Newsletter

CANCER RESEARCH UK | MANCHESTER INSTITUTE

Winter 2015

FEATURE - Fundraising and Engagement Activities

Meet the New Students

NCRI Meeting

Colloquium 2015

Core Facilities

Publications

MANCHESTER 1824
The University of Manchester

Director's Introduction

Last month, many of our scientists attended the NCRI meeting which is a multidisciplinary conference held annually in the UK with the aim of discussing the latest and most exciting developments in cancer research. A number of prizes are awarded there each year and I am delighted that two of our scientists were honoured at this year's event.

First, one of our Junior Group Leaders, John Brognard was awarded the Cancer Research UK Future Leaders prize. This well-deserved honour reflects the high level of success that John and his team have achieved during his first five years at the Institute. The second award went to Romina Girotti from the Molecular Oncology group who was presented with the British Association for Cancer Research Translational Research Prize, which recognises the contributions made by young scientists to translational cancer research.

During the summer, Angeliki Malliri and her Cell Signalling group underwent a successful quinquennial review of their research programme and have recently secured external funding from Worldwide Cancer Research to help progress one of their studies. I would like to extend my congratulations to all on this success.

Santiago Zelenay has joined the Institute as a new Junior Group Leader. He will lead the Cancer Inflammation and Immunity group which will explore the complex balance between the tumour-promoting and tumour-suppressing properties of the immune system. Santiago has recently published an exciting study in Cell describing his post-doctoral research work at the CRUK London Research Institute where he discovered how certain cancer cells can dampen down the immune response. You can read more about his future research plans in this issue.

In order to support the Institute's expanding portfolio of research, we have also established two new core research services. The first is a transgenic production facility that will provide a complete service from experimental design to generation and cryogenic storage of transgenic lines and we welcome Natalia Moncaut who will be heading the team. The second facility will allow us to perform small molecule and RNAi screening which will aid our ambitions to accelerate the translation of our research. Ian Waddell from the Drug Discovery Unit is taking the lead on experimental design for this activity.

A number of events were held over the summer to mark the official opening of the Manchester Cancer Research Centre Building. It was a great opportunity to thank many of the donors and fundraisers who have made this project possible and to invite the general public to look around this fantastic space. We look forward to a number of our teams moving into the building in the New Year. Many of our scientists took part in the recent Manchester Cancer Research Centre Autumn School which was an opportunity to invite young scientists from other CRUK centres to Manchester to learn more about how we are working towards implementing personalised medicine for cancer patients. I would like to thank everyone who participated in, and helped to organise this event which was a great success.

Another opportunity to highlight activity in Manchester was the annual CRUK student conference which was held here during the summer and organised by the Institute's PhD students. I had the pleasure of attending some of the meeting and was very impressed by the hard work that had gone into hosting this event. It offered our students an excellent opportunity to develop additional skills and I am very proud of their achievement.

In October, Sive Finlay joined us as our new Research Engagement Manager. Sive got off to a flying start as this is a particularly busy time for engaging with our supporters with the Institute's annual open day and the Manchester Science Festival as well as our on-going programme of lab tours. I would like to welcome Sive to the Institute and to thank all who have taken part in these important events.

The past year has been a particularly successful one for the Institute both in terms of the quality of publications produced but also our success in external funding applications and with prizes awarded to Institute scientists. The coming year promises to be just as exciting as Manchester takes on the mantle as the European City of Science. Part of the associated activities will involve the biannual meeting of the European Association of Cancer Research taking place in the centre of the city and I look forward to seeing many of you there.

Finally, I would like to thank everyone for their hard work during the year and to wish you all a Happy Christmas and a very successful 2016.

Richard Marais
Director

Cover Image: John Brognard with his Cancer Research UK Future Leaders' Prize

Fundraising and Engagement activities

#sciencecakes creations

The annual #sciencecakes competition in aid of Stand Up to Cancer returned to the Institute in early October. Scientists from CRUK centres across the country whisked, baked and iced their way to cake glory for their research-inspired creations. An entry from the Signalling in Cancer Networks group was a deserving winner of the Institute's coveted wooden spoon for their impressive multi-cake creation.

The cakes showed the generalised MAP Kinase signalling pathway, whereby the receptor tyrosine kinase (malteser cake) within the plasma membrane (chocolate truffles) is activated by a ligand (chocolate star). This activates a GTPase (passion fruit and blueberry cheesecake) starting a cascade of phosphorylation events through the MAP kinases (chocolate mousse trifles), which are held together by a scaffold protein (ginger loaf).

After a national competition via twitter, #edinburghcake won the overall prize while #newcastlecake took victory in the public vote. Get your creative juices flowing to bid for a Manchester victory next year!

The MAP Kinase signalling cake

Natalie Stephenson and Wendy Trotter with their #sciencecakes prize of a CRUK MI wooden spoon.

Virtual Reality lab tour

Stuart Pepper enjoying the virtual reality lab tour

The Manchester Institute hosts hundreds of supporters on lab tours every year. Now we're extending our reach even further by being the first location to offer virtual reality lab tours.

Armed with a set of google cardboard glasses and an app they can download to their phone, visitors are expertly guided on a tour of the Drug Discovery Unit and the Leukaemia Biology lab by Marina Parry from the Molecular Oncology group. The tour is being shown at public events across the country to great acclaim; congratulations to everyone involved.

Movember fundraising

For the 5th year running, David Jenkins has led a fantastic fundraising effort for Movember. David's Great British Bake Off Halloween special included some ghoulish treats with green Cyclops and spiders from Mars cupcakes.

The ever-popular David's Lucky Dip had a great selection of unusual prizes and his raffle included even more special offerings with a top prize of a signed copy of Nigella Lawson's latest cook book. This brings David's total to a fantastic £540 for Movember so far with more fundraising plans in store. Combined with regular November Mo-Yoga sessions led by Lisa Waters, everyone at the MI is doing a great job of supporting our Movember Centre of Excellence.

David Jenkins, Movember fundraiser extraordinaire!

Images left to right: Sara Menegatti and Victoria Tessyman at our science spectacular stand; Kate Hogan and Marina Parry catching circulating tumour cells in the hurricane tube at the Cravings Exhibition; Alice Greenhalgh, Clare Dickinson and Aida Sarmiento-Castro at a lab tour in the MCRC Building.

Manchester Science Festival

The Manchester Institute was well-represented with four events for the Manchester Science Festival. Our CRUK Grand Challenge evening at Manchester Art Gallery asked members of the public to give their views on how CRUK should spend large grants of £20 million to tackle some of the toughest questions in cancer research.

After introductory talks from the Grand Challenge team and a patient representative, visitors were invited to learn more about some of the seven grand challenges through hands-on activities involving science cluedo, ball pools, UV torches and a dark tent. The unusual props were a great way to bring the science behind the challenges to life.

As part of the festival, the Institute and the MCRC Building opened their doors for an afternoon of public lab tours. Dr Allan Jordan from the Drug Discovery Unit gave a welcome presentation involving a sweet-themed (and delicious) introduction to epigenetics after which visitors explored the MCRC Building, Drug Discovery Unit, Molecular Biology Core Facility, Clinical and Experimental Pharmacology laboratory and the Imaging Facility.

We joined the CRUK London team for the Manchester Museum of Science and Industry's lates' event on the theme of cravings. Our contribution focused on tobacco-related cancers with activities based on epidemiology, impacts of tobacco policy control and basic research into lung cancer, particularly the Clinical and Experimental Pharmacology group's work on circulating tumour cells. It was also great to see the never-ending queue of people keen to experience our new virtual reality lab tour.

We rounded off the science festival by taking part in the University of Manchester's Science Spectacular at Manchester Museum. This family-friendly science fair features interactive stands from more than 200 researchers. At our stand, visitors could take #cellfies with smartphone microscopes, play "hook a duck" to learn about personalised medicine and make their own cell balloons to learn about how their bodies work.

A huge thank you to everyone who helped out with the science festival activities. It was a fun, busy week and a great opportunity to showcase our research. Many visitors commented on how lovely it was to chat to friendly, knowledgeable and enthusiastic researchers.

Research Engagement Manager – Meet Sive

Sive Finlay joined the Institute in October 2015 as our new Research Engagement Manager, taking over from Hannah Leaton. Sive joins us from a maternity-cover research engagement post at the CRUK Cardiff centre. Prior to that she worked in science communication roles in Dublin after studying tenrecs (look them up!) in the forests of Madagascar.

Sive's office is on the ground floor, last door on the left before the stairs down to the basement. She has lots of public engagement opportunities, activity ideas and an endless supply of CRUK branded goodies so if you would like to get involved with any of our public engagement or volunteering opportunities please come in and say hello!

Race for Life volunteer thank you

On Saturday 14th November, we said a massive thank you to the wonderful volunteers who help run Race for Life and Pretty Muddy events across the North West. Keeping to early start times, long days and braving the Great British weather, these volunteers ensured that everything ran smoothly for the 17,760 women who took part in local events this year.

CRUK events' staff wait to welcome race for life volunteers across the finish line after their lab tours.

Open Day

Cancer Research UK relies entirely on generous donations from our supporters. The Institute Open Day is our opportunity to thank our fantastic fundraisers and to show how we're spending their money.

Over 100 visitors joined us for our most recent open day in November, many of them visiting the beautiful new MCRC building for the first time. After a warm welcome from CRUK staff including a video reel of fundraising highlights from the last year, guests received a scientific update from Allan Jordan. He gave an inspirational talk about recent research successes at the Institute and highlighted how none of it would be possible without the tireless work of CRUK fundraisers.

Visitors then headed off for tours of the labs. They got an insight into the crucial services provided by the core facilities, carried out strawberry DNA extractions and tried their hand at pipetting and loading gels. Guests also had a chance to go on virtual reality lab tours and to admire the "Descience" dress based on Esther Baena's research into prostate cancer.

The day wrapped up with an inspirational story from a cancer survivor and details about upcoming fundraising plans for next year. Thank you to everyone who volunteered to host and guide lab tours and who helped visitors to get a first hand view of the impact that their support is having on cancer research.

Genny Filliciotto enjoying the new virtual reality lab tour

The "Descience" dress designed to represent progression of prostate cancer.

Featured Publications

Teasing apart the specifics of blood cell development

Institute scientists have explored the role played by a particular protein in the development of blood cells in early embryonic development.

The Stem Cell Haematopoiesis and Stem Cell Biology groups, led by Dr Valerie Kouskoff and Dr Georges Lacaud respectively, worked together to investigate FOXF1, belonging to the forkhead family of transcription factors, and how it controls the beginning of haematopoiesis – the process by which blood components are formed.

They looked at embryonic stem cells - growing in the lab in petri dishes - and found that expression of FOXF1 was lacking in the blood cells. Further experiments showed an inverse relationship between FOXF1 and commitment to blood cell formation.

Their study, published in the journal *Development*, shows that this particular transcription factor is responsible for 'holding back' the differentiation of stem cells into early blood cells.

Understanding the process of cell specification in embryonic development is crucial for researchers hoping to create patient-specific blood products in the lab for therapeutic applications in the clinic.

Fleury M, Eliades A, Carlsson P, Lacaud G, Kouskoff V. (2015) FOXF1 inhibits hematopoietic lineage commitment during early mesoderm specification *Development* 142(19):3307-20

Divide by two

Dr Angeliki Malliri's Cell Signalling group have made a significant discovery in relation to how cells divide, with important implications for certain drugs that are undergoing clinical trials.

Their study – published in the journal *Nature Communications* – focuses on tiny structures called centrosomes. These are the white dots in the middle of the image of the cell, seen down a high-powered fluorescence microscope.

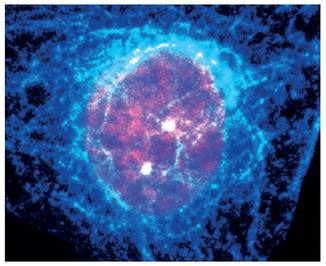


Image of a cell with the centrosomes shown in white

Centrosomes are the cell's scaffolding engineers, responsible for building long, tube-like structures called microtubules. They play a fundamental role as cells divide, generating a moving molecular scaffold that pulls apart the DNA.

Each cell usually has just one centrosome, but when it's time for a cell to divide the single centrosome gets duplicated, along with the cell's DNA. Next, one centrosome moves to each end of the cell and together they start constructing a network of microtubules, reaching towards the DNA in the centre.

The microtubules then grab hold of the DNA and pull the two copies apart. Finally the cell splits down the middle, producing two identical 'daughters', each with one full set of DNA and one centrosome. And so the cycle repeats.

Angeliki and her team have been studying a molecule called Kinesin-5 (also known as Eg-5), which is essential for centrosomes to function properly. Without it, the centrosomes don't separate after they've been copied, remaining in the centre of the cell rather than moving to each end. This molecular chaos is too much for cells to cope with – they get stuck, and eventually die. Because of this, researchers have wondered whether interrupting this process could help target cancer cells.

This, in turn, has led to experimental drugs that target Kinesin-5, and at least five have undergone early stage clinical trials. One of these is called Monastrol. In their new paper, the Cell Signalling team have discovered that reducing the levels of two other molecules, Pak1 and Pak2, enables cells to somehow carry on and divide, even in the presence of the drug.

Their finding has important implications for the development of Kinesin-5 blockers, because it suggests a way that cancer cells could develop resistance to them. Tumour cells are constantly evolving, so if they develop any genetic faults that block Pak1 or Pak2 then they might be able to keep growing, regardless of the treatment.

This could be used to help predict which patients will benefit most from these treatments. And understanding how cancers develop resistance to drugs – in this case while the treatments are still in early trials – will help the development of new strategies to overcome resistance and treat the disease more effectively.

Whalley HJ, Porter AP, Diamantipoulou Z, White GRM, Castañeda-Saucedo E, Malliri A (2015). Cdk1 phosphorylates the Rac activator Tiam1 to activate centrosomal Pak and promote mitotic spindle formation *Nature Communications*, 6, 7437.

Learning more about treatment resistance in melanoma

Scientists from the Molecular Oncology group, led by Professor Richard Marais, have found that certain melanoma cells change the way they produce energy for growth – offering an insight into drug resistance and a potential way to treat resistant tumours in the clinic.

Cancer cells require considerable energy to support their growth, in conditions that are typically deprived of oxygen. This means they frequently switch their metabolism to alternative energy sources and this change, driven by specific genetic mutations, is seen as one of the key hallmarks of cancer.

Around 45% of melanomas contain a mutation in a gene known as BRAF, which encourages the growth of cancerous cells. By targeting and blocking this mutation, recently developed drugs known as BRAF inhibitors have improved survival. However, many patients unfortunately develop resistance to treatment and their disease returns.

Researchers at the Institute, working in collaboration with a team in Glasgow, have now explored how metabolism changes in treatment-resistant BRAF-mutant melanoma cells.

The group found that BRAF-mutant melanoma cells that had developed resistance to BRAF inhibitors had a preference for glutamine as an energy source, instead of glucose. The resistant cells also depended much more on their mitochondria for survival.

By blocking the breakdown of glutamine, or by poisoning the mitochondria, the team were able to stop the growth of treatment resistant tumours. Their findings could lead to new combinations of therapies to treat or prevent resistance in melanoma patients.

Baenke F, Chaneton B, Smith M, Van Den Broek N, Hogan K, Tang H, Viros A, Martin M, Galbraith L, Girotti MR, Dhomen N, Gottlieb E, Marais R. (2015) Resistance to BRAF inhibitors induces glutamine dependency in melanoma cells *Molecular Oncology* S1574-7891(15)00149-0. doi: 10.1016/j.molonc.2015.08.003.

Leukaemia gene stops blood cells 'growing up'

The Leukaemia Biology group, led by Dr Tim Somervaille, has identified a gene – FOXC1 – that, if switched on, causes more aggressive cancer in a fifth of acute myeloid leukaemia (AML) patients, according to a study published in the journal *Cancer Cell*.

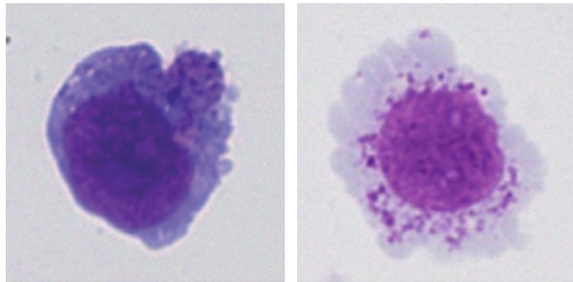
The FOXC1 gene is normally switched on during embryonic development and is needed to turn cells into specialised tissues, like the eyes, kidney, brain and bone.

But this new research found that in certain patients with AML – a type of blood cancer that affects white blood cells and the bone marrow – this gene was wrongly switched on inside the patient's cancer cells.

When it is switched on in blood cell tissue, FOXC1 stunts the development of blood cells and stops them maturing into normal specialised blood cells. This triggers the cancer to be more aggressive, as young cells are able to replicate more than mature cells – causing cancer cells to grow faster and become more difficult to treat.

Around 2,900 people were diagnosed with AML in the UK in 2011. Of these, around 20 per cent would have had the FOXC1 gene wrongly switched on in their cancer. This important finding helps us understand how acute myeloid leukaemia develops and why some cases of AML are more aggressive than others.

Somerville TD, Wiseman DH, Spencer GJ, Huang X, Lynch JT, Leong HS, Williams EL, Cheesman E, Somervaille TC. (2015) Frequent derepression of the mesenchymal transcription factor gene FOZC1 in Acute Myeloid Leukaemia *Cancer Cell*, 28(3):329-42



Two different blood cells: the left hand side shows a non-specialised 'blast' cell with FOXC1 switched on. The right hand side shows a cell with FOXC1 switched off and specialising into an infection fighter.

Education News

Meet the new students

Mairah Khan

Hi, I am Mairah, originally from Lahore in Pakistan. I completed my undergraduate degree in Biology at the Lahore University of Management and Sciences, and for my undergraduate final year project I developed tools to study post translational modifications in PcG/TrxG proteins in Drosophila melanogaster.

Following my undergraduate degree, I moved to Manchester to pursue an MRes in Biological Sciences at the University of Manchester, where I was introduced to the world of long non-coding RNAs (lncRNAs) and for one of my MRes projects I characterised the function of a novel lncRNA in Drosophila embryos. After my masters, I worked for a few months at the University of Manchester studying the effect of a putative anti-cancer drug on notch signalling by looking at genetic notch phenotypes (again in Drosophila!). I am starting my PhD in the RNA Biology group under Crispin Miller, with my project incorporating both of my interests: lncRNAs and cell signalling. I will be working in collaboration with John Brognard's group looking at novel long non-coding RNAs that affect kinase signalling pathways in lung adenocarcinoma. I am very excited to be starting a PhD at the Institute, where I have the wonderful opportunity to learn and accomplish great science.

Elizabeth Hogg

Hi, I'm Lizzy, and I'm from Guildford, in Surrey. I have recently completed my undergraduate degree in Biomedical Sciences from the University of Southampton.

I took a year out from my degree to work as a placement student at GlaxoSmithKline in the area of immuno-inflammation. I learnt a lot about industry and enjoyed the experience, but was really more interested in cancer, which I confirmed during my final year research project on Chronic Lymphocytic Leukaemia. I am pleased to be accepted into the Drug Discovery Unit for my PhD, particularly as the research is translational to the patient. For my project, I will be applying the collateral vulnerability hypothesis to genomic datasets from pancreatic cancer patients, with the aim to identify and validate targets for novel cancer drug discovery. I am enjoying my time here, getting involved with the University cricket and tennis clubs. There is a lot to explore in Manchester and the surrounding areas, which I am looking forward to.

Denys Holovanchuk

Hi, I'm Denys Holovanchuk, a Portuguese student with Ukrainian origins. That's why my accent doesn't match my looks.

I obtained my degree in Biochemistry, from the University of Lisbon, where I also completed my master's degree in Medical Biochemistry. During the last year of my MSc, I worked with drug delivery systems, so called liposomes, for active targeting of tumour cells. This project combined biotechnological and pharmacological approaches to cancer treatment, which drove my interest in translational research. Following this project, I spent some time at the Institute Gulbenkian of Science, as a research assistant, working with mice models of chronic metabolic diseases in Carlos Penha Gonçalves' team. I have recently moved to England and I am very excited to start my PhD in the Molecular Oncology group, under the supervision of Professor Richard Marais. The main goal of my project is to study molecular mechanisms that drive melanoma resistance to targeted therapies. I will be focusing on NRAS mutant melanoma and on combination therapies, in vitro and in vivo, using patient-derived xenografts in mice. In spite of being far away from the sunny shores of the Atlantic, I am confident that Manchester will become a warm and familiar city to start my career and to enjoy in my free time.

Colin Hutton

Hi, my name is Colin and I've just started my PhD in Systems Oncology, led by Claus Jorgensen. I'm originally from Hemel Hempstead and completed my undergraduate chemistry degree at UCL.

After a student placement at AstraZeneca, I worked in Nottingham for a biotech company developing chemical probes to inhibit human telomerase. I then moved to the CRUK MI Drug Discovery Unit where I've been involved in a project identifying novel drug-like inhibitors of PARG – an enzyme required for the normal function of DNA single-strand break repair. Whilst in DDU, I became aware of the great studentships the Institute offers and I'm now looking forward to the next 4 years! My PhD project is investigating cancer-associated fibroblast (CAF) heterogeneity in pancreatic cancer with a focus on using mass spectrometry-based proteomics to characterise functionally distinct CAFs. Outside of research I really enjoy rock climbing. Manchester is perfectly located for this sport, when there's a break in the drizzle. If there are any keen climbers currently in the Institute please get in touch!

Joe Maltas

Hi, I'm Joe and I have just started my PhD with the Cell Signalling Group. I am originally from Cambridge and then I ventured north to complete my degree in Human Physiology at the University of Liverpool.

Here, I gained some lab experience during a project looking into the relationship between Nrf2 and K-Ras in cancer. This motivated me to continue studying within the field of cancer research. I am excited to start my PhD project at the CRUK Manchester Institute, identifying novel nuclear interactors of Tiam1. I am really enjoying living in Manchester so far, and I look forward to heading out to the Peak District on a regular basis. I also aim to eat at every curry house on curry mile over the next 4 years!

Renaud Mevel

Hi, my name is Renaud and I come from the south west of France (Bordeaux). There, I completed a master's degree in Biotechnology Engineering, and then moved to Toulouse to undertake a research oriented MSc in Oncology.

In 2013, I embarked on an internship in a spin-off company called Recombinant Antibody Technology Ltd, based in the Babraham Institute (Cambridge, UK). My thesis focused on the characterisation of the antibody repertoire of a transgenic rat strain producing heavy-chain only antibodies. This experience reinforced my strong interest and passion for research. Last year, I completed another internship at the Cancer Research Center of Toulouse, where I worked on the implication of PI3K isoforms in the induction of chemoresistance in ovarian cancer cells by mesenchymal stromal cells. Fulfilling my great interest in solid tumours, I am now delighted to start a PhD on prostate cancer in Georges Lacaud's laboratory, working in close collaboration with Esther Baena's group. The aim of my project will be to investigate the role of Runx proteins in the development of normal prostate and prostate cancer. In my free time I greatly enjoy outdoor sports (triathlons, skiing...) and look forward to further discovering the UK's National Parks.

Sakis Paliouras

Hi, my name is Sakis, which is short for my double first name (Athanasios-Rafail). I come from Greece, where I completed my undergraduate degree in Molecular Biology and Genetics, at the Democritus University of Thrace.

During my undergraduate studies, I had the great opportunity to work on a research project on the dynamics of the mitotic spindle during cell division, under the guidance of Associate Professor Margy Koffa. There, I experienced first-hand the beauty of biological research and decided to continue studying for a PhD. Eager to explore the world of translational research, a project in cancer was a very tempting choice, so I was very excited to be accepted in a Cancer Research UK core funded Institute. I am the newest member in the group of Transcriptional Networks in Lung Cancer, led by Dr Michela Garofalo. The group's main goal is to identify and characterise the roles of microRNAs in lung cancer. My focus will be on whether some microRNAs can influence acquired resistance to targeted therapies in Non Small Cell Lung Cancer. As far as the city is concerned, I love being part of the University of Manchester and enjoying all it has to offer, while getting involved with extracurricular activities. I particularly like the main campus and regularly spend time there. All in all, I expect to spend four memorable years here.

Fabrizio Simeoni

Hello, my name is Fabrizio and I am originally from Rome, Italy.

I recently completed my master's degree in Genetics and Molecular Biology at the University of Rome, La Sapienza and I also undertook my undergraduate studies at the University of Rome, Tor Vergata. As part of my master's degree, I was a trainee in the group of Professor Isabella Screpanti, where I worked on the molecular mechanisms leading to Notch3 gene deregulation in T cell acute lymphoblastic leukaemia (T-ALL), so my real interest has always been cancer. As a result, I applied for a position at the Cancer Research UK Manchester Institute and here I am! I am really excited to start my PhD and be part of the Leukaemia Biology group, led by Tim Somervaille. The aim of my project is to study the role of FOXC1 in Acute Myeloid Leukaemia (AML) and to try and unveil the molecular mechanism by which FOXC1 is able to block monocyte lineage differentiation, accelerating leukaemia onset. I just

arrived in Manchester two months ago but I love the city so far. I will definitely enjoy this experience and try to explore as much of what Great Britain has to offer as possible.

Ivana Steiner

Hi, I'm Ivana and I come from Croatia. There I graduated from the University of Zagreb with a master's degree in Molecular Biotechnology.

My research career started with another deadly disease - anthrax. During my placement in Melbourne, Australia, I spent most of my days in a BSL3 lab performing SNP genotyping of B. anthracis. However, I knew it was not to be my life's calling. I was hopelessly fascinated by the endless complexity of cancer, and I wanted to contribute to the fight against it. Before applying for a position at the Cancer Research UK Manchester Institute, I have been working as a Junior Research Associate in Dr Osmak's Laboratory for Genotoxic Agents at the Ruđer Bošković Institute, where on one of my projects I was investigating the molecular mechanisms of integrin-mediated response of human melanoma cells to targeted therapy. I was delighted when I heard that I was accepted for a PhD position in the Prostate Oncobiology group led by Dr Esther Baena. The aim of my research is to investigate the role of certain epigenetic regulators in prostate cancer (PCa) initiation and how they drive carcinogenesis towards castration resistant (CR) disease. I want to evaluate their tumorigenic potential in human CRPC cells and perform selective genetic targeting to develop new therapeutic strategies for patients with advanced PCa. Only three months in, and I am already completely smitten by Manchester and its people and I am discovering there is so much more to this wonderful city than great music and football.

Mark Williams

Greetings, my name is Mark and I'm originally from Rugby in the Midlands. I studied medicine at Cambridge, worked in East Anglia for a couple of years and moved up to Manchester in 2009 for my specialist training in clinical haematology.

I have always wanted to be a clinical academic, so when I relocated to the North I set about trying to find a suitable mentor and potential supervisor. Happily I found Tim Somervaille who gave me lots of good career advice and helped me to secure a Clinical Research Fellowship from the Kay Kendall Leukaemia Fund. My PhD with the Leukaemia Biology group will focus on identifying mechanisms of chemoresistance in acute myeloid leukaemia. I have cared for hundreds of patients with this condition and am motivated by their courage to try and advance our understanding of this devastating malignancy. I have two young children so my current interests include futile attempts at imposing discipline and trying to get out of the house as often as possible. Despite initial reservations (principally climatic) I have been fully converted to the northern lifestyle; Manchester is a great city and all food is better with gravy on it.

Matthew Howell

Hi, I'm Matt and I am originally from South Wales. I completed medical training at the University of Bristol before moving to Manchester to start work as a junior doctor.

I have just started a PhD as clinical fellow in the Signalling Networks in Cancer Group, led by Dr John Brognard. As a junior doctor I developed an interest in oncology and have spent the last three years working as a medical oncology registrar in the Christie Hospital. My PhD is looking for novel genetic drivers of lung cancer that can be targeted pharmacologically. This is a really exciting area of research and I am looking forward to the next few years greatly. Manchester has been home now for the last ten years and just keeps getting better.

Sam Humphrey

I'm Sam, I come from Stockport and studied an undergraduate Masters in Physics degree at the University of Manchester. Now working at CRUK MI, I haven't exactly travelled far!

I went into my degree with the intent of learning about how the universe works, from the fine grain structure of atoms in a lattice to how massive gravitational structures warp space-time. I learnt that the more knowledge you acquire about a subject, the more questions arise in that area. Towards the end of my degree I became excited by the idea of biological and medical physics. My Masters project was making computational simulations of electrical flows in the human atria and identifying potential drug targets for the treatment of atrial fibrillation. These ideas led me to take on a PhD in the RNA Biology group looking at developing high performance computing tools for the analysis of lung cancer data. I'm looking forward to using the mathematical and computational knowledge from my undergraduate degree in a biological environment, ever more showing that modern science is not just three independent subjects.

Pontecorvo Prize for Marija Maric

Marija Maric

Congratulations to Marija Maric who has been awarded the prestigious Pontecorvo Prize by Cancer Research UK. The prize, which was also won by a student at the University of Oxford, is worth £500 and is open to CRUK-funded students across the country.

It is awarded to the student who has produced the best PhD thesis and made the most outstanding contribution to scientific knowledge in their field. The award takes its name from the geneticist Professor Guido Pontecorvo, who worked at the Lincoln's Inn Fields laboratories in London from 1968-75. Funding for the prize is a result of the generosity of Professor Peter Goodfellow FRS, formerly Head of the Human Molecular Genetics Laboratory at the Lincoln's Inn Fields laboratories. Marija completed her PhD in Karim Labib's laboratory which moved to the University of Dundee during her final year. Her work has helped to uncover the molecular details underpinning a key step in the process of DNA replication. Defects in replication can lead to cancer-causing mutations so it is essential that we fully understand the mechanisms which control these events. Her work was published in the prestigious journal *Science* and Marija will shortly be embarking on the next phase of her career as a post-doctoral researcher at the newly established Francis Crick Institute in London.

9th International PhD Student Cancer Conference

By Julie Edwards, CRUK MI Postgraduate Manager

Congratulations to all CRUK Manchester Institute PhD students for organising an inspiringly successful student conference held during the summer.

The aim of this annual conference is to allow high calibre students from top cancer research institutes across Europe to organise and present at their own scientific conference. Manchester was chosen as the host Institute for the 9th International PhD Student Cancer Conference (IPSCC) and the CRUK MI students certainly took on this challenge with vigour. For those of you who have been involved in the organisation of a conference you will know the amount of hard work it can take to bring such an event together. Our students received a crash course in transferable skills with enthusiasm, culminating in exceptional results, producing an impressive scientific programme not to mention the highly successful networking and lively social events in Manchester. Arranging the weather posed no barriers for the organising committees, despite previous weeks of heavy downpours, they also managed to pull off sunshine and bright blue skies!

A huge thanks to all the CRUK MI students involved in the organisation - you should be extremely proud of your immense achievements in organising such a successful event. I hope you all enjoyed the experience!

Travel Award for Kate Hogan

Congratulations to PhD student Kate Hogan, who was awarded a Travel Award from the Society for Melanoma Research (SMR).

These awards are designed to help young scientists attend the annual Society for Melanoma Congress. With a grant of $1500, Kate travelled to the 12th SMR International Congress, which took place during November in San Francisco. It is the most important melanoma meeting in the calendar, and Kate was really excited about presenting her work on the role of UVA and UVB in melanoma, interacting with top scientists in the field and discovering the latest breakthrough research that will greatly benefit her career development.

Kate Hogan

CRUK MI students with Bruce Alberts.

IPSCC – the Students' view

By Emma Williams

This year it was our students' turn to organise and host the 9th International PhD Student Cancer Conference (IPSCC). The IPSCC is a student-led conference aimed at fostering scientific discussion and networking between PhD students from cancer research institutes in the UK as well as from other European countries.

All delegates are required to present a talk or a poster, thus this event often serves as the attendees' first opportunity to present their work at a scientific meeting.

The bar was set high following a fantastic 2014 conference at the DKFZ in Heidelberg, so the students commenced their planning early. Our team of 18 students split into sub-committees of finance, logistics, social and publications, overseen by our Postgraduate Manager, Julie Edwards. This was our first experience of planning such an event, and it was our responsibility to organise everything, from sponsors and abstract books to accommodation and catering!
One of our immediate priorities was to secure our keynote speakers, so we were delighted when Bruce Alberts and Mariann Bienz accepted their invitations. We also secured the youth hostel in Castlefield early on to accommodate our delegates. Our finance committee made great work of the difficult task of obtaining funds through grant applications and sponsorship package sales, whilst the publications committee managed the registration process and selected student speakers.

By the evening of 3rd June, after a last-minute re-arrangement of poster boards and conveyer belt-style packing of sponsorship bags, we were ready to greet our delegates. The next morning, 100 delegates arrived at The Christie NHS Foundation Trust Education Centre to commence our three-day meeting. UK-based delegates from CRUK institutes and The Francis Crick Institute joined students from DKFZ (Heidelberg), SEMM (Milan), NKI (Amsterdam) and MDC (Berlin).

A fantastic series of 20 student talks covered a range of basic and translational cancer research topics, including epigenetics, tumour microenvironment and the non-coding genome. The prize for best talk went to Kristyna Kotynkova from The Francis Crick Institute, who presented her work on the control of cleavage furrow formation by the Ect2 RhoGEF during cytokinesis. Our own Kate Hogan from Molecular Oncology received runner-up prize for her talk entitled 'Gene-environment interactions in melanoma'.

The keynote lectures were thoroughly enjoyed. Bruce Alberts gave a biography of his distinguished career and current focus on science education, whilst Mariann Bienz talked to us about her work on Wnt signalling. Our breakout sessions also proved extremely popular, with a careers-based focus and informal Q&A style. They were highly praised by our delegates, and we would like to thank everyone who came along to host one.

Logistically the conference ran very smoothly. We were especially proud of our success in transiting our delegates down Oxford Road to the youth hostel without losing a single one! Evenings were well spent, with live music on the first night and a formal dinner in Castlefield on the second.

Anna Woroniuk and Alekh Thapa at the registration desk.

Overall we were thrilled with how well the conference went and the great feedback we received. We look forward to the 10th IPSCC in Summer 2016, which will be hosted by the CRUK Cambridge Institute.

Postgraduate Showcase Success for Kate Hogan

We are pleased to announce that PhD Student Kate Hogan, from the Molecular Oncology group, won the prize for best oral presentation at the University of Manchester's Faculty of Medical and Human Sciences Graduate School/Graduate Society 3rd Annual Postgraduate Research Showcase.

The event, held in September provides postgraduate students with the opportunity to present their data via poster or oral presentations before an audience of their peers. Presentations were judged by a panel of PGR Directors, Tutors and Supervisors. During her talk, Kate explained how UVB but not UVA accelerates melanoma in a mouse model driven by the melanoma oncogene V600EBRAF.

Awards and Events

Funding success for John Brognard

John Brognard

Congratulations to Dr John Brognard, head of the Signalling Networks in Cancer group, who has been awarded a grant from the Lung Cancer Research Foundation (LCRF) to follow on investigations seeking to identify a novel target for therapeutic intervention in lung cancer.

Lung squamous cell carcinoma (LSCC) accounts for nearly 25% of lung cancer cases and causes approximately 400,000 deaths per year worldwide. Although targeted treatments are being used to treat other types of lung cancer, this is not currently the case for LSCC. Having previously identified a protein kinase (TNIK) that is important for sustaining survival in LSCC cell lines, John received funding from the LCRF. Preliminary data highlighted the important role TNIK plays in promoting proliferation and survival of LSCC cells, suggesting that it is an oncogene, a gene that has the potential to cause a normal cell to become cancerous. With this latest LCRF funding, John and postdoc Dr Pedro Ayuso-Torres aim to further validate TNIK as a novel target for therapeutic intervention in LSCC and to elucidate the molecular mechanisms through which TNIK mediates its functions.

Biochemical Society Travel Award

Congratulations to Natalie Stephenson from the Signalling Networks in Cancer group who has been awarded a travel grant from the Biochemical Society towards her attendance at the ASBMB conference on kinases and pseudokinases in San Diego. Natalie will be giving a talk and a poster presentation on her research into the molecular dynamic simulations of mutated kinases, and how these provide structural insights into the functional consequences of various mutations.

CRUK Research Travel Award Winner

Congratulations to Romina Girotti, a post-doc in Molecular Oncology, who has been awarded the CRUK Research Travel Award. This funding will provide her with the fantastic opportunity to travel to Argentina and expand her research.

She will spend three months with collaborators in Buenos Aires studying how the activation of galectins (a family of proteins that help tumour-immune escape and abnormal vascularisation) contributes to immune escape in metastatic melanoma patients resistant to targeted therapies and immunotherapies, with the ultimate goal of developing novel therapeutic strategies. The study aims to reveal new insights to improve our understanding of why melanoma patients fail on targeted therapies and hopes to pave the way for the development of new therapies capable of enhancing the anti-tumour immune response in melanoma.

Young Investigator's Award

Romina at the ECCO meeting

Romina Girotti, a postdoctoral researcher in the Molecular Oncology group, has been awarded the Young Investigator's Award by ECCO (the European CanCer Organisation) and EJC (the European Journal of Cancer). She received her award at the 18th ECCO - 40th ESMO European Cancer Congress in Vienna, which took place in September.

The Award is given to a young scientist or doctor in the field of basic, translational or clinical oncology research for recent original work in cancer research, treatment or care. Romina's research aims to establish new tools for personalised medicine in melanoma patients. Under the mentorship of Professor Richard Marais, Romina has contributed significantly to the field and produced a number of important publications. Her work has provided crucial insights into the molecular mechanisms underlying resistance to targeted therapies in melanoma and developing new therapeutics to treat resistant patients, in collaboration with The Institute of Cancer Research. As a result of this research, a Phase-I clinical trial started in 2015 in Manchester and London assessing novel panRAF inhibitors.

Academia Europaea

Institute Director Professor Richard Marais has been elected to the Academia Europaea. The academy covers a variety of academic disciplines including sciences and is composed of individual members. Membership is by invitation, which is made through peer group nomination followed by confirmation by the Council of the Academia.


Richard Marais

UM Cure 2020 consortium

Congratulations to Professor Richard Marais who is part of the successful consortium, UM Cure 2020, that has received EU funding through the Horizon 2020 scheme to develop new therapeutic approaches to treat metastatic uveal melanoma (UM), which at present is incurable.

UM is a rare intraocular disease, with an incidence of five cases per million individuals per year, and while the primary tumour can often be treated effectively, there is currently no effective treatment for its metastases. Half of UM patients develop metastases, most often in the liver, which are invariably fatal.

The multidisciplinary, pan-European consortium comprises specialists involved in UM patient care and expert academic scientists in basic, translational and clinical UM research, as well as a number of small and medium enterprises. With over €6 million, they propose to develop new therapeutic approaches for metastatic UM patients by identifying novel drugs or drug combinations. Richard and his team will apply their expertise in the generation of transgenic mouse models that recapitulate the physiopathology of UM progression and metastases formation; and in biochemistry and blood-borne biomarker detection to help describe the genetic landscape of the metastatic disease, giving further insight into tumour heterogeneity of metastases, all of which will ultimately help stratify patients with UM.

Travel Bursary for Melanie Galvin


Melanie Galvin

Melanie Galvin from the Clinical and Experimental Pharmacology group has been awarded a travel bursary from the NC3Rs to attend the IAT Animal Technicians Symposium. Here Melanie describes her attendance at the meeting and how this experience is helping her research.

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) and the Institute of Animal Technology (IAT) are organisations dedicated to the care and welfare of animals in science by advancing knowledge and promoting new discoveries and approaches to replace, reduce and refine the use of animals for scientific purposes. Attending the NC3Rs/IAT Animal Technicians' Symposium in London was of great interest to me, not only from a development perspective for myself but also for the Institute, therefore to be awarded a travel bursary enabling me to attend was a fantastic opportunity.

The Clinical and Experimental Pharmacology Group at CRUK MI have designed a protocol to extract Circulating Tumour Cells (CTCs) from Small Cell Lung Cancer (SCLC) patients, enabling the growth of tumours in mice which mimic the chemotherapy response seen in the patients. Having these mouse models has enabled us to trial novel compounds/ drug combinations with the aim to provide more effective treatment regimens for patients whose current prognosis is bleak.

A highlight of the Symposium was "best practice in rodent surgery". Passaging of the SCLC tumour models requires me to conduct rodent surgery on a regular basis, so hearing presentations address this very area was a great opportunity for me to ensure my team and I are working to the highest standards: performing careful aseptic technique; providing adequate peri-operative care; and always making the welfare of the animal the highest priority. With this in mind, the team have developed a new method of tumour passage, which eliminates the need for rodent surgery. By disaggregating the tumour, we are able to isolate the tumour cells and implant them into a mouse without performing an invasive surgical procedure. This decreases the severity of the procedure carried out and complies with the 3Rs principles.

The Institute also has a new NTCO (Named Training and Competency Officer) so I was also interested to hear the presentation "Working with the NTCO". The overview given at the symposium has enabled me to work alongside our new NTCO to improve training, competency and compliance within my team.

Recent Events

FLS – CRUK MI Away Day

The second joint Faculty of Life Sciences – Cancer Research UK Manchester Institute Away Day was held at the King's House Conference Centre in September, following on from the success of the inaugural meeting in 2013.

This year's event was attended by more than 50 researchers from across the two sites who all enjoyed the programme of talks presented by Allan Jordan, Angeliki Malliri, Iain Hagan, Crispin Miller, Tim Somervaille and Georges Lacaud from our Institute, along with a number of scientists from FLS. Topics ranged from the challenges facing drug discovery to cell signalling in breast cancer. The day provided a wonderful opportunity for everyone involved in cancer-related research, from basic biology right through to translational approaches, to enhance their knowledge, and importantly, to network and discuss their science. Already a potential collaboration has emerged between Iain Hagan and Alan Roseman from FLS to investigate whether it will be feasible to use cryo-EM – Cryo-electron microscopy, a form of transmission electron microscopy where the sample is examined at cryogenic temperatures – to study the structure of Protein Phosphatase 2A (PP2A) complexes purified from yeast. This would be an exciting and breakthrough pilot project which may challenge current thought on the structures of PP2A and transform this field of research. Mutations in PP2A have been associated with a very large number of cancers.

CRUK MI Junior Group Leader John Brognard receiving his Cancer Research UK Future Leaders' Prize from CRUK Chief Scientist and CRUK MI Group Leader Nic Jones

NCRI meeting

Researchers from the Institute enjoyed the recent National Cancer Research Institute (NCRI) Cancer Conference in Liverpool in November.

The NCRI was set up in 2001 with a mission to bring together all the key players in cancer research in the UK to identify where activity is most needed and where it is most likely to contribute to progress. More than ten years on, it comprises 22 partner organisations that collectively spend more than £500m on cancer research each year. As part of their activities, the NCRI organise an annual conference to provide a forum for the partners to exchange ideas across the cancer research spectrum. As previously, the conference took place over four days, with the very latest cancer research from across the UK, and further afield, presented in posters and talks and there was much to celebrate for the Institute.

John Brognard, leader of the Signalling Networks in Cancer group, was awarded a prestigious Cancer Research UK 'Future Leaders in Cancer Research' prize. He has been a Junior Group Leader at the Institute since September 2010 and has focused on identifying novel driver mutations in kinases. The prize recognises John's important discoveries concerning oncogenic and tumour suppressing cell signalling.

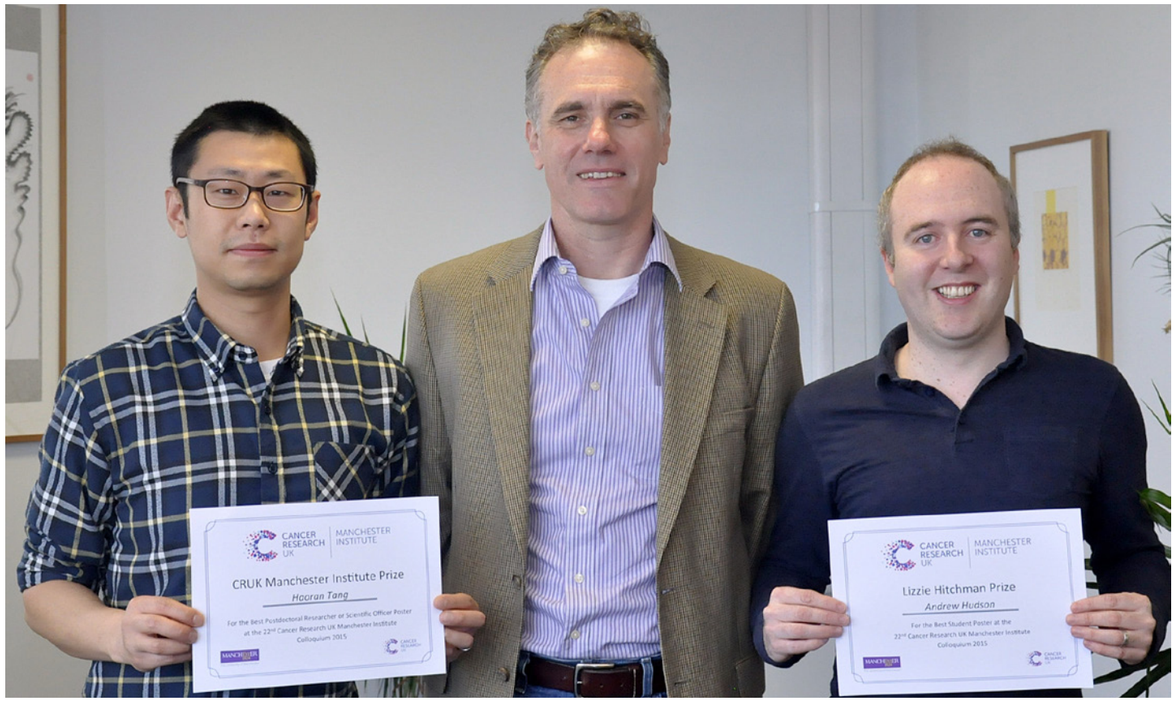
Another high profile prize went to Romina Girotti in the Molecular Oncology group, who received the British Association for Cancer Research (BACR) Translational Award for her work to implement personalised medicine for melanoma patients. Romina presented her progress at the conference during the 'Liquid biopsies with a twist' session. New Institute group leader Santiago Zelenay gave a great talk on his research into how tumour cells evade the immune system in the 'Immune checkpoints and cancer' session.

During the two poster sessions, there was strong Institute representation from the Clinical and Experimental Pharmacology group and the Drug Discovery Unit. Three popular posters from the DDU covered their latest advances in developing novel inhibitors of RET, PARG and IDH1 and highlighted the benefits of collaboration and industry partnership. Much of CEP's work focused on their pioneering research into circulating tumour cells, particularly in lung cancer.

Looking ahead, Caroline Dive will be chair of the scientific committee for the 2016 meeting, and she gave a brief speech to close the conference.

Fellowship for Dan Wiseman

Congratulations to Dan Wiseman, a Clinical Fellow in the Leukaemia Biology group led by Tim Somervaille who has been awarded a Clinical Research Training Fellowship from Bloodwise to continue his research in the group. Dan will be studying the interplay between mutations in the IDH and SRSF2 genes and the impact that this has on the development of Acute Myeloid leukaemia.



Poster Prize winners Haoran Tang and Andrew Hudson receiving their awards from Institute Director Richard Marais

Colloquium 2015

In September, the Institute Colloquium once again took place at Lancaster University. An annual event, the Colloquium offers the chance for our staff and PhD students to present and discuss their work and to develop collaborations with each other. Across three days, there were oral and poster presentations covering all aspects of cancer research taking place within the Institute.

Opening the first session, Institute Director Richard Marais gave an excellent overview of his group's progress in developing a personalised medicine approach for melanoma patients. In the subsequent sessions, talks covered a variety of topics on both fundamental and translational research. Among these was a fascinating presentation by new group leader Santiago Zelenay on his work exploring inflammation and immunity in cancer.

Each evening, a poster session took place. The best of these posters were chosen to receive one of two prizes. Winning the Lizzy Hitchman prize for best poster by a PhD student was Andrew Hudson of the Signalling Networks in Cancer group. Andrew is a Clinical Research Fellow and has been looking at large scale cancer genomics datasets. His latest work was to create a screen to identify key tumour suppressing proteins and potential new targets for the development of novel therapeutics.

The prize for best poster by a post-doctoral researcher or scientific officer was Haoran Tang from the Molecular Oncology group. He has investigated the role played by an enzyme known as LOX in cancer. LOX is known to cross-link collagen and elastin, and can therefore alter the structural support surrounding cells. HaoRan found that it regulates growth factor receptor signalling, allowing it to control tumour growth and progression.

New Group Leader - Santiago Zelenay

Santiago Zelenay

Santiago Zelenay joined the Institute this summer as a Junior Group Leader to form the Cancer Inflammation and Immunity Group, which will investigate the mechanisms that control natural and therapy-induced anti-tumour immunity.

Born in Argentina, Santiago studied Biology at the University of Buenos Aires where he started his career in immunology working as an undergraduate student on vaccines based on immunisation with DNA. He then moved to the Gulbenkian Institute of Science in Portugal where he obtained his PhD in Immunology studying the origin and function of regulatory T cells. In 2008, Santiago joined the group of Caetano Reis e Sousa at the Cancer Research UK London Research Institute. There he was awarded EMBO and Marie Curie postdoctoral fellowships to examine how damaged and dead cells are recognised and processed by immune cells in order to activate T cell responses against infectious organisms and tumours.

His most recent work on tumour immunity was published in the journal *Cell* last September and constitutes the basis for some of the current research questions of his group. This study highlighted the view that there are two types of cancer-associated inflammation. One 'bad' usually found in aggressively growing tumours that promotes several key aspects of malignant growth and one 'good', with cancer inhibitory properties, characterised by increased levels of anti-tumour immune factors typically associated with improved prognosis and clinical benefit following treatment. Notably, this work suggested that anti-inflammatory drugs such as aspirin, could be used to manipulate the type of inflammation and to enhance the efficacy of immune-based cancer therapies. Thus, combining the use of genetically engineered cancer models with the analysis of patient samples, a main objective of the recently established Cancer Inflammation and Immunity Group is to identify and examine cellular and molecular mediators that regulate the balance between 'good' cancer-preventive and 'bad' tumour-promoting inflammation.

Post doc Eduardo Bonavita will be soon joining Chikkanna-Gowda CP and Santiago in an actively recruiting team, whose ultimate goal is to improve our understanding of the immune response to cancer in order to design new therapies for patients.

Lung Cancer Centre of Excellence Summer Conference

The Centre successfully held its first "CRUK Lung Cancer Centre of Excellence - Student/Post Doc Summer Conference" during the summer at the Royal York Hotel in York.

For the first time the two-day conference brought together PhD students, Clinical Research Fellows and Post-doctoral Research Fellows from Manchester and London working in lung cancer to meet and share their research and ideas.

There were two excellent keynote presentations – Professor Charlie Swanton, Chair in Personalised Cancer Medicine at the Francis Crick Institute, who spoke about "Lung Cancer Evolution- Implications for Drug Development" and; Professor Sam Janes, Professor of Respiratory Medicine at UCL, who gave an insight into "Unlocking the pathogenesis of early squamous cell lung cancer".

Sessions covered all eight of the Centre's research themes and gave students/post docs the chance to present and receive feedback from the Centre's leading academics, find out about possible lung cancer career routes and fellowship opportunities, and talk informally to Cancer Research UK staff and senior academics about potential research ideas.

Over 75 PhD students and Post Docs from both Manchester and University College London attended the conference, along with a number of the Centre's senior academics and research theme leads. It was great to see everyone interacting, asking questions and making the most of the two days; with delegates already talking about potential joint research collaborations and ways to take the research forward.

The conference ended with a prize giving presentation for the 'Best Oral Presentation' and 'Best Poster' for both PhD students and Post Docs alike. Our congratulations go to this year's winners:

- Garima Khandelwal (CRUK Manchester Institute) – Best Post Doc Poster
- Laura Succony (UCL) – Best PhD Poster
- Laura Bennett (CRUK Manchester Institute) – Best Post Doc Oral Presentation
- Nicholas McGranahan (Francis Crick Institute) – Best PhD Oral Presentation

Manchester Lung Cancer Research Features at Royal Society

Visitors to the Royal Society learn about CTCs

Cutting-edge research from the Cancer Research UK Manchester Institute that could improve treatment for lung cancer patients was recently showcased at the Royal Society's Summer Science Exhibition in London.

A prestigious annual event, the exhibition offers the opportunity for research organisations from across the UK to present aspects of their work to the general public and highlight the best of British innovation in science and technology. This year it took place during the summer at the Royal Society's headquarters in central London. The Manchester exhibit was entitled 'Beating cancer' and focused on circulating tumour cells (CTCs), which could hold the key to better diagnosis and treatment of lung cancer.

CTCs are cancer cells that have broken off a patient's tumour and are floating in their blood. Pioneering work by Professor Caroline Dive's Clinical and Experimental Pharmacology group has shown that the level of CTCs in patients with small cell lung cancer relates to their survival – patients with fewer CTCs live longer.

The research could lead to the use of a blood test that allows doctors to predict how a patient will respond to a particular drug, and to monitor their treatment. It also potentially offers the chance for minimally-invasive genetic profiling, leading to more personalised therapies.

Visitors were invited to explore how scientists capture and investigate these CTCs, through an interactive 'hurricane tube' and giant labyrinth game. Researchers from Manchester and other Cancer Research UK-funded scientists were on hand to explain and discuss the exhibit and the science behind it.

The exhibit was funded by Cancer Research UK and The Physiological Society and developed by Cancer Research UK's Research Engagement team.

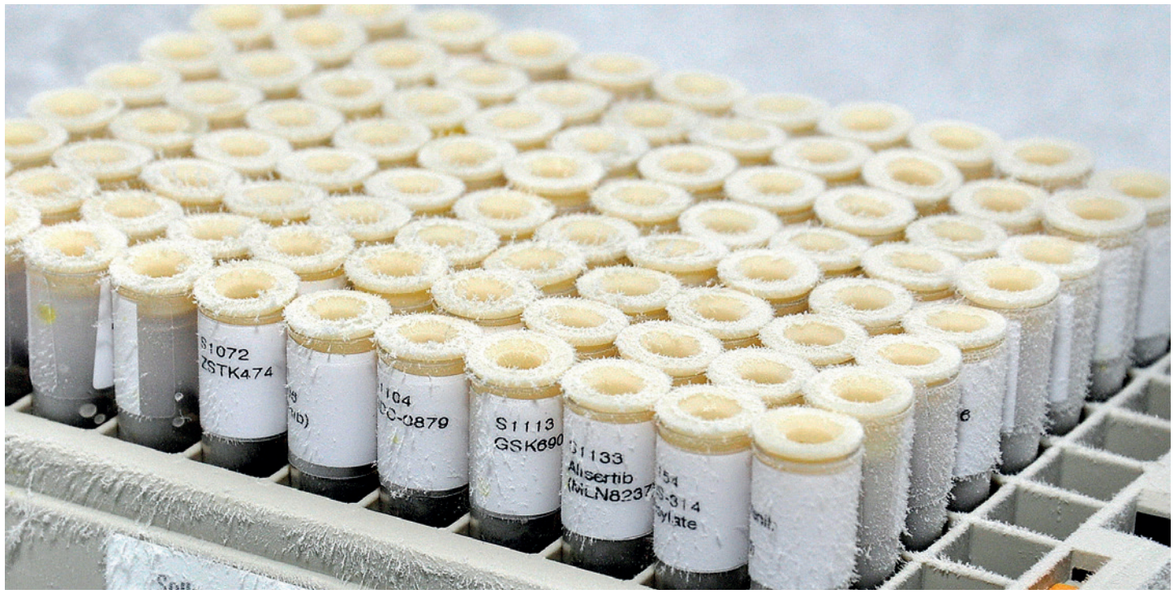
Inaugural MCRC Autumn School

Following the appointment of the Cancer Research UK Manchester Centre to Major Centre status – an investment that will help Manchester transform personalised medicine for cancer treatment – the Centre hosted an Autumn School to promote the centre, network with other centres and showcase its research strengths.

Postdocs and final-year PhD students were invited from the five CRUK Research Institutes (Manchester, London, Oxford, Cambridge, and Glasgow) as well as from Edinburgh, Belfast, UCL and Leicester. The event, held in October, comprised a comprehensive programme dedicated to personalised medicine, including talks from Dr Liz Patton (from the Edinburgh CRUK Centre), Professor Richard Marais and Professor Caroline Dive amongst many others.

The event started off with a plenary talk presented by Professor Rene Bernard from the Netherlands Cancer Institute and was followed by an enjoyable evening of viewing posters and discussing science. Over the subsequent two days, the audience learned about personalised medicine, drug discovery, clinical trials and biomarkers. These sessions were broken up by tours around facilities in the Paterson Building as well as The Christie NHS Foundation Trust Clinical Trials Unit and the University of Manchester's Wolfson Molecular Imaging Centre. Feedback was very encouraging with many people commenting on how much they enjoyed the event.

Core Facilities Update



Midas Library

Looking for Drugs with the Midas Touch

Identifying potential new anti-cancer drugs often entails some sort of screening process. Scientists will try and find a compound that targets the protein responsible for driving a particular type of cancer.

The growth of cancer cells will be assessed in the presence of many different small molecules, which together form a library that will be compiled from selected compounds based on their novelty, diversity, drug-like properties, and chemical structure.

The MIDaS (Manchester Institute Diversity Set) compound collection has been specifically designed to allow screening with around 22,000 compounds with the capacity for the collection to expand. The library was chosen based upon computational analysis of commercially available compounds to select chemicals with the correct physicochemical properties whilst avoiding those that are known to cause interference and false positive hits that often plague screening applications. The chemists in the Drug Discovery Unit examined the selected compounds in order to remove any rogue undesirable compounds that may have slipped through the computational filtering. This "cleaned" or curated library was then clustered such that closely related compounds were grouped together and a single representative of each cluster chosen to be included in the collection.

In addition to the MIDaS library, the compound collection also includes subsets such as an FDA approved 1200 compound set and a target-focused collection of clinical, pre-clinical and literature compounds which are known to interact with either kinases or epigenetic targets.

The MIDaS collection is now available for use by the Institute's scientists to identify potential new drugs for their targets of interest. Screening so many small molecules is facilitated by suitable automation that is now available in the Institute's Molecular Biology Core Facility through the Echo acoustic dispensing platform.

New Transgenic Production Facility

Natalia Moncaut and Mark Willington

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

At the Cancer Research UK Manchester Institute, the only animals we use in our research are mice and we use them only when there is no alternative. Most of the mice we use have altered genetics, which enables us to study and identify the genetic basis of different cancers and target ways in which these might be treated. In order to facilitate this work, we have set up a new core research facility to produce transgenic mice. This is led by Natalia Moncaut who joined the Institute in September.

After completing her PhD in molecular biology at the University of Porto in Portugal, Natalia was introduced to mouse transgenesis while working as a postdoctoral fellow first with Moises Mallo at the Gulbenkian Institute of Science in Portugal and later with Peter Rigby at the Institute of Cancer Research in London. In both labs, she generated transgenic mouse models on a routine basis in order to understand the transcriptional regulation of muscle genes during development and how hox genes pattern the axial skeleton.

More recently, Natalia became a member of the CRUK London Research Institute Transgenic Services where she expanded further her expertise in mouse transgenesis. Natalia was responsible for introducing and establishing the new CRISPR-Cas system to the facility and successfully generated several genetically modified mouse lines using this technology.

The objective of the new Transgenic Production Facility at the CRUK Manchester Institute is to work closely with research groups to design the targeting approach based on their needs and provide fully customisable support to enable the successful achievement of the experimental aims. The facility will be responsible for the targeting strategy design, generation of required reagents, breeding, genotyping and cryopreserving new mouse lines. It will use three main approaches to generate new transgenic mice: DNA pronuclear injection, ES cell targeting and CRISPR-Cas.

CRISPR-Cas is a simple and flexible genome editing technology that has the potential to speed up the generation of mouse models and as such, has revolutionised the field of transgenic mouse production.

Mark Willington from the Biological Research Unit has also joined the Facility bringing all his years of expertise in mouse work, and a third post will be added soon.

New Research Building Open and Ready for Science

The MCRC Building as seen from the green swathe

Early this year, construction finished on the new Manchester Cancer Research Centre (MCRC) building. The new building offers state-of-the-art laboratory space for cancer research scientists alongside offices for clinical trials support staff and clinical academics.

The cutting-edge facility, located opposite The Christie NHS Foundation Trust and the Cancer Research UK Manchester Institute, is set to pull in more world-class researchers to the city, boosting scientific progress and helping to get improved treatments to patients faster.

In May, the first office-based occupants from the University of Manchester and The Christie moved in, and during June there was a week of events to celebrate the opening. This included an exclusive preview evening for major donors and key staff from the MCRC's partner organisations. Guests were invited to take a tour around the building, have a look inside the laboratories and hear from current MCRC scientists.

Throughout the week, events were held for many other groups, including staff from all three partner organisations of the MCRC (The Christie NHS Foundation Trust, The University of Manchester and Cancer Research UK), fundraisers, school children and local residents. The end of the week featured a public open day that included fascinating talks on drug discovery and proton beam therapy on top of a variety of hands-on activities and tours of the building.

September saw the opening of Café VIVO in the building's atrium. The café is open to the public and offers a range of hot and cold drinks as well as sandwiches, soup and jacket potatoes.

Over the summer, there has been additional internal building work to make minor modifications to some of the laboratory space, in preparation for occupation by scientists. In particular, the facilities for cell culture have been increased. Research groups have begun to move into the new building and by early 2016, most of the laboratories will be occupied by various teams from the CRUK Manchester Institute and the Institute of Cancer Sciences.

The building has been fitted out with all new specialist equipment, including large -80°C freezers, laminar flow cabinets and incubators. In addition, a flow cytometry machine was recently installed.

CRUK Chief Scientist and MCRC Director Nic Jones gives the opening address at the start of the week's events.

Images left to right: Emma Williams demonstrates gel loading to a scientist of the future; the MCRC Building by night; Esther Baena explains her research on prostate cancer to guests including Harpal Kumar, the CEO of Cancer Research UK; guests enjoy the opening reception in the atrium; the central staircase. MCRC Building photos by David Millington.

Staff News

Climbing the highest mountain in Africa

Jason at the summit of Kilimanjaro

Jason Farrand, a new Scientific Officer in the BRU, had an exciting adventure this summer. In June he climbed the largest freestanding mountain in the world, Mount Kilimanjaro.

He completed the trip over 13 days, 7 days on the mountain and the rest in the hotel in Tanzania. It was certainly a challenge, especially on days when the group was trekking for over 8 hours, and when altitude sickness meant that some of them couldn't complete the climb, but the friendly group kept each other going.

Jason said: "It is something that I have wanted to do for a while. The whole trip was an experience I will never forget, the sights you see each day are spectacular. I would definitely recommend it to others, and even do it again myself."

CRUK Shine Night Walk

Mandy, Richard and Ellie ready to Shine!

Mandy Watson, Lead Biologist in the Drug Discovery Unit, completed the CRUK Shine Night Walk in September along with her husband Richard and daughter Ellie.

The event is a night-time walking marathon around London which set off from Southwark Park and the participants lit up the streets with glow-sticks, neon face paint and bright clothes. Mandy and her family raised a tremendous £1746 for CRUK.

Social Events

Bar Rally

The equine winners and highland losers

The Bar Rally is an annual event that takes place every Autumn in which the Institute's various groups engage in a bit of friendly competition.

The groups adorn themselves in fancy dress and embark on a mystery tour of the local bars, completing fun tasks and quizzes along the way. Each year there is a theme and this year it was 'sports'; we had Highland Gamers, bowlers, jockeys and their horses, bullfighters and bulls, Quidditch players and equipment (goal posts, brooms and a golden snitch!)

It is a fun event and a great way for the new students and staff to get to know their colleagues outside of the lab.

The victors this year were the Leukaemia Biology/ Prostate Oncobiology groups and the unlucky losers were the Signalling Networks in Cancer group who now take up the challenge of organising next year's event.

Summer Party and Newcomers' Party

For the third year the Director's office has organised social events that continue to be enjoyed by staff across the whole Paterson Building.

The Summer party was held on a lovely sunny evening in July in a local pub, which supplied a delicious Mexican feast. At the party Allan Jordan was presented with his CRUK Inspiring Leadership in Research Engagement Award.

The Newcomers' party was held in October and is a chance for staff to welcome new students, scientists and others workers to the building. We like to give a warm welcome especially to the new PhD students starting their research projects in October who will be spending the next four years at the Institute.

In the spotlight with Alba Marques-Diaz

Alba Marques-Diaz is a post-doctoral researcher in the Leukaemia Biology group. Originally from Madrid in Spain, Alba received her PhD from the Spanish National Cancer Research Centre (CNIO)/ Universidad Autónoma de Madrid moving to the Manchester Institute in 2014. Her research is focused on understanding the mechanisms of action of LSD1 inhibitors which have potential for treating Acute Myeloid Leukaemia.

1. **What is your favourite part of the UK?**
   Difficult to choose only one! I love all the countryside I've visited so far (Lake District, Peak District...). I'm impressed with all the tones of green that you see everywhere.

2. **What was your best ever holiday and why?**
   A month in an international camp in Beirut (Lebanon) when I was 17 years old. It opened my eyes and made me see the world differently.

3. **Which website do you always check, and why?**
   I can't live without Spotify, life sounds better with a soundtrack.

4. **What is your favourite film?**
   "Mujeres al borde de un ataque de nervios" (Women on the Verge of a Nervous Breakdown) from Almodovar.

5. **What is your favourite band/singer?**
   Nina Simone, especially the song "Ain't got no/ I got Life".

6. **If you had to change careers tomorrow, what would you do?**
   I would (love to) be a Clown.

7. **What is the most important lesson that you have learnt from life?**
   Happiness is handmade.

8. **Name three things you would take with you to a desert island?**
   Photos from my family and friends, my boyfriend and a good mattress.

9. **What is your greatest fear?**
   Global warming and all conflicts that will come (and are already happening) associated with the shortage of natural resources (such as water, food...).

10. **How would you like to be remembered?**
    With a big smile.

11. **If you could change one thing in your past what would it be?**
    Learn earlier that achieving something is to a great extent, a matter of believing in yourself.

12. **What is your signature dish to cook?**
    Tortilla de patatas, in my grandmother's style!

13. **You've just won the lottery and have £5 million pounds to spend. What do you buy first?**
    I would throw a big party and send money to the refugees.

14. **What is your idea of perfect happiness?**
    To be doing what I want to do in each moment.

15. **What keeps you awake at night?**
    It's quite difficult to keep me awake at night...but if there is one thing, it would be family issues.

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