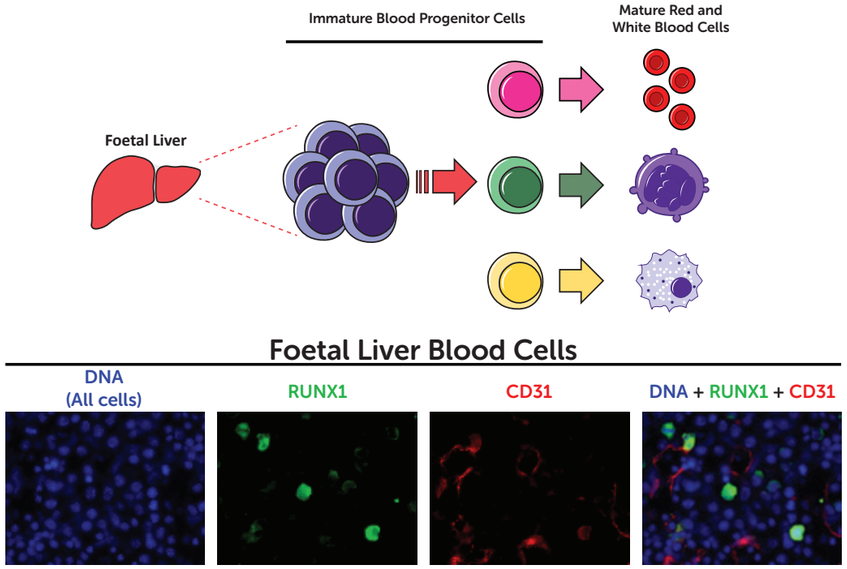
Featured Publications

More accurate method to study blood cell development

Researchers in the Stem Cell Biology group have developed a new, more accurate method to separate out the precursors of different blood cells during foetal liver haematopoiesis.

In order to identify the underlying causes of blood disorders that originate in the womb, such as infant leukaemia, scientists need to understand how immature progenitors differentiate into different types of blood cells in the foetal liver (the main site of blood cell production in the midgestation embryo). This permits the determination of how genetic mutations affect the production of each individual sub-class of cells, causing imbalances and, ultimately, the development of leukaemia.

Scientists at the Institute, including Dr Julia Draper and Professor Georges Lacaud, characterised the expression of two different genes in mouse foetal liver progenitor cells. They showed that these genes allow us to better define the generation of different types of blood cells and could therefore be used to track foetal blood cell development. They demonstrated the power of this new approach by studying the effect of deleting *Runx1*, a key blood development gene, and identifying the underlying gene networks responsible for the defects observed.



Studying blood cell production in the foetal liver

The foetal liver contains numerous distinct blood progenitor cells with the potential to produce different mature red and white blood cell populations (top). The identification and classification of these progenitor cells is aided by analysing the expression of blood development-associated genes, including RUNX1 and CD31 (bottom).

Blood test could help predict skin cancer's return

Scientists in the Molecular Oncology group have discovered that testing skin cancer patients' blood for tumour DNA could help predict the chances of an aggressive cancer returning.

Published in the *Annals of Oncology*, the findings could pave the way to identifying patients who are most at risk of their disease returning, and who might benefit from new immunotherapy treatments.

Led by researchers from the Institute and The Christie NHS Foundation Trust, the team studied blood samples taken after surgery from 161 patients with stage 2 and 3 melanoma. They then looked for faults in two genes that are linked to 70% of melanoma skin cancers – BRAF and NRAS.

After five years, 33% of patients who had a positive blood test for faults in either of the two genes were alive, compared to 65% of those who did not.

The results also revealed that skin cancer was much more likely to return within a year of surgery in patients who had faults in either of the two genes.

Potential approach to stop growth of lung cancer identified

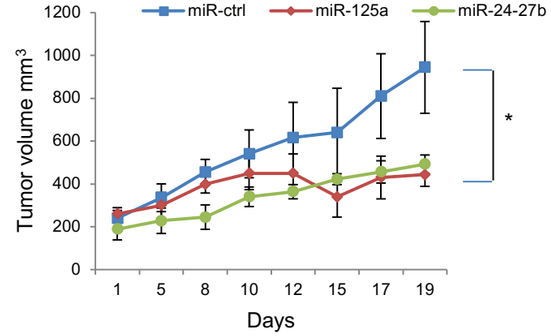
Institute lung cancer researchers have found a way to suppress tumour growth in non-small cell lung cancer (NSCLC).

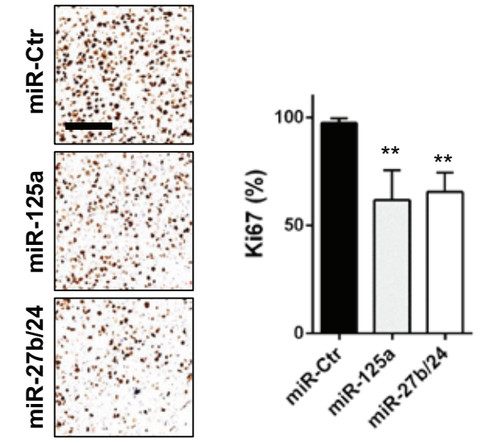
The Transcriptional Networks in Lung Cancer group, working with scientists from the Clinical and Experimental Pharmacology group, looked at microRNAs that are known to be regulated by a molecule called PDGF Receptor (PDGFR).

In patients with NSCLC, PDGF receptors mark out those with worse prognosis, but they are yet to be successfully targeted by drugs. New treatments for this disease are desperately needed, with fewer than 20% surviving more than five years.

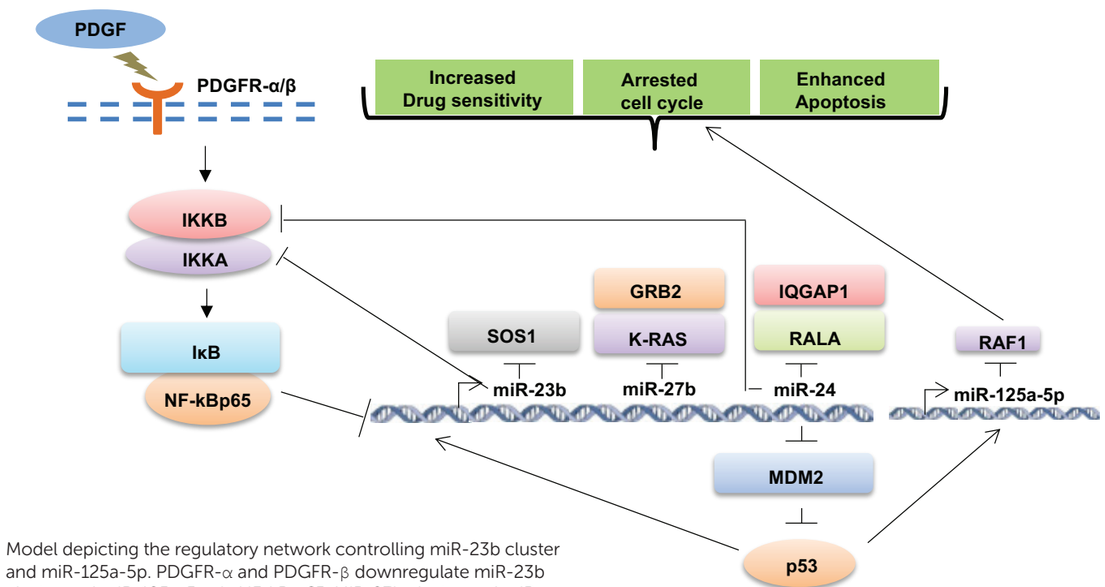
The team identified some miRNAs of interest - miR-23b cluster and miR-125a-5p – as modulated by PDGFRs. These microRNAs silence important oncogenes involved in the KRAS pathway. By analysing a large *in vivo* dataset, they found an inverse correlation between the miRNAs and target genes in lung cancer patients.

In addition, they used a CTC-derived xenograft (CDX) model to further test the potential of these microRNAs *in vivo*. Members of miR-23b cluster or miR-125a-5p significantly blocked the growth of this aggressive lung cancer model, suggesting that they could be potential therapeutic tools to halt lung tumorigenesis.





Top: Tumour volume of cohorts of CDX mice treated with a control miR (ctrl), miR-125a-5p or miR-27b/24. Bottom: Representative images of Ki67 expression in CDX tumors treated with control miR versus miR-125a-5p or miR-27b/24.



Model depicting the regulatory network controlling miR-23b cluster and miR-125a-5p. PDGFR-α and PDGFR-β downregulate miR-23b cluster and miR-125a-5p via NF-kB p65. MiR-23b cluster and miR-125a-5p are transcriptionally activated by p53 and silence several important oncogenes involved in the KRAS and NF-kB pathways.

New leukaemia target found

Scientists from the Institute's Leukaemia Biology group have shown how the transcription factor IRX3 contributes to a key aspect of acute leukaemia.

IRX3 is known to play a role in the growth of the embryonic nervous system, heart and limbs, but it is generally absent in healthy bone marrow in adults.

The group found that it is expressed in high levels in a third to a half of patients with various types of acute leukaemia.

Their experiments demonstrate that IRX3 blocks the development and maturation of blood cells, leading to the characteristic symptoms of acute leukaemia.

The researchers now aim to identify ways to target IRX3, and previously investigated FOXC1, in order to improve patient outcome.

Meet our new research teams

Translational Oncogenomics group

Rob Bristow and the Translational Oncogenomics group

Professor Rob Bristow has joined the Institute as a Senior Group Leader, alongside his roles as Director of the Manchester Cancer Research Centre and Chief Academic Officer at The Christie.

Before his move to Manchester last year, he was a Clinician-Scientist and Professor within the Departments of Radiation Oncology and Medical Biophysics at the University of Toronto and a Senior Scientist at the Princess Margaret Cancer Centre.

His primary research interests are in tumour hypoxia, DNA damage signalling and DNA repair in tumours, and the genomics of prostate cancer progression and cancer treatment response. He is particularly interested in novel clinical trials that intensify cancer therapy to prostate cancer patients whose tumours harbour aggressive genetic changes and hypoxic sub-regions.

Control of genome stability requires careful coordination between cell cycle checkpoint control and DNA repair mechanisms. Defects in the repair of DNA double-stranded breaks have been associated with acquiring genetic instability, particularly in genes responsible for homologous recombination such as BRCA1 and BRCA2. Defects in these genes lead to an increased risk of ovarian and breast cancer in women and prostate cancer in men. BRCA2-associated prostate cancers have a particularly poor outcome with survival of less than 50% at five years after local therapy. More recently, other DNA repair gene mutations or dysfunction have been linked to aggressive prostate cancer leading to the castrate resistance and metastatic phenotype.

Recent findings suggest that in untreated BRCA2-associated prostate cancers, pathways are already upregulated that herald resistance to hormone therapy and genetic instability. His group are now looking to address the mechanism by which BRCA2 mutations and dysfunction leads to genetic instability within primary prostate epithelium. They will also explore the additional mechanistic role of hypoxia in the acquisition of aggressive prostate cancer phenotypes on the background of BRCA1/BRCA2 genetic deficiency.

Joining the Translational Oncogenomics team are Senior Scientific Officer Steve Lyons, previously in Professor Nic Jones' group, PhD Student Ronnie Rodrigues Pereira, and Richard Rebello, a Postdoctoral Fellow who moved from Australia in February. Two further PhD Students will arrive in September.

Patricia Muller and the Tumour Suppressors group

Tumour Suppressors group

Patricia Muller is one of our new Institute Fellows at the Cancer Research UK Manchester Institute.

Patricia is a biologist who has studied the role of mutant p53 proteins in cancer. After a PhD in copper metabolism at the University of Utrecht, she started her postdoctoral career at the Cancer Research UK Beatson Institute in Glasgow in Karen Vousden's lab.

Following a personal Rubicon fellowship from the NWO (Netherlands Organisation for Scientific Research) to work on mutant p53 function in metastasis for three years, she continued her career with a Sir Henry Dale Fellowship from the Wellcome Trust/Royal Society in 2013 at the MRC Toxicology Unit in Leicester on the function of mutant p53 in chemoresistance, and received an early career award from the Biochemical Society in 2015.

Dr Muller is continuing her Sir Henry Dale Fellowship here and is now building her Tumour Suppressors group at the Institute.

Small cell lung cancer (SCLC) is dominated by mutations in the tumour suppressor gene *TP53*. These mutations result in the loss of p53 expression or expression of a mutated or truncated p53 protein. A mutated protein has lost most of its wild type functions, but can also exert new functions in promoting tumourigenesis, conferring chemoresistance and inducing invasion. Despite the important role of p53 as a tumour suppressor, p53 status is currently not used in the clinic for therapeutic decisions. Insufficient knowledge of mutant p53 gain-of-function as well as insufficient understanding of the differences between mutant p53 proteins could be a reason for this lack of clinical use.

The Tumour Suppressors group aims to characterise the molecular pathways underlying mutant p53 gain-of-function and to classify different mutant p53 proteins occurring in SCLC based on molecular function and patient characteristics.

Patricia is now joined by Postdoctoral Fellow Yannick von Grabowiecki, and Graduate Student Callum Hall.

Maximiliano Portal and the Cell Plasticity & Epigenetics group

Cell Plasticity & Epigeneitcs group

Maximiliano Portal is another of our new Institute Fellows to have joined the Cancer Research UK Manchester Institute last year.

Maxi joined the Institute to establish the Cell Plasticity & Epigenetics lab, focusing on unravelling the role that non-coding RNA molecules play in the genesis and propagation of non-genetic information through the acquisition of drug-tolerance in cancer relevant settings.

He is a biotechnology-trained molecular biologist and obtained his degree from the University of Quilmes, Buenos Aires, Argentina. Following his initial studies, he pursued his PhD at National University of Cordoba, Argentina where he worked unveiling the molecular basis underlying non-canonical signalling/metabolic pathways governed by the transcription factor c-Fos during tumorigenesis.

Immediately after his PhD, he joined the Institute of Genetics, Molecular and Cellular Biology (IGBMC) in Strasbourg, France where he focused his research into the biology of non-coding RNAs. During this period Maximiliano unveiled the crosstalk between miRNAs and the basal transcriptional machinery during cell division and further discovered a novel family of non-coding RNAs termed as natural double-stranded RNAs (ndsRNAs).

The widespread ramifications of this novel discovery led to two international patents and dedicated funding to develop a platform that enables the use of ndsRNAs as molecular diagnostic tools.

The Cell Plasticity & Epigenetics lab is envisioned as a multidisciplinary team that takes advantage of high-throughput sequencing and imaging technologies as well as more traditional molecular and cellular biology techniques to analyse the role of non-coding RNA molecules in the generation and propagation of epigenetically encoded molecular "memories".

Maxi is now joined by his Postdoctoral Fellow, Yelyzaveta Shlyahktina, who will be working on a project aiming to elucidate how tumorigenic cells escape therapeutic paradigms by diversifying its epigenetic makeup and thus generating alternative molecular landscapes without modifying their genetic background. Their ultimate goal is to unravel the network of molecular systems supporting cell plasticity and to shed light onto the core mechanisms underlying the inheritance of epigenetically encoded traits in cancer.

Meet the new Director of the Drug Discovery Unit

Caroline Springer

Professor Caroline Springer joined the Institute in October last year to become the new Director of our Drug Discovery Unit.

One of the leading experts in cancer therapeutics, Caroline took over from Dr Donald Ogilvie who retired in April last year after leading the DDU for eight years since its inception in 2009.

She completed her PhD in biological chemistry at University College London before moving to the Institute of Cancer Research (ICR) where in 1993 she became an independent Team Leader and established the Gene and Oncogene Targeting Team, with a multidisciplinary focus that combined medicinal chemists, biochemists, pharmacokinetics bioanalysts and molecular biologists.

Caroline was awarded tenure in 1994, the title of Reader in 1997 and in 2000, Professor of Biological Chemistry. She has co-authored over 120 primary research papers, 21 book chapters, edited a book on suicide gene therapy and is an inventor on 30 patents. Caroline was elected Fellow of the Royal Society of Chemistry in 1999 and Fellow of the Royal Society of Biology in 2010.

Caroline has been involved in all stages of the drug discovery process in a wide variety of novel therapeutic areas. Over the last 25 years she also ran the development of various cancer treatments, including antibody, oncolytic viruses for gene targeting, metastases inhibitors and cancer stem cell inhibitors. Her work has led to five clinical trials including antibody-directed and small molecule cancer therapies as well as nine preclinical candidate nominations and collaborations with pharmaceutical companies including AstraZeneca, Novartis and GSK.

Caroline initiated and led on the drug discovery for ADEPT, an antibody-directed enzyme prodrug therapy, that led to four colorectal cancer clinical trials with two different prodrugs and different antibody-enzyme conjugates and fusion proteins. She also developed gene-directed enzyme prodrug therapy, a suicide gene therapy designed for the treatment of a wide range of cancer types. With Institute Director Professor Richard Marais, Caroline has demonstrated efficacy in their GDEPT systems in a range of human tumour xenograft models that include head and neck, breast, and lung cancers, colorectal carcinoma, hepatoma, as well as mouse melanoma.

A key area of Caroline's research has been to discover panRAF inhibitors designed to treat naive and mutant BRAF or mutant RAS melanoma and other tumour types driven by these mutant oncogenes.

In collaboration with Richard, she has discovered and developed orally bioavailable, well-tolerated panRAF/SRC inhibitors that are effective in pre-clinical patient derived xenograft models at therapeutic doses. These agents were licensed to Basilea Pharmaceutica Ltd in 2015 and BAL3833 is currently undergoing clinical trials at The Christie and The Royal Marsden NHS Foundation Trusts with biomarker analysis performed by Deputy Director Professor Caroline Dive. Caroline Springer is also working with Richard investigating lysyl oxidase inhibitors to prevent and treat metastases in a range of tumour types. A series of LOX inhibitors are now in late lead optimisation.

As Director of the DDU, Caroline plans to strengthen the collaboration with CRUK Manchester Institute Group Leaders to translate their exciting biological work into new drug discovery programmes. She is increasing the integration of the DDU with the Clinical and Experimental Pharmacology group led by Caroline Dive such that every drug discovery project is underpinned by biomarkers of target engagement and predictive of response.

Caroline plans to expand the medicinal and computational chemistry capability of the DDU and bring significant Drug Metabolism and Pharmacokinetics (DMPK) Studies and in vivo capability within DDU. Our drug discovery will form the basis of integrated clinical development with the Christie NHS Foundation Trust.

Digital Experimental Cancer Medicine Team

by Siobhan Southam

Some of the digitalECMT team members

Patient Engagement and Digital Innovation in clinical trials

www.digitalecmt.org

Health technology is moving from general wellbeing, such as step counters, to clinical trials and the digital Experimental Cancer Medicine team is leading the way.

Established in 2016 as part of Professor Caroline Dive's Clinical and Experimental Pharmacology group, the digital Experimental Cancer Medicine Team now comprises 14 members of staff. We are doing things differently and our mission is to innovate and apply digital science to change decision-making in early clinical trials and the patient's role.

Patient voices in early clinical trials

In September 2017 we set up a *Patient Design Lab* in the Phase I Clinical Trial Unit at The Christie NHS Foundation Trust. We have some exciting news from the Patient Design Lab:

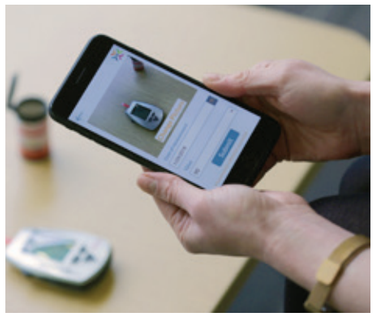
- The PROACT trial started at The Christie in September 2017. Patients report how they feel during an experimental (early phase) clinical trial, through video, audio, or text messages using PROACT (Patient Reported Outcomes About Clinical Tolerability).
- Together with patients we have started a 'hospital-in-the-home' approach to monitor kidney function. This means that patients could monitor their kidney function at home using a device and an app. The aim is that more patients could take part in early clinical trials in the future.

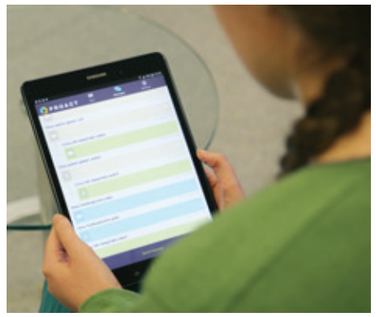
Going digital

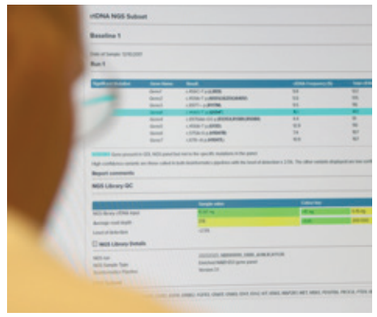
The digitalECMT developed the eTARGET digital tool to support the Manchester Molecular Tumour Board as part of the TARGET trial. This digital tool shows genetic results alongside clinical data for each patient in an easy to use visual display.

TARGET (Tumour chARacterisation to Guide Experimental Targeted therapy) is an innovative trial. It is investigating the molecular profile of tumours by genetic analysis of tumour tissue and circulating tumour DNA from blood samples to match patients to experimental (early phase) clinical trials.

Achieving patient engagement and digital innovation in early clinical trials needs partnership and expertise. The digitalECMT also delivers the leading iDecide research programme, a 5-year, £11.5M collaboration between four strategic partners in cancer research; the Manchester Centre for Cancer Biomarker Sciences, The University of Manchester, The Christie NHS Foundation Trust and AstraZeneca.







Education News

Meet the New Students

Charlotte Bell

Hi, I'm Charlotte and I'm originally from Stamford in Lincolnshire. I have recently completed an integrated Master's degree in Pharmacology at the University of Bath. During my degree I completed an industrial placement year at MedImmune, with a project focused on developing a novel mouse tumour model to investigate mechanisms underlying response to anti-PD-L1 immunotherapy. I'm therefore very excited to be further pursuing my interests in both cancer and immunology as part of the Cancer Inflammation and Immunity group led by Santiago Zelenay. My project is investigating the potential role of COX-2 and PGE2 signalling in enhancing tumour-promoting inflammation, immune evasion and cancer cell repopulation during cytotoxic therapy-induced tumour cell death. In my spare time I enjoy going to gigs and for walks in the countryside, so I definitely want to make the most of the music scene in Manchester and venture out into the Peak District! I'm looking forward to spending the next four years at CRUK MI.

Christopher Below

My name is Christopher Below and I've joined CRUK MI as a PhD student with Claus Jørgensen in the Systems Oncology group. Before starting my PhD, I completed my Bachelor in Biotechnology at the Brandenburg University of Technology (BTU) in Germany. During my Bachelors, I worked at Indiana University, USA and the Institute of Cancer Research in London where I gained a deep interest in the tumour microenvironment and its role in cancer progression and evolution. Here in Manchester, I will pursue this scientific interest and study the influence of the tumour's matrix in pancreatic cancer aggressiveness and intratumour cross-communication. Manchester is a great place for pursuing scientific endeavours but also to have a really good time as it offers lots of special places to be discovered. If you are up for a nice hike on the weekend, it's the best place to go.

Hasse Bossenbroek

My name is Hasse. I completed my undergraduate studies in Molecular Life Sciences and a Master's in Molecular Mechanisms of Disease in the Netherlands, but fell in love with the UK when I did an internship in Cambridge and decided that I wanted to come back here for a PhD. In January I joined the Epigenetics of Haematopoiesis group led by Kiran Batta, where I'm studying the epigenetic mechanisms at play in CMML, a rare type of leukaemia. So far working here has been great. I love living in Manchester – it's a very friendly city with much to offer. Also, being from the completely flat Netherlands, I find being so close to the Peak District very exciting. I'm hoping to spend a great deal of free time there. I've already spotted a couple of nice hikes and scrambles that I would love to try! Manchester also seems to be a good city for cycling, climbing and live music, so I'm sure I'll have a wonderful time here.

Chris Bromley

Hi, my name is Chris and I grew up on the Wirral near Liverpool. I am delighted to have joined the Cancer Inflammation and Immunity group led by Santiago Zelenay. I graduated in 2015 from the University of Sheffield with a degree in biomedical science. During my degree, I spent a year working at GlaxoSmithKline in Stevenage where I first realised my interest in immunology working with tonsil-derived B cells to understand their response to epigenetic agents. After my degree, I joined the graduate programme at AstraZeneca where I undertook three different job rotations. I firstly worked at Alderley Park in an in vivo capacity before moving to Cambridge where I worked in oncology target validation. Finally, I worked within early clinical development where I helped to manage externally sponsored research trials. I am now thoroughly excited to begin my PhD project combining my key interests of cancer and immunology. For my project I will use bioinformatic approaches to dissect tumour-promoting and tumour-inhibitory inflammation. Manchester is a fantastic place in which to study with so much exciting science going on in the region.

Francesco Camera

My name is Francesco and I am from Reggio Calabria in the deep south of Italy. For my bachelor's degree I studied Biology at the University of Messina and then I moved to Trieste for my masters in Functional Genomics. There I joined a research group focused on "antimicrobial peptides", which represent a promising alternative to antibiotics for infectious diseases. I next undertook a postgraduate internship at the Weatherall Institute of Molecular Medicine at the University of Oxford, where I worked on the identification and characterisation of cis-regulatory elements underlying cranial neural crest formation. This experience led to my interest in the molecular aspects of neoplastic disease in humans and so I joined the Leukaemia Biology group to study the characterisation of abnormal expression of specific genes in Acute Myeloid Leukaemia. I really like being part of the Institute; it's an excellent environment. I have been living in Manchester for almost a year now and I am really enjoying my time here where I can easily indulge my interest in music, cinema, theatre and comedy.

Alicia-Marie Conway

Hello I'm Alicia and I am originally from the West Midlands. I moved to Manchester in 2004 to undertake my medical degree at The University of Manchester. I chose to stay in Manchester for my postgraduate training and I am currently half way through my Medical Oncology specialist training at The Christie. Having previously undertaken an MRes in viral oncology as an undergraduate I am thrilled to be back in the lab as a clinical fellow in Caroline Dive's group. My PhD will evaluate liquid and tissue biomarkers in Cancers of Unknown Primary, an under-researched metastatic cancer with a dismal prognosis and limited treatment options. Our aim is to discover prognostic and predictive biomarkers to elucidate novel therapeutic options for these patients and determine the molecular origins of this heterogeneous group of cancers.

I love Manchester not only for its world-class cancer research but also its diversity, friendliness and food. Four years ago I took up aerial hoop and haven't stopped practicing since, although I'm not quite good enough to join the circus yet...

Sarah Craig

Hi, my name is Sarah and I'm a Clinical Fellow working in the Skin Cancer and Ageing group. I'm originally from Birmingham but completed my undergraduate medical degree in Sheffield. I've worked around Yorkshire for the last few years as a junior doctor and am now a specialist registrar in Dermatology.

I have been privileged to witness how novel targeted and immunotherapies have revolutionised the treatment of metastatic melanoma. There remains, however, a need to unpick biological differences between tumour types to appropriately stratify patients for therapy. It is the elderly who are the most vulnerable to melanoma with the highest incidence and mortality. These patients are also more likely to develop keratinocyte malignancies such as cutaneous squamous cell carcinoma. I am interested in how elderly and sun damaged skin coordinates homeostasis and how this microenvironment impacts tumourigenesis, growth and metastasis. Studying this will help us to understand if certain cutaneous malignancies may be prevented and could help identify prophylactic and/or adjuvant therapies that may benefit this patient group. I am delighted to be working at the Institute where world-leading bench to bedside research takes place. I am also glad to remain living around the beautiful Peak District where I enjoy climbing, cycling and running.

Alex Du Feu

Hi, my name is Alex and I'm from the island of Jersey. I recently completed my undergraduate degree in Biomedical Science at Cardiff University, during which I had the exciting opportunity to experience first-hand the combined efforts of researchers in the fight against cancer. I began my scientific journey into the molecular biology of cancer by investigating the phenomenon of vasculogenic mimicry in solid tumours, in particular the mechanisms surrounding its occurrence. Whilst working on this project alongside researchers at The Institute of Cancer and Genetics and the European Cancer Stem Cell Institute in Wales, I became increasingly captivated by the means and extent to which cancers evolve to circumvent current therapeutic strategies, resulting in insensitivity to previously successful treatments. As a result, I'm excited to be starting my PhD in the Prostate Oncobiology group under the supervision of Esther Baena, where I will be exploring the functional significance of a prospective marker of therapeutic resistance in aggressive prostate cancer and assessing its candidacy as a therapeutic target. My first impressions are that Manchester is brimming with tantalising new experiences for anyone who is willing to try anything – something that I'm eager to take full advantage of over the next four years!

Callum Hall

Hello, my name is Callum. I am originally from Glasgow but spent the last half a decade in Dundee. I did my BSc in Biomedical Sciences at Abertay University, where I spent some time working on the role of GNβ3 in metastatic breast cancer. I then completed my MRes thesis at Dundee University on the role of p53 isoforms in chemotherapeutic resistance in breast cancer. Moving to Manchester for my PhD is the first time I've ever lived in England, and I am loving it so far. When I'm not in the lab, I am a keen climber, cook and reader, so you can talk to me about bouldering, baking or science fiction. I also host an American Football podcast during the gridiron season.

Zoe Lee

My name is Zoe Jane Lee and I am from Sandiacre (Nottingham). I studied Chemistry at the University of Nottingham prior to starting my PhD here in Manchester. I have joined Iain Hagan's Cell Division group at the CRUK Manchester Institute to undertake my PhD project investigating how protein phosphatase 1 is regulated. Protein phosphatase 1 is a highly conserved serine/threonine phosphatase that is widely used within the cell to reverse the impact of protein kinase driven phosphorylation. I will be using fission yeast to establish core principles of protein phosphatase 1 control, once key results have been defined in yeast, parallel experiments will be conducted in human cell lines.

My personal interests include taking part in gym classes (toning classes and spin) and walking in the Peak District – which happily is easily accessed from Manchester. Manchester has a lot going on; the nightlife is great and the Trafford Centre is a perfect place to go shopping. I also really like Didsbury, it is a pleasant place with plenty of entertainment options to meet with friends.

Hannah Reed

Hello. My name is Hannah and I'm from a small town called Ware in Hertfordshire. I studied Biochemistry at The University of Bristol, and graduated with first class honours. During the third year of my undergraduate degree I completed a year in industry at Eli Lilly, where I developed assays to test drugs in development for Alzheimer's disease. I thoroughly enjoyed working in a lab-based environment, which is why I decided to carry out a PhD. I have now joined Angeliki Malliri's Cell Signalling group, and during my PhD I will be investigating the role of the Rac1 activator STEF in non-small cell lung cancer. I will be generating CRISPR knockouts of STEF in NSCLC cell lines to determine whether this effects cancer cell migration and invasion. Outside of work I enjoy rock climbing and am enjoying the many rock climbing opportunities Manchester has to offer, and am excited to visit the Peak District in summer.

Ewan Selkirk

Hi, I'm Ewan and I have just started my project in the Stem Cell Biology group, where I will be investigating the role that long non-coding RNAs play in leukaemia and haematopoiesis. I grew up in St. Albans, Hertfordshire, before undertaking my undergraduate degree in Molecular and Cellular Biochemistry, at Hertford College in Oxford University. As part of my degree I completed a lab project investigating the role that long non-coding RNAs played in neurogenesis of mice - this helped confirm my interest in pursuing research, as well as introducing me to the fascinating field of long non-coding RNAs. Outside of research I am a keen sportsman, playing rugby for much of my childhood; and more recently taking up the more unusual sport of Australian Rules football. Luckily I have found a team in Manchester in order to continue playing. Living in Manchester also provides the ideal location for hill walking, either in the Peak District or in the Lake District, both areas I'm hoping to explore soon. The ability to easily go climbing a few hills is a welcome change after living in flat St. Albans and Oxford.

Matt Wilson

Hi I'm Matt and I'm a PhD student in the Molecular Oncology group currently working on understanding the role of Lysyl Oxidase-Like family proteins in the tumour microenvironment, which is an incredible opportunity for me. I'm originally from Yorkshire, so for me moving to Manchester was quite the challenge (roses are white!). Putting aside old rivalries, I still think it is a lovely place to be and very exciting, especially with such a fantastic focus on cancer and a strong consortium of researchers all working together, you really get a sense that everyone is one large family with one admirable aim. I am a recent graduate from the University of York where I completed a degree in Biology as a mature student. During my time at York I completed a Year in Industry where I was working as an Analytical Bioscientist at the Laboratory of the Government Chemist (LGC) to develop methods to quantify levels of analytes in samples from clinical trials in order to generate PK and PD data. Being an avid climber I'm also really fortunate to be in a city that has the largest indoor bouldering centre in Europe so you'll often find me on the walls at The Depot.

Awards and Events

Caroline Dive is awarded the CBE

In the New Year's Honours list for 2018, our Deputy Director Professor Caroline Dive was named Commander of the Order of the British Empire (CBE) for her services to cancer research. In particular, she was recognised for her pioneering work on developing blood tests known as liquid biopsies.

Speaking to CRUK about this recognition, Caroline says her most defining moment in her career was her decision in 2003 to move away from more basic science to set up a new translational research team focused on biomarkers, an area at the time that needed investigation.

Caroline and her Clinical and Experimental Pharmacology team are developing 'liquid biopsies' that hunt for cancer cells or molecules within cancer cells that have broken free from tumours and are circulating in the bloodstream. These liquid biopsies are less invasive for the patient than tumour biopsies and offer clues about how cancer develops, grows and spreads, what treatment might be best and how tumours can become resistant to treatment.

Professor Dive says, "Whilst I know this is a personal award, it really does reflect the work of a number of people working at the Cancer Research UK Manchester Institute. They are a great team and I am lucky to work here."

Institute Director Professor Richard Marais adds, "We are all incredibly proud of Caroline's achievements and for the public recognition of her contribution to cancer research".

On 6 March, Caroline went to Buckingham Palace to collect her CBE from the Queen.

Success of second CRUK Lung Cancer Centre of Excellence Conference

We would like to thank and congratulate all those who contributed to the huge success of the second CRUK Lung Cancer Centre of Excellence Conference, held at the Midland Hotel in Manchester, in December 2017.

The Conference brought together 196 international delegates, including experts from across a wide range of disciplines, to discuss the latest advances in lung cancer research and how we can continue to drive forward progress. Among those in attendance were over 70 PhD students and post-doctoral researchers from a number of institutes across the UK.

Manchester hosted several world-leading lung cancer researchers, speaking in sessions which reflected our Centre's broad research focus, including Discovery Science and Target Identification, Immunology and Tumour Evolution, and Heterogeneity. We were excited to host keynote speakers Professors Mark Krasnow (Stanford University) who spoke about dissecting 'lung stem cells and cancer initiation at single cell resolution', Tyler Jacks (KOCH Institute For Integrative Cancer Research at MIT), Harry de Koning (ERASMUS MC) who discussed the 'Dutch-Belgian lung cancer screening trial (NELSON)' and Julien Sage (Stanford University) who gave a talk on 'intra-tumoral and inter-tumoral heterogeneity in SCLC'.

In addition to invited speakers, delegates were invited to submit an abstract for short talks and four were featured and included our own Sumitra Mohan (CRUK Manchester Institute) for her work on 'cfDNA in small cell lung cancer'.

During the three day event, PhD students and post-docs working in lung cancer took part in thought provoking and insightful poster sessions which offered them an opportunity to showcase work and receive feedback from experts and other researchers in the field. Furthermore, the event hosted a Careers Workshop, highlighting some of the funding opportunities available for early career researchers and clinicians with CRUK. Overall, the Conference was a great opportunity for networking and potential joint research collaborations. The feedback for our second conference has been excellent, and we are very excited to be hosting our Student/Postdoc School this autumn.

Institute postdoc awarded Kay Kendall Leukaemia Fund Junior Research Fellowship

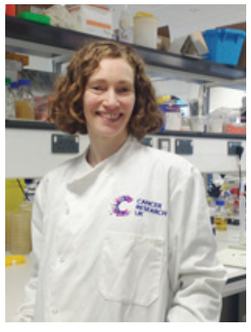

Isabel Romero-Camarero

Dr Isabel Romero-Camarero has been awarded a prestigious Kay Kendall Leukaemia Fund Junior Research Fellowship. This fellowship programme supports outstanding individuals wishing to pursue research into haematological malignancies.

Working as a Postdoctoral Fellow in the Leukaemia Biology group led by Professor Tim Somervaille, Isabel focuses on myeloid malignancies and has been working on FOXC1- a protein that acts as a transcription factor to turn genes on and off. She has been elucidating its mechanisms of de-repression in acute myeloid leukaemia (AML), a type of blood cancer. FOXC1 is not expressed in normal blood cells but is frequently expressed in AML.

The project to be funded by KKLF aims to understand how FOXC1 is turned on in AML, which in the longer term it is hoped will lead to new treatment approaches to turn gene expression off, allowing AML cells to resume more normal differentiation.

Best Lab Manager 2017


Clare McManus

Clare McManus, from the Molecular Oncology group, received the Proteintech 'Best Lab Manager Award 2017' for her outstanding work after the fire at the Paterson Building. She was nominated by her colleagues for being "efficient and supportive" and for "been literally amazing in keeping the lab together after the fire", helping find alternative solutions and assisting with the relocation.

Clare was the only British finalist out of five candidates and the CRUK Manchester Institute was the only non-American institution in the finals.

As part of her prize, Clare received a care package and US$1000 for use in her research.

3Rs Star wins the 2018 Andrew Blake Tribute Award


Melanie receives her award

Most of our research does not involve animals but some animal research is essential if we are to understand, prevent and cure cancer.

Our animal technicians work hard to ensure that the animals receive the highest standard of care. So we are delighted to announce that Senior Scientific Officer Melanie Galvin has been honoured with the Andrew Blake Tribute Award for 2018. The award, given by the Institute of Animal Technology and sponsored by The Association of the British Pharmaceutical Industry, recognises animal technicians throughout the UK and their contributions to improving laboratory animal welfare.

Melanie has made a significant impact on animal welfare by targeting all three of the 3Rs' principles (replacement, reduction and refinement of animals). She has reduced the number of mice required as donor and recipient animals for large scale efficacy studies, refined tumour passage by eliminating invasive surgery, and hopes that the ex vivo growth of these disaggregated cells could replace in vivo studies in the future. It is vital that good welfare practices and improvements carried out by technicians are widely disseminated and Melanie presented her valuable work at the IAT Congress in March 2018, where she was presented with a glass trophy and £250 award.

About the award, Melanie says: "As animal welfare is my passion, it is a great honour to be recognised for the work we are doing to not only refine the procedures we carry out, but to reduce the number of animals used in our research."

The Andrew Blake Tribute Award commemorates the work and life of Andrew Blake, who suffered from Friedrich's ataxia, a hereditary condition described as one of the "worst of neurological diseases". Andrew died in May 2002 aged 39. Andrew was passionate about the need to support scientists in their work and his commitment to speaking out against animal rights activists took up much of the last ten years of his life. He died shortly before he was to collect his MBE.

SMR Congress comes to Manchester

The Society for Melanoma Research (SMR) will be holding their 15th International Congress in Manchester this year.

Taking place 24-28 October 2018, this will be the first time the prestigious annual meeting comes to the UK. Previous host cities have included Amsterdam, Sapporo, Boston, Zurich, and Brisbane.

The SMR is a diverse, all-volunteer group of scientists working to find the mechanisms responsible for melanoma and, consequently, new therapies for the cancer. The Congress is a global meeting that unites leading melanoma clinicians and researchers to focus on multidisciplinary management of skin cancer and discuss cutting edge data.

Manchester's successful bid was supported by the Cancer Research UK Manchester Institute, The Christie NHS Foundation Trust, The University of Manchester, Marketing Manchester and Manchester Central.

Institute Director Professor Richard Marais, said: "The SMR does some vitally important work to encourage interdisciplinary collaboration and drive forward progress in melanoma research, and it's very exciting to be welcoming them to Manchester this year. It is sure to be a stimulating few days."

Professor Paul Lorigan, leading melanoma oncologist at The Christie, said: "We're very much looking forward to welcoming the SMR's annual congress to Manchester this year. It comes as recognition not only of the important work the Christie does in the field of melanoma research, but of also of the global significance of Manchester's wider scientific community." This is a fantastic opportunity to showcase our strengths in melanoma and our collaborative working between clinical and basic research.

Institute researcher invited to give prestigious conference lecture


Amaya Virós

Dr Amaya Virós was chosen to deliver the Rising Star Lecture as the representative of the European Society for Dermatological Research (ESDR) at the 2018 International Investigative Dermatology Meeting in May this year. The Rising Stars Lectures celebrate the best of emerging dermatological science throughout the world.

Amaya was selected as a prominent young researcher engaged in high-impact science in her respective field to provide a short overview on her current work entitled 'the aged skin microenvironment'.

Amaya combines her research with clinical work as a dermatologist at Salford Royal NHS Foundation Trust in Manchester. Her research has focused on the mechanisms driving secondary keratinocytic tumours in metastatic melanoma patients treated with the BRAF inhibitor vemurafenib, as well as on dissecting the specific contribution of ultraviolet radiation to distinct subtypes of melanoma defined by their driver oncogene. In 2016, she became a Wellcome Trust Intermediate Clinician Scientist Fellow and is establishing her research group as an Institute Fellow at CRUK MI. Her Skin Cancer and Ageing group focuses on how ageing influences melanoma initiation and progression and developing rationales of adjuvant care for patients at high risk for melanoma progression.


Denys and Katharina alongside Rachel Eyre from the Division of Cancer Breast Biology group receive their awards

Meeting bursary award winners

PhD Student Denys Holovanchuk and Postdoctoral Fellow Katharina Mahal, both from the Molecular Oncology group, were awarded an EACR-Worldwide Cancer Research Meeting Bursary to support their attendance at the Seed and Soil conference in November last year. The meeting was held in Berlin and focused on in vivo models of metastasis. They each presented a poster on their work and received complimentary registration and €190 towards their travel costs.

Institute Director Richard Marais presents the Dexter Award 2018 to Melanie Galvin

Dexter Award

We are delighted to announce that the winner of the 2017 Institute's Dexter Award for Young Scientists is Melanie Galvin.

Melanie is a Senior Scientific Officer in the Clinical and Experimental Pharmacology group and has been awarded the prize for her extremely valuable contributions to the in vivo programme in CEP, together with the external recognition of her work in the 3Rs (the replacement, reduction and refinement of use of animals in research). Melanie took over running the in vivo team in 2016 leading a team of five. As a result of her efforts, over 55 patient derived models, including 46 CDX models of lung cancer have been developed, which have underpinned much of the work across CEP's preclinical team as well as contributing to the programme of work undertaken by the Nucleic Acid Biomarkers group. Her interactions with various clinicians are also a key component of this success. She has continued to generate further models while the experimental part of the BRU has been based at The University of Manchester Stopford Building in the aftermath of the fire, while simultaneously helping the BRU team to set up the new in vivo facility at our temporary site in Alderley Park.

Her impact is not confined to CEP but felt more widely across the Institute through her valuable participation on the Institute's Animal and Welfare Ethical Review Body. Melanie is a keen advocate of the 3Rs and has won awards in this area for her work on the disaggregation of tumours prior to passage leading to the application of the reduction and refinement principles to CEP's work. In 2016, she was awarded the Steve Moore Memorial Poster Prize at an Institute of Animal Technology meeting, which enabled her to present this work at the American Association for Laboratory Animal Science meeting. In 2017, she was asked to speak at the IAT congress in Wales and also awarded the Andrew Blake Tribute Award, which she received at the IAT congress in March this year. Melanie was also part of the team that was awarded a national research engagement prize in 2016 from Understanding Animal Research for communicating how animals are used at the Manchester Science Festival.

This is an extremely impressive list of contributions to the Institute for whom Melanie is a tremendous ambassador. We would like to congratulate her on receiving the Dexter Award for 2017.

Alumni of the year

Sara Valpione

Sara Valpione, from the Molecular Oncology group, was distinguished with the University of Padua Alumni of the Year Award 2017 for her PhD work.

Amongst Sara's achievements, the University highlighted that during her studies she received an ESMO Fellowship and the Conquer Cancer Foundation Merit Award 2017 for her innovative studies on the treatment of patients with melanoma.

Talking about this award, Sara said: "I was very pleased to receive such a prestigious recognition from the University of Padua for the work done during my time there. I have to thank all the people who have supported me during these years, both in my private life and at work (including my Mancunian mentors), because they made this possible."

University Medal of Honour for Professor Nic Jones

The University of Manchester has awarded Professor Nic Jones, a world-leading cancer researcher, with its highest medal, the Medal of Honour.

Following the receipt of his PhD from Edinburgh University, Nic pursued his research career in the USA initially at the University of Connecticut Health Centre and subsequently at Purdue University. After 12 years he returned to the UK and joined the ICRF laboratories in London as a Principal Scientist where he continued his research on DNA tumour viruses and the mechanisms they employ to transform normal cells into cancer cells.

In 1999, he moved to Manchester to become Director of the Paterson Institute (now the Manchester Institute) which is core funded by Cancer Research UK. He remained in that role until 2011 when he became the CRUK Chief Scientist with the responsibility of overseeing the scientific strategy of the organisation. He has also been a Senior Group Leader at the Institute leading the Cell Regulation group until the end of 2017.

In 2006 he also became the inaugural Director of the Manchester Cancer Research Centre, a partnership between The University of Manchester, the Christie and CRUK and oversaw its development into one of the foremost cancer centres in Europe. He stepped down from this role in August 2017. Nic is continuing to work closely with the University advising on major strategic initiatives and research awards.

Staff News

New arrival

Pablo García Martinez, from the Molecular Oncology group, and his wife Mar are overjoyed with the arrival of their first son, Naël García García, who was born on 17 February, weighing 3.23 Kg (7.12 pounds).

Naël García García

Newcomers Party

Once again the CRUK Manchester Institute welcomed the new staff with our annual Newcomers Party, which took place last October in the MCRC Building.

This event was a great opportunity for our staff to meet the people who have joined our team in the last year, helping to make new connections and getting to know each other better over some food and drinks.

From new Group Leaders and Institute Fellows to new PhD Students, science and administrative staff, we had plenty of new starters who joined us in 2017 and we were delighted to give them a very warm welcome.

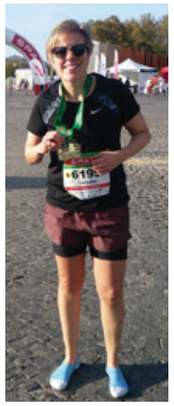
A warm welcome to the newcomers

Marathon and fundraising success

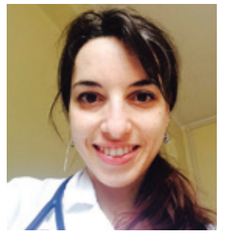
Rachel Craven, Recruitment Coordinator at the Institute, successfully completed her first marathon last October in Budapest, raising £972 for CRUK.

She describes it as "the most difficult but incredible experience. I'm really glad to have finished and raise so much for CRUK."

Despite a heat wave, which meant it was 25 degrees instead of the expected 13 degrees, she managed to finish the race in 5 hours 6 minutes.



Rachel after running her first marathon



Sara Valpione

New member of the EORTC MG Steering Committee

Sara Valpione, Clinical Fellow in the Molecular Oncology group, is honoured to become part of the European Organisation for Research and Treatment of Cancer (EORTC) Melanoma Group (EORTC MG) steering committee. From April, she has been sitting as co-chair of the early career investigators.

This is a great achievement since the EORTC MG is one of the largest melanoma networks in the world, and conducts clinical trials and translational research in the melanoma field. Its objectives are to improve clinical care of patients suffering with cutaneous or ocular melanoma, and to increase knowledge about melanoma acquisition and progression.

Denys talking to students at Benavente High School

Back to high school to engage with the future scientists

Denys Holovanchuk, from the Molecular Oncology group, was invited to go back to his former high school. But this time, as a guest speaker.

Denys presented an hour seminar about his academic path, the main mechanisms driving cancer initiation and progression, and the CRUK Manchester Institute.

The students, who were part of a science and technology course, really engaged with the talk, asking many questions. "They actually made a little circle around me asking things like how our immune system fights cancer, which was very exciting and unexpected", remembers Denys, who has already been invited to repeat the experience next year.

In the spotlight with Tom Bolton

Tom Bolton is our Web Developer and he is responsible for designing and maintaining our external website and intranet, as well as the website for the Manchester Cancer Research Centre. Tom recently launched our new-look website, which we are all incredibly pleased with. After the fire, he provided invaluable help to IT by assisting our users with various computer related problems while their time was taken up establishing new IT infrastructure at Alderley Park.

1. What is your favourite part of the UK?
I have many – I love Oxfordshire (where I grew up), and the south-west and Devon in particular. Manchester is the one place I keep returning to though.

2. What was your best ever holiday and why?
A chance connection landed us a once-in-a-lifetime shot at proper luxury on a very posh island resort in the Maldives some years ago. During which, by a much bigger chance, Mrs. B. happened to say 'yes' when I proposed.

3. Which website do you always check, and why?
The spoof-news site Daily Mash for laughs, the Guardian for news. Given recent years' events, some days it can feel like it's the other way around.

4. What is your favourite film?
The Blues Brothers.

5. What is your favourite band/ singer?
Band, Pearl Jam; singer, Aretha Franklin.

6. If you had to change careers tomorrow, what would you do?
Something that doesn't involve computers!

7. What is the most important lesson that you have learnt from life?
Your family, friends, and health. These are what's important, everything else is a bonus.

8. Name three things you would take with you to a desert island?
My father's old Martin guitar, a gift to say sorry to my father for taking his guitar. A lifetime's supply of plectrums (all of which will be lost by week three).

9. What is your greatest fear?
Heights. Realising that you forgot your wife on the way to a desert island. That "I heard you!" grin you get from our band's bass player when you hit the wrong chord in the middle of a gig.

10. How would you like to be remembered?
A decent human being.

11. If you could change one thing in your past what would it be?
I would have paid attention in language classes at school - I can just about order a couple of beers in French. It's beyond embarrassing.

12. What is your signature dish to cook?
Curries, chillies, that sort of thing. Bloke food.

13. You've just won the lottery and have £5 million pounds to spend. What do you buy first?
I'd take everyone important in my life somewhere tropical and hot and have a big party.

14. What is your idea of perfect happiness?
That party sounds like a good start!

15. What keeps you awake at night?
The computer programmer-levels of caffeine in my bloodstream.

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