Winter 2014

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Director’s Introduction

Last month it was my privilege to chair the National Cancer Research Institute (NCRI) conference which took place in Liverpool. This meeting is an annual international multidisciplinary meeting held in the UK with the aim of airing the most recent and exciting developments in cancer research.

The NCRI brings together stakeholders from across the cancer research spectrum, including scientists, clinicians, healthcare professionals and patient advocacy groups, a breadth that allows broad discussion of many of the issues relevant to cancer research. This year marked the 10th anniversary of the meeting, a milestone that allowed the opportunity to reflect on the progress made during the decade that the conferences have been running, and also to look forward to what the future may hold. It was particularly pleasing to see a high level of participation at the meeting from members of the Institute and you can read more about this later on in the newsletter.

Our recent research engagement events have been a tremendous success so many thanks to everyone involved. October was a particularly busy month as we hosted lab tours as part of the Manchester Science Festival, and our Open Day in November was attended by over 100 CRUK supporters. We held a public engagement lecture in the centre of Manchester about the future of prostate cancer research and treatment, which was attended by over 100 members of the public. The event was held to celebrate the establishment of our November Prostate Cancer Centre of Excellence which is a joint venture with Queen’s University Belfast. The evening offered an excellent opportunity to discuss our ambitions with many local prostate cancer patients and survivors.

I am also pleased to note that the success of last year’s national science cakes’ competition was replicated this year with Gemma Forrest a very worthy winner of the Institute’s prize for her creation of a cake depicting a laboratory.

As 2014 draws to a close, there is much to look forward to in the coming year. Santiago Zelenay will join the Institute in spring as a new Junior Group Leader, working in the area of melanoma immunology. The 9th International PhD student conference will be held in Manchester and promises to be an exciting and rewarding experience. Our students will be organising and hosting the event, so good luck to them. In early 2015, the new NCRI building is set to open allowing for expansion of cancer research activity on this site.

Finally, I would like to thank everyone for their hard work during the year and to take this opportunity to wish everyone a Happy Christmas and a very successful 2015.

Richard Marais
Director

Thank you to Darren Roberts

We would like to say a big thank you to Darren Roberts as this is his last issue as a member of the editorial team. As well as all of his efforts on the newsletter, Darren has also been a committed host of the Institute’s post-doctoral seminar series for many years as well as putting in a lot of work organising teams for the Keswick to Barrow walk for a number of years. Thank you Darren!

In November, scientists from the CRUK Manchester Institute and others based within the Paterson building attended the 10th annual National Cancer Research Institute (NCRI) Cancer Conference in Liverpool.

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 who collectively spend more than £500m on cancer research each year. As part of their activities, the NCRI organise an annual meeting to provide a forum for the partners to exchange ideas across the cancer research spectrum.

The 10th annual meeting took place over four days, with the very latest cancer research from across the UK presented in posters and talks and Manchester certainly had a lot to contribute.

Professor Richard Marais, Director of the Institute, was 2014 Chair of the Scientific Committee. Along with the rest of the committee, he was responsible for developing and organising the programme for this year’s conference.

There were also workshops and symposia hosted by other group leaders from Manchester: Professor Caroline Dive led a session looking at circulating biomarkers, Dr Claudio Jorgensen chaired an afternoon of talks discussing developments in pancreatic cancer research, and Dr Donald Ogilvie introduced a series of presentations on cancer drug discovery.

Several institute members were chosen to give oral presentations at the conference: in the cancer drug discovery session, Romina Girotti from the Molecular Oncology group spoke about her exciting work investigating the use of pan-RAF inhibitors to treat those melanomas that are resistant to BRAF or BRAF/MEK inhibitors. The Clinical Trials Showcase offered Corinne Fairefinn, a clinician scientist who works both at the University and The Christie hospital, the chance to talk about the practice-changing international REST trial that looked at the use of thoracic radiotherapy in late stage lung cancer. Louise Carter, from the Clinical and Experimental Pharmacology group, presented her work exploring molecular status and heterogeneity of small cell lung cancer using circulating tumour cells in the lung cancer session.

Many more Manchester scientists presented their research in the poster sessions. Highlights from the Institute included Natalie Stephenson from the Signalling Networks in Cancer group with her work on MLK4 mutations in colon cancer, and Amaya Viros and Kate Hogan from Molecular Oncology both presenting studies investigating UV radiation in BRAF-driven melanoma.

There were also several posters from the Drug Discovery Unit – amongst these Phil Chapman, Gemma Hopkins and Dominic James. The Clinical and Pharmacology group contributed a selection of posters: Rob Metcalfe’s abstract on using tissue analysis software to automate characterisation of CTCs was shortlisted for the BACR poster prize, and others looked at techniques for enrichment of CTCs and studies involving small cell lung cancer.

Thank you to Darren Roberts

NCRI Meeting 2014

By Katy Holliday

Cover Image: Allan Jordan, Head of Chemistry in the Drug Discovery Unit, was presented with his Flame of Hope Special Commendation Award for Research Engagement, by Richard Marais, at the Institute’s Summer Party. Allan’s awe-inspiring and outstanding efforts to raise awareness for CRUK and engage with the public make this a very worthy award. Find out more about Allan’s engagement work in our Fundraising pages.

Allan Jordan receives his award from Richard Marais.

Feature Article - NCRI Meeting 2014

By Katy Holliday

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Images left to right: Caroline Dive who gave a presentation as well as chairing the Circulating Biomarkers session, PhD student Kate Hogan presenting her work, Professor Richard Marais opens the meeting.
New Clues to Skin Cancer Development Show Sunscreen is not Enough

The Molecular Oncology group has shown that sunscreen cannot be relied upon alone to prevent malignant melanoma, the most deadly form of skin cancer. The work, published in the journal Nature, supports the approach taken by public health campaigns that call for people to use a combination of shade and clothing to protect their skin, applying sunscreen to the areas you can’t cover.

The research explains more about the mechanism by which UV light leads to melanoma and also explores the extent to which sunscreen is able to prevent UV light from damaging healthy cells. The study, carried out at the Manchester Institute and at The Institute of Cancer Research in London, examined the molecular effects of UV light on the skin of mice at risk of melanoma and whether disease development was blocked by sunscreen.

UV light directly damages the DNA in the skin’s pigment cells, increasing the chances of developing melanoma. Crucially, the research showed that it causes faults in the p53 gene, which normally helps protect from the effects of DNA damage caused by UV light. The study also showed that sunscreen can greatly reduce the amount of DNA damage caused by UV, delaying the development of melanoma in the mice. But, importantly, the study also found that sunscreen did not offer complete protection and UV light could still target p53 to induce melanoma, albeit at a reduced rate.

Professor Richard Marais, who led the study, said: “UV light has long been known to cause melanoma skin cancer, but exactly how this happens has not been clear. These studies allow us to begin to understand how UV light causes melanoma.

“UV light targets the very genes protecting us from its own damaging effects, showing how dangerous this cancer-causing agent is. Very importantly, this study provides proof that sunscreen does not offer complete protection from the damaging effects of UV light.

“This work highlights the importance of combining sunscreen with other strategies to protect our skin, including wearing hats and loose fitting clothing, and seeking shade when the sun is at its strongest.”


Insight into Control of Blood Cell Creation

The Stem Cell Biology and Stem Cell Haematopoiesis groups have discovered more about the role of a particular gene in the formation of blood cells – work that could help improve understanding of cancer development.

New blood cells are created through a process known as haematopoiesis. The RUNX1 protein has a critical function in enabling precursors of blood cells to emerge from specialised cells called the haemogenic endothelium (HE). However, HE cells are rare and short-lived, making them hard to study. Now our researchers have looked at a new method to assess how RUNX1 controls the haematopoietic process.

Dr Georges Lacaud, who led the study, said: “We’ve known for a while that RUNX1 is important in haematopoiesis, but the rapid changes in the cells involved in the process mean that so far scientists have only been able to explore a small part of its activity. We wanted to try a different approach in order to capture more information about how RUNX1 controls the behaviour of cells in HE.”

The team used a technique known as DamID (DNA adenosine methyltransferase identification) to deposit ‘tags’ at points on the DNA that interact with the RUNX1 molecule, and then detected the location of these tags. By looking at the location of the tags, they could identify which genes were switched on by RUNX1. The work found an unexpected role for RUNX1 in regulating cell adhesion- and cell migration-associated genes within the HE, as it had previously been thought to be more of a haematopoietic regulator. They also identified that one form of the protein, RUNX1b, specifically activates binding and migration of HE cells.

“A key step in HE-mediated haematopoiesis is the formation of HE cell clusters, which are essential for the release of cells that go on to become blood cells. This study suggests that RUNX1 is responsible for organising these clusters. Our technique will allow further study of RUNX1 that could inform both cancer research and regenerative medicine,” added Dr Lacaud.


Mixing it up for Resistance in Melanoma

The protein BRAF has been shown to contain the mutation V600E in several tumours and this mutation results in a constant “on” signal being sent to the cell via the RAF pathway driving the tumour’s progression. In melanomas, the use of drugs such as vemurafenib (BRAF inhibitors) switching this pathway off can lead to rapid and large reductions in the tumour.

Within two to eighteen months, however, the tumour has often adapted to avoid these drugs and returns in a resistant form. Work led by the Signalling Networks in Cancer Group has shown how some tumours bypass the drug’s “off” signal and provides a strategy to treat these tumours. Their work demonstrated that tumours upregulate a family of kinases, the mixed-lineage kinase (MLKs), which work to bypass the proteins targeted by the RAF inhibitors and switch the pathway back on allowing the tumours to once again grow.

The work demonstrated that MLKs are responsible for re-activation of the MEK/ERK pathway downstream of the RAF inhibition and directly phosphorylate MEK. Introduction of MLKs-4 into V600E positive cell lines led to resistance to RAF inhibitors and increased survival. In addition MLKs were shown to increase resistance to RAF inhibitors in an in vivo model and MLKs were found to be upregulated in melanoma patients with acquired drug resistance. As previous MLK mutations had been described, these were investigated and found to be mainly gain-of-function mutations which would confirm the role of MLKs in the development of resistance to RAF inhibitor therapy and may imply a role in melanoma formation.

Additional work may lead to therapies which target the MLKs allowing the treatment of melanomas which have developed resistance to RAF inhibitors.


New Drug Active Against Most Aggressive Type of Lung Cancer

Scientists from the Clinical and Experimental Pharmacology group have shown that a new drug could prove useful in treating small cell lung cancer - the most aggressive form of lung cancer. They teamed up with experts at AstraZeneca, as part of a collaboration agreed in 2010, to test a drug – known as AZD3965 - on small cell lung cancer cells. The research also helps identify which patients are most likely to respond to the treatment.

One treatment approach currently being investigated by cancer scientists is finding drugs that exploit the change in energy production in tumours. In cancer cells there is a switch to using glycolysis, a process that requires less oxygen and produces lactate as a by-product. Certain molecules – monocarboxylate transporters (MCTs) – are involved in the movement of lactate out of cells and drugs that target MCTs have been shown to stop tumour growth. The team tested a new drug that targets one of these molecules, MCT1, in lung cancer cells and in mouse models.

Professor Caroline Dive, who led the research, said: “Small cell lung cancer has a dismal prognosis and we have seen little improvement in treatment for many years. More targeted therapies are needed to help those patients whose tumours become resistant to chemotherapy. This new drug – AZD3965 – is currently in clinical trials, but it has not yet been tested in small cell lung cancer.”

The team investigated the sensitivity of small cell lung cancer cells to AZD3965 and showed that in those cells lacking an alternate lactate transporter, MCT4, the drug had an effect. They then found that the drug increased the level of lactate in cells and, more importantly, reduced tumour growth. They then looked at tumour samples taken from lung cancer patients and found that high levels of MCT1 were linked to worse patient prognosis.

Professor Dive added: “We propose that this drug will be most useful in this subset of patients who have elevated MCT1 levels and need more effective treatments. Our laboratory results are promising and certainly provide encouragement to test this treatment clinically in patients with small cell lung cancer.”


New Blood Cells Created Through a Process Known as Haematopoiesis

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Insight into Control of Blood Cell Creation
New Groups

This summer, we welcomed two new Junior Group Leaders to the Institute. Esther Baena and Michela Garofalo. Michela is originally from Italy and joins the Institute from Ohio State University. Esther is from Spain and joins us from Harvard Medical School where she was a post-doctoral research fellow. Here they introduce their groups and describe their future research plans.

Transcriptional Networks in Lung Cancer

By Michela Garofalo

Currently the group includes Peter Magee, who has been appointed as a scientific officer and Srivatsava Naidu, a post-doctoral fellow. Peter got his Ph.D. from Salford University in 2011. Srivatsava obtained his Ph.D at the Justus-Liebig University, Germany in 2009. Another post-doctoral fellow, Lei Shi will be joining us in January from the Institute of Pathology, Munich University.

Lung cancer still represents a very deadly disease with non-small cell lung cancer (NSCLC) accounting for 85% of all lung cancer cases and an overall ten year survival of only 5%. Therefore, there is an urgent need for new and effective therapeutic approaches. In this context, TRAIL may represent an alternative therapeutic molecule for this type of cancer. Several TRAIL inhibitors have recently entered clinical trials and seem to be effective in a small fraction of lung cancer patients; however, as with other molecularly targeted agents, resistance is likely to develop. We have recently found several dysregulated miRNAs in cells with acquired TRAIL-resistance compared to the parental sensitive cells. A set of the up-regulated miRNAs is transcriptionally activated by NF-kB. Combination of TRAIL and NF-kB inhibitors have shown, in vitro and in vivo, increased apoptosis and reduced cell proliferation in TRAIL resistant cells compared to treatments involving TRAIL or NF-kB inhibitors alone.

The application of miRNAs to cancer therapeutics and diagnostics is emerging as an important field of gene therapy. Both miRNA replacement and miRNA inhibition strategies have been successfully used to restore normal gene networks in vitro and in vivo, evidencing the huge potential of miRNAs as therapeutic tools in the fight against cancer. At the moment we have identified a p53-regulated microRNA cluster whose modulation drastically potentiates the response to chemotherapy. The biggest challenge in small RNA therapy remains the efficient and specific delivery to the desired target tissues. We are currently working on the generation of new delivery systems to be complexed with microRNAs and tested in vitro and in vivo in mouse models of lung cancer.

Prostate Oncobiology

By Esther Baena

The aim of the Prostate Oncobiology group is the identification of the signalling pathways and cellular subtypes supporting prostate tumour progression to the lethal castration-resistant stage - which occurs when the cancer becomes resistant to hormone therapy.

Prostate cancer (PCa) is the third leading cause of cancer-related mortality. Prostate carcinomas exhibit a remarkable diversity in behaviour and lack of pathological subclasses associated with patients’ outcome. A central challenge in PCa is the identification of those patients with cancer whose disease will eventually progress to the lethal stage. In advanced disease, first-line therapies are initially effective, but progression to castration-resistance PCa is inevitable. Thus, the variation in prostate cancer clinical heterogeneity represents an opportunity to identify and understand molecular features that can be used to stratify patients into clinical subgroups.

Understanding molecular events leading to castration-resistant prostate cancer is key for the development of improved therapies for such patients. Our previous work suggested that cellular metabolism alterations promote disease progression to the castration-resistant stage. We are currently working to identify which metabolic pathways are critical to castration-resistance acquisition, and how disruption of the selected pathway by gene targeting and drug treatment affects tumour growth and progression in vivo.
**Manchester Science Festival**

The Manchester Cancer Research Centre kicked off the Manchester Science Festival with an evening of immersive theatre. Guests were able to inspect their own cheek cells under a microscope, use a simulator to have a go at keyhole surgery, and learn about personalised medicine, before enjoying a play about the life of Henrietta Lacks.

Henrietta was born into a poor farming family in Virginia in the 1920’s and died of cervical cancer just thirty years later with no idea that she was about to make an immense contribution to the world of science. Her cancer cells – so called HeLa cells – were immortalised and grown in the lab, and have been used for research into cancer, polio, TB and AIDS ever since. They are still being used in Manchester today.

The Institute then opened its doors for an afternoon of public lab tours. During a welcome to the building from Dr Allan Jordan, guests got to grips with epigenetics using a delicious demo involving marshmallows, strawberry laces and jelly tots! Visitors then had the chance to explore our Drug Discovery Unit and our Molecular Biology Core Facility.

Scientists from the Institute also took part in Science Spectacular. This is a huge family fun science fair at Manchester Museum, featuring interactive stands from more than 200 different researchers from across the North West. At our stand, children were able to make cells from balloons in order to learn about how their bodies work.

**Institute Open Day**

Over 40,000 people fundraise for Cancer Research UK every year in the North West alone. Whether they hold a coffee morning or a car boot sale, run Race for Life or busk in local town centres, we are so grateful for their support.

The Institute Open Day is our opportunity to say a huge thank you to these incredible fundraisers, and to show them that we’re spending the money wisely.

Over 100 guests joined us for our most recent Open Day in October. After an inspirational welcome from a cancer survivor, guests heard from Institute Director, Professor Richard Marais. He revealed some of our recent successes as well as our exciting plans for the future, before taking questions from the audience. Guests then headed off on tours of the labs. They learnt about our important research into cancers of unmet need, tried their hand at pipetting and loading gels, and discovered some of the exciting new equipment in our core facilities. They explored some of our newest labs, examined their own cheek cells under a microscope, and most importantly were able to see first-hand the impact that their support is having on cancer research.

One supporter said, “Thank you for such an inspiring day. Everything I’ve seen and heard has just blown me away!” Another commented, “I’ve met so many enthusiastic and knowledgeable people. I’ve had a wonderful day, and it has absolutely increased my motivation to continue supporting Cancer Research UK!”

**The Great Science Bake Off**

To celebrate Stand Up to Cancer, the Great Science Bake Off returned to the Institute, and a number of our scientists baked fantastic representations of their research as part of a national competition between CRUK Centres. It was a close contest in Manchester, but Gemma Forrest’s ‘Battenberg Lab’ was a deserved winner! Other highlights included a retweet from a ‘Great British Bake Off’ finalist, and Breast Biology’s sweet interpretation of 100 Years of Notch. Happily nobody was put off by the idea of eating a giant fruit fly, and with the help of David Jenkins’ lucky dip, the Institute raised over £300 for Stand Up to Cancer.

To mark the launch of the new Cancer Research UK brand campaign, Dr Allan Jordan from Drug Discovery stepped in front of the camera to explain why he believes we will beat cancer sooner.

His videos have been viewed over 600,000 times, received over 40,000 ‘likes’ and have been shared nearly 7,000 times.

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Watch this space for more upcoming brand activity featuring yet another familiar face from the Institute!

**Funding Events and Activities**

It’s been a busy few months at the Institute, with a record number of people coming through our doors for lab tours! Our scientists have also been out speaking to supporter groups and delivering hands-on science activities for families and school children.

**Bollington Science Festival**

Scientists from the Institute took part in the 50th Annual Bollington Science Festival.

Over the course of a weekend, more than 300 children and their parents extracted DNA from strawberries and learnt about targeted therapy through fun hands-on activities.

**Pint of Science Festival**

Pint of Science is an annual festival that brings the best academic scientists in the UK to local pubs so that they can explain their latest research.

As part of this event, Professor Caroline Dive spoke to a packed audience about her team’s research into lung cancer.

**We Will Beat Cancer Sooner**

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Race for Life thank you event

Race for Life raises £50,000,000 every year for Cancer Research UK, and it would be impossible to run these events without the support of dedicated volunteers.

To say thank you to these fantastic volunteers, we welcomed them into the Institute for a behind the scenes look at our labs. They extracted DNA from strawberries with Steve Lyons in Cell Regulation, learnt about the ‘make, test, refine’ process of Drug Discovery with Dr Allan Jordan, before Clare Dickinson, Lead Nurse for Manchester, explained how all of this research is being transformed into tangible patient benefit.

Charity of the Year

Dr Ali Raoof and Dr Kate Smith from Drug Discovery recently helped Cancer Research UK secure a new corporate partnership with Thomson Airways!

They filmed a video explaining the urgent need for more cancer research and asked Thomson Airways staff to please vote for CRUK as their charity of the year. This video helped CRUK win the staff vote, and the partnership will be worth about £50,000 over the course of the year! Thank you Ali and Kate!

Flame of Hope

Dr Allan Jordan from the Drug Discovery recently received a Flame of Hope Special Commendation Award from Cancer Research UK in recognition of his research engagement work.

The award celebrates the exceptional contribution and achievements of dedicated CRUK ambassadors and volunteers.

He says “I was both delighted and incredibly humbled when I found out I had been awarded a Special Commendation for Research Engagement. One of the highlights of working with Cancer Research UK is explaining our research to fundraisers, sharing the successes they have allowed us to deliver and showing them where we hope to deliver further breakthroughs in the future. It is incredibly rewarding to share their stories and experiences and to see how our research has touched their lives”.

We asked Research Engagement Manager Hannah Leaton why she nominated Allan for the award…

“Allan is a fantastic ambassador for Cancer Research UK. He takes part in countless events and activities every year, spreading the word about the charity’s achievements to anyone who will listen! He cannot fail to inspire you and fundraisers regularly say they are determined to raise even more money after meeting him. This is because his desire to beat cancer sooner is so energising and so clearly what drives him.

I am thrilled that the time and energy he devotes to championing CRUK, way above and beyond his job description, has been recognised”.

Relay for Life

Congratulations to the team from the Institute who took part in this year’s Stockport Relay for Life, walking alongside survivors and local supporters for 24 hours straight.

The Relay raised over £50,000 which will go towards equipment for the new Manchester Cancer Research Centre.

Although the first few laps were bravely walked in torrential rain, the weekend finished in lovely sunshine, and our team of Relaxers enjoyed being able to share our science with supporters.

John Castle from CEP took part in the event and said “We’re so grateful to the organisers for working so hard throughout the year to raise such a fantastic amount of money. It was an honour and a pleasure to share the weekend with them. We returned to our institute with muddy labcoats but some great memories, inspired by the people we met”.

The date for the 2015 event has been set as 4th – 5th July. Please speak to Steve Lyons if you’d like to join the Institute’s team.

Recent Awards and Events

EACR Presidency for Richard Marais

We are delighted to announce that our Director, Professor Richard Marais, has recently become the President of the European Association of Cancer Research (EACR), sitting from 2014 to 2016.

During his presidency, Professor Marais will take the lead role in organising the 24th EACR Biennial Congress, which will be held in Manchester from 9th – 12th July 2016. This prestigious event will help raise the profile of cancer research in Manchester on a global level.

The European Association for Cancer Research has over 9,000 researcher members and aims to advance cancer research. Founded in 1968, it is Europe’s largest member society for cancer research. It sets out to raise the profile of cancer research and cancer researchers in Europe and the need for sustained political and economic support.

Professor Marais said “It is an honour to be elected President of the EACR and I look forward to leading the Association and its activities over the next two years. I am particularly delighted that my presidency will culminate with bringing EACR 24 to my home town and I look forward to seeing many from the University of Manchester there.”

Poster Prize for Andrew Porter

Congratulations to Andrew Porter from the Cell Signaling group who won the Post-Doctoral poster prize at the ESF-EMBO Cell Polarity and Membrane Trafficking meeting, which was held in Poland earlier this year.

His poster was entitled “CASK, a novel Tiam1 interactor, regulates MDCK lumen formation and mitotic spindle orientation” and included former PhD student Natalie Mack as a co-author as well as Angeliki Malini, who heads the Cell Signaling group.

Coming in 2015

- Lung Cancer Panel Debate
- Institute Open Day
- Cancer Campaigns Ambassador Day
- Lab tours and more!

Grant Success for John Brognard

John Brognard, head of the Signalling Networks in Cancer Group, has been awarded a grant from the Lung Cancer Research Foundation (LCRF) to support a research project that aims 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. Recent work by the Signalling Networks in Cancer Group has identified a protein kinase that is important for sustaining survival in LSCC cell lines. The grant from the LCRF will allow John and a postdoctoral researcher within his team, Pedro Ayuso-Torres, to understand more fully the role of this kinase and how it cooperates with other key oncogenic drivers. Working together with the Drug Discovery group, they hope to develop small molecule inhibitors of the kinase that will allow them to assess its suitability as a therapeutic target.

Grant Success for CEP

Our Clinical and Experimental Pharmacology group, led by Professor Caroline Dive, has recently been awarded funding from the Roy Castle Lung Cancer Foundation.

The study, to be led by Dr Phil Crosbie, a clinician based in CEP who also works out of the North West Lung Cancer Research Centre, the University Hospital of South Manchester, will focus on a novel circulating tumour cell (CTC) detection method in patients with early stage lung cancer. The overall aim is to evaluate its effectiveness in detecting and enumerating CTCS, and to determine the diagnostic performance in comparison to other circulating biomarkers. The reliable measurement of CTCS in early stage patients may provide a way of evaluating newly formed tumours that have spread to other sites in the body that are otherwise too minuscule to be detected, the reason why so many patients’ tumours recur after radical treatment. This method could potentially result in more effective stratification of adjuvant therapy for early stage lung cancer patients and could also be used for other cancer subtypes.
Travel Award Success

ASH Abstract Achievement Award for Tim Somerville

Tim Somerville has been awarded a travel award to attend the 56th American Society of Hematology (ASH) meeting in San Francisco in December.

The ASH meeting is a major event in non-malignant and malignant haematology with more than 3,000 haematology professionals attending and more than 3,000 scientific abstracts submitted. Tim, who is working towards a PhD in the Leukaemia Biology group, has won an ASH Abstract Achievement Award which is a merit-based prize of $500 for trainees with high-scoring annual meeting abstracts. He will be presenting a poster on his work entitled ‘TOXIC1 is Derepressed to Functional Effect in Human Acute Myeloid Leukemia (AML)’.

BACR Travel Award for Ewelina Testoni

Ewelina Testoni is a third year PhD student in the Signalling Networks and Cancer Group led by John Brognard, where she investigates novel mutational drivers in non-small cell lung cancer (NSCLC).

NSCLC accounts for approximately 90% of lung cancers and worldwide affects 1.37 million patients each year. The molecular mechanisms underlying the majority of NSCLCs remain unknown and currently only a small proportion of lung cancer patients benefit from targeted therapies. Hence, there is a need to identify novel driver mutations that can be targetable in lung cancer patients. Ewelina is investigating the role of somatically mutated ABL kinases as a novel genetic dependency and therapeutic target in NSCLC.

Ewelina was recently granted a BACR travel award to attend the International Union of Biochemistry and Molecular Biology (IUBMB) sponsored 48th Miami Winter Symposium, to be held in January 2015. The meeting will be dedicated to Personalised Cancer Medicine and provide an overview of recent developments in cancer research and novel therapeutic approaches. The symposium will address multiple research topics including areas such as cancer heterogeneity, genetics, epigenetics, molecular mechanisms, targeted therapies, immune therapies and translational research. Ewelina is delighted BACR is sponsoring her attendance and providing her with an incredible opportunity to present her work on ABL kinases and also to network with world leaders in cancer research from both academia and industry.

Travel Award for Romina Girotti

Romina Girotti of the Molecular Oncology group has won a $1000 travel award from the Society for Melanoma Research for the abstract that she produced for the 2014 SMR congress, which was held on 13th – 16th November in Zurich.

Romina presented her work on the development of preclinical models that reflect the complexity and heterogeneity of melanoma, in order to help advance new therapies for individual patients that don’t respond, or become resistant to, current targeted therapies. The DNA and proteins of patient tumours, which have also been grown in mice that are treated with the same therapies, are analysed to investigate mechanisms of resistance. This research aims to explain why some patients respond to treatment, whilst others are refractory, and has the potential to revolutionise the future management of melanoma patients.

When Science Meets Fashion

When Esther Baena, who leads the Prostate Oncobiology group, decided to enter the first Descience competition – a project that pairs scientists and fashion designers to make cutting-edge research tangible – she hoped to transform her research into something palpable and visually appealing with the help of Arielle Gogh.

Esther focuses on prostate cancer, the second most diagnosed cancer among men. Prostate cancer is graded using the Gleason system, which provides information on the aggressiveness of the cancer and relies entirely on the architectural pattern of cancerous glands (carcinomas). This grading process became the main focus of their Descience project, ‘Transmutation’. The diverse characteristics of carcinomas were represented in their garment by the colour heterogeneity in the ice-dyed fabric, and cellular malignant transformation was represented by the changing volume of the dress. Cleverly, creation of an additional, separate arm piece conveyed bone metastasis. Esther was both surprised and delighted that tumour growth, invasiveness and progression to distal metastases could be so accurately represented through a beautiful and fashionable dress. She said “I am grateful to Descience for challenging me to work with the talented Arielle Gogh, and for allowing me to present tumour heterogeneity, and progression to metastasis, to the world as a scientific piece of art.” Transmutation was a selected finalist among four other teams.

Institute Colloquium 2014

A warm welcome was extended to all those attending the colloquium for the first time – this included new group leaders Esther Baena and Michela Garofalo.

In the opening session, both gave excellent talks introducing their areas of interest. Over the three days there were six sessions where we heard presentations by PhD students and group leaders from across the Institute and from other University researchers based in the Paterson building.

Alongside the fantastic talks, two poster sessions took place. Winning the prize for the best poster presented by a Post-doc/Scientific Officer was Anna Marusiak in the Signalling Networks in Cancer Group, for her work exploring mutations in MLK4 in colon cancer. Many of these mutations are known to be loss-of-function and can act in a dominant negative manner. Anna investigated whether these inactivating mutations were critical for cancer development and found that by reintroducing the unmutated form of MLK4, she could slow tumour growth in a mouse model.

The Lizzy Hitchman prize for best poster by a student went to Danish Memon of the RNA Biology Group. His fascinating work looked at the role of non-coding RNAs in the regulation of tumour response to hypoxia. Tumour hypoxia is linked to poor outcome and resistance to treatment, and Danish hypothesised that non-coding RNAs may well be involved in regulating the hypoxic response. He examined colorectal cancer cells that had been subjected to a hypoxic environment and found substantial genetic changes.

Focusing on one non-coding RNA in particular, HINCR1, he showed that it had increased expression in various models of hypoxia and that its levels could predict survival in patients. This could be used as a target for anti-cancer treatment.
Core Facilities Update

The start of November saw the departure of Mike Hughes, a valued member of Flow Cytometry – one of the Institute’s Core Research Facilities. After 39 years and 5 months of committed service to the Institute, Mike is hanging up his lab coat and heading home for the last time.

Mike was infamous around the Institute for his lunchtime run. Rain or sunshine, he would always go for a run in the local park, which Mike reflects on below. We all wish Mike a happy and healthy retirement.

A Fond Farewell
By Mike Hughes

I visited the Institute for an interview in February 1975 after working at Withington Hospital for 18 months doing research into Platelet Aggregation. Little did I know at the time that this was to be my last job interview.

I started work in June 1975 as a Scientific Officer with Drs Boris and Lea Cercek, who were researching an early detection test for cancer. This involved measuring the fluorescent polarization of a well-defined population of Lymphocytes to determine changes in the structure of the cytoplasmic matrix.

In 1980, the Cerceks relocated to Beckman in Los Angeles and although I was offered a position with them, I decided to remain at the Paterson. Lazlo Lajtha, who was the Director at that time, offered to redelegate me to start the FACs service. My first thought was, would I be behind the receptionist’s desk sending out messages for the Paterson but I soon learned otherwise. I was sent to Sunnyvale, California for a week’s training and the new Flow Cytometry service gradually took shape. Our first sorter, a FACS IV was the second machine in the laboratories challenging any over 35’s to race me over 100m in Fog Lane Park. I think there were about seven competitors and about 80 spectators for the big event. I finished 3rd but Ric Swindell who won the race was then employed by the hospital so only Alan McGowan from the laboratories beat me. After this I organised the annual Paterson sports’ day for five years in the park with events ranging from a slow bike race to a ‘dream’ mile to finish the evening. I also helped organise other sports’ events which included tennis, table tennis, darts, snooker, rounders and non-stop cricket.

After more than 39 years, it is time for me to leave the Institute. My wife has some decorating jobs lined up and I am looking forward to spending more time working at my church, Poynton Christian Fellowship. I will still keep active running and playing Badminton but you will probably miss me looking the worse for wear on the Paterson steps at lunchtimes. Many thanks to everyone I have known over the years for your friendship and help. I will miss you all and no doubt will keep in touch.

A Warm Welcome

Two new members of staff have been appointed into the core facilities, Toni Grady in Molecular Biology and Toni Banyard in Imaging & Cytometry.

High Content Screening: From Cell Populations to Numbers
By Steve Bagley

Toni Grady

I originally came from a customer service background and worked in the virgin media complaints office, a very challenging but rewarding environment, however I wanted a complete career change so I went back to study science A-levels at a local college and secured a position at The University of Manchester to study Physiology.

After studying, my first job was within the Centre for Integrated Genomic Medical Research at Manchester University, then onto the Institute in July where I am involved with Sanger sequencing, genotyping, mycoplasma and MHV testing, and will soon be trained in cell line authentication, qPCR and Fluidigm.

I have an older daughter and son who are 21 and 16. My daughter is at university studying animal behaviour and my son wants to follow in my footsteps with a career in science. In my spare time I enjoy arts and crafts and always have many projects on the go!

Toni Banyard

My first degree was in marine biology and in my final year I was involved in a project to extract and sequence the attachment protein of mussels with the view to producing marine glue!

This started my great interest in translational science. This has carried on in my career from my time working at Cambridge Antibody Technology producing GMP standard humanised antibodies for clinical use and then onto Syngenta working on T cell interactions in respiratory allergies where I first used flow cytometry.

Outside of the lab, I have been a keen scuba diver for many years from university days, so much so, I got the chance to run a dive company over in Cairns which I jumped at and was there for 2 years, although I fear I am too wussy to brave the UK waters now! I enjoy hill walking so it’s great to be so close to the Lake District, and love skiing (and boarding too) so always try to get to the slopes every year, even to Scotland which I can recommend.

Abi is Now Certified!

Abi Johnson has successfully completed the International Cytometry Certification, a series of study and examination covering flow cytometry theory and practice, from instrumentation and safety through quality control and experimental design. Congratulations, Abi!
**Education News**

**New Students**

The last year of my undergraduate degree, and for the subsequent two years of my MSc, I was a trainee in the group of Professor Alberto Bardelli. There I worked on mechanisms of acquired resistance to anti-EGFR monoclonal antibodies in metastatic colorectal cancer patients. It was very exciting and this amazing experience pushed me to carry on my career in the translational side of cancer research. Thereby I applied for a position at the Cancer Research UK Manchester Institute and now I am here! I am working in the Clinical and Experimental Pharmacology group led by Professor Caroline Dive where I will have the chance to study the mechanisms of resistance to standard chemotherapies in SCLC patients, taking advantage of circulating tumour cell (CTC) and CTC-derived xenograft (CDX) models. In my free time I hope to make the most of the exciting opportunities that Manchester has to offer and also to explore as much as possible of the large island that is Britain.

**Alice Lallo**

Hi, my name is Alice Lallo and I am from Italy. I was born in Torino and there I completed both my undergraduate degree in Biotechnology and my MSc in Molecular Biotechnology.

Andrew Jenkins

Hello! I’m Andy from south Wales. I’ve just completed an undergraduate Master’s degree in Pharmacology at the University of Bath.

As part of my studies, I spent a year on placement at UCB Pharma in Brussels working on the identification of a transcriptomic biomarker signature for drug abuse-liability testing, which I really enjoyed. This may seem a far cry from cancer research (I) but it kindled a deep interest in noncoding RNA, and I am delighted to be starting a PhD with Crispin Miller in the RNA Biology group, to follow up that interest. I am very excited about my project, starting a PhD with Crispin Miller in the RNA Biology group, which is entitled ‘Noncoding RNA systems in small cell lung cancer’. I have a deep interest in noncoding RNA, and I am delighted to be working on the identification of a transcriptomic biomarker signature for drug abuse-liability testing, which I really enjoyed. This may seem a far cry from cancer research (I) but it kindled a deep interest in noncoding RNA, and I am delighted to be starting a PhD with Crispin Miller in the RNA Biology group, to follow up that interest. I am very excited about my project, starting a PhD with Crispin Miller in the RNA Biology group.

**Sara Menegatti**

My name is Sara and I come from Italy. I received my bachelor’s degree in Biology at the University of Ferrara, my hometown, and then moved to the Netherlands for an MSc in Biomedical Sciences, at the University of Maastricht.

As part of my degree, I attended an 8-month internship in Paris at the UPMC (Université Pierre et Marie Curie), where I first encountered the world of haematopoiesis. My master’s thesis focused on the production of haemagogenous endothelium and haematopoietic stem cells (HSCs) from cultured embryonic tissues. This challenge encouraged my interest in blood formation and stem cells, but I was still missing a more direct contact with the clinics. So I am happy that the PhD project I secured in the Stem Cell Haematopoiesis group, led by Valenia Koukou, fulfills those wishes. Our aim is to optimise differentiating conditions leading to the production of long-term repopulating HSCs from mouse embryonic stem cells (ESCs) and to identify novel markers to define repopulating progenitors. Thus, the optimisation will be translated to human ESCs and induced pluripotent stem cells, providing the basis for future cancer treatments. Besides research, I will explore Manchester and its surroundings, enjoying the unique experiences on offer in England.

**Amy McCarthy**

Hi, I’m Amy, originally from a very tiny village in rural Berkshire. I did my undergraduate degree at Cambridge University, specialising in Cell and Developmental Biology.

During my degree I did a project in Developmental Biology looking at the contribution of cell lineage to neuro-transmitter specification in Drosophila, and after graduating I worked for a year in Cambridge, also in a Drosophila lab. However my real interest has always been cancer, so I was really excited to be accepted for a PhD in the Systems Oncology group here in Manchester. My project is looking at heterogeneity in tumour-stroma signalling, trying to understand how genetic heterogeneity in tumours might result in different stromal activation. I’ve only been living in Manchester in few months but I love it so far – it’s a real change from anywhere I’ve lived before and I’m excited to explore it properly!

Manon Pillai

Hello, my name is Manon and I am originally from North Wales. I completed my undergraduate medical degree at Imperial College in London before moving to Chester and Liverpool to undertake my core medical training.

I developed an interest in Medical Oncology and re-located to Manchester to train as a Specialist Registrar at the Christie Hospital. During my time in Manchester I obtained an interest in immunotherapy for cancer and I recently began a 2 year MD here in the Paterson Building with the Institute of Cancer Sciences, working in Professor Robert Hawkins and Dr Dave Gilham’s group evaluating PDI and T-cells in renal cell carcinoma. I feel very lucky to be part of such a dynamic group and look forward to developing many new skills during my time here. Being part of the University of Manchester also offers the opportunity to join and participate in many extra-curricular activities and I hope to take full advantage of these over the next 2 years.

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8th International PhD Student Cancer Conference

By Alekh Thapa

Each year students from leading European cancer research institutions organise and host the International PhD Student Cancer Conference. In June, CRUK MI students joined delegates from other CRUK research institutes, along with those from the SEMM (Milan), NKI (Amsterdam), HBIGS (Heidelberg) and the ICR (London) for the conference’s 8th edition which was hosted by the German Cancer Research Centre (DKFZ) in Heidelberg.

Talks focused on key areas in cancer research, such as metastasis, drug resistance and tumour heterogeneity. Amongst many interesting talks, Danish Memon, from Crispin Miller’s group here at the CRUK Manchester Institute, presented his work identifying and characterising the hypoxia induced long non-coding RNA transcript HANCRI. His data suggests this non-coding RNA may play an important role in the regulation of hypoxia related genes, hypoxia being a common microenvironmental condition at the site of tumours. Sally Dewhurst, from Charles Swanton’s group at the CRUK London Research Institute, discussed her use of isogenic diploid and tetraploid colorectal cancer cell lines to demonstrate that tetraploidy allowed tolerance for chromosomal instability. After 18 months in culture, tetraploid clones developed similar genomic changes to those observed in chromosomally unstable human colorectal tumours. This year, two plenary lectures were given. Gottfried Schatz, who gave an engaging talk on his own career, researching mitochondrial DNA, and his views on the state of science today. Lutz Gissmann gave an overview of the successes of HPV vaccination and the future of this programme of cancer prevention. Breakout sessions focused on communication in science both between scientists and also in the form of public engagement and patient information services. A tour was also led viewing the 7 Tesla experimental MRI system which is being developed at the DKFZ for more detailed imaging of tumours. The DKFZ students put together a conference dinner held on a restaurant boat cruising the river Neckar which was accompanied by fantastic weather.

In June 2015 we, the students from the CRUK Manchester Institute, will be hosting the 9th annual conference at the Christie Hospital’s Education Centre. We aim to foster some exciting scientific dialogue between young researchers whilst also hosting two key note speakers including Mariann Blenz, who will be speaking about her work in the field of Wnt signalling.
Belfast-Manchester Movember Centre of Excellence Launch Night

By Ruth Perkins

Earlier this year we announced the launch of the Belfast-Manchester Movember Centre of Excellence in partnership with Prostate Cancer UK. We organised a launch night at the end of October to allow members of the public and fundraisers to hear about the work that we are doing to change the face of men’s health.

The event took place on a wet and windy night at The Albert Square Chophouse, Manchester. The public event about “The future of prostate cancer research – powered by the moustache” was part of the Manchester Science Festival. Despite the weather, there was a healthy attendance of curious members of the public, fundraisers, advocates and staff from Movember and Prostate Cancer UK and our own prostate cancer scientists, all present to celebrate this pioneering joint enterprise between CRUK MI and Queen’s University Belfast.

Festivities kicked off with a short Q&A with Mike Summerbee, an ex-Manchester City football player and prostate cancer survivor, who declared George Best to be his favourite moustache wearer in history. An inspiring speech by Adam Garone, co-founder of the Movember Foundation, explained how the original idea of growing a moustache to raise money for men’s health was conceived by a group of friends in a Melbourne pub in 2003. He outlined their vision of funding scientific collaborations to improve prostate cancer patient survival. A subsequent triple act of Prof Richard Marais (Director of CRUK MI), Prof David Waugh (Queen’s University Belfast) and Prof Noel Clarke (The Christie NHS Foundation Trust) covered the basics of cancer development, the challenges of prostate cancer, and current and future treatment options for men with the disease.

The talks were swiftly followed by drinks and delicious ‘manapes’ and the fundraisers, scientists and members of the public stayed to chat and discuss all they had heard that evening.

Mo Sista

By Marina Parry

As a newly appointed Movember-funded postdoctoral researcher, I was keen to support the charity’s activities during their flagship month.

I gave a short talk to almost 40 members of staff at the Marks and Spencer’s Business Support Centre in Manchester with Damian Shannon, Community Engagement Coordinator for Movember. We were there to raise awareness of the huge impact that fundraising has, and to talk about the Centre of Excellence’s objectives in increasing knowledge and improving treatments for men with prostate cancer. I also organised a couple of lunchtime Mo Yoga sessions at the Institute with qualified Iyengar yoga teacher Jackie Taylor, who generously donated her time and helped to raise over £100 for Movember.

Mo Bro Baker

In his 4th year as a Mo Bro, Purchasing Officer David Jenkins, arranged lots of great activities to raise money for Movember. He held a Mo-themed raffle and cake sale and raised over £300! A fantastic effort!

Mo Sista Marina Parry

Mo Bro Baker David Jenkins (centre) with Pat Mo Bros and Mo Sistas at David’s bake sale

By Ekram Aidaros

Graduation Ceremony at Stockport Town Hall at the end of September.

Congratulations to Julie Jarratt on successfully completing the CIPD Level 7 Advanced Diploma in Human Resource Development.

Completion of this Diploma provides Julie with the knowledge required to work towards Chartered CIPD Membership (MCIPD). The Chartered Institute for Personnel and Development (CIPD) is the professional body for HR and people development.

Julie celebrated her success in style by dining at Albert’s Restaurant in Didsbury and then attending her Graduation Ceremony at Stockport Town Hall at the end of September.

Social Events

The second annual CRUK MI Summer Party was held this July, on a splendid summer’s evening. The party, which was held in a nearby pub, allowed all Paterson Building staff to step away from their work and enjoy the company of their colleagues, some wonderful sunshine and a few slices of delicious pizza.

The party was a great success, with plenty of laughter, conversation and, even though the day proved hotter than was expected, no sunburn.

In the last few months we also held our Newcomers’ Party, which took place in October and it is a chance for old staff to meet and welcome new staff to the Building. The party, in its second year like the summer party, is a great way for new PhD students especially who start their projects in October, to meet other members of staff and labs, and put names to faces.

Babies!

Catriona Tate celebrated the birth of her baby boy, Arthur Tate, earlier this year. Born on the 21st January 2014, Arthur is now a happy and healthy 10 month old.
In the spotlight with David Stanier

David joined the Institute as the Operations Administrative Assistant in 2013 having previously worked in similar roles elsewhere following a degree in English at Lancaster University. He helps the Institute to run smoothly in a number of ways by providing administrative support to the Operations department as well as undertaking a number of duties within Human Resources and covering reception.

1. What is your favourite part of the UK?
   I have a soft spot for my hometown Stoke-on-Trent but I’ve loved Manchester since I moved here in 2010.

2. What was your best ever holiday and why?
   New York. It’s very exciting. I felt like I was in Friends.

3. Which website do you always check, and why?
   BBC News, to see what is going on out there.

4. What is your favourite film?
   Jurassic Park

5. What is your favourite band/singer?
   Kanye West

6. If you had to change careers tomorrow, what would you do?
   Am I being fired? I would do my secret other career which I do at night, stand up comedy.

7. What is the most important lesson that you have learnt from life?
   If you have good thoughts they will shine out of your face like sunbeams and you will always look lovely.

8. Name three things you would take with you to a desert island?
   A parasol, a jet ski and a buffet.

9. What is your greatest fear?
   Snakes. Snakes in my bed.

10. How would you like to be remembered?
    With a huge statue and the plaque reads “Thank You David, Love from Humanity”

11. If you could change one thing in your past what would it be?
    Giving up piano lessons but they were soooo boring.

12. What is your signature dish to cook?
    Nachos, which might give you an insight into my culinary prowess.

13. You’ve just won the lottery and have £5 million pounds to spend. What do you buy first?
    A horse. No more taking the bus for me.

14. What is your idea of perfect happiness?
    Sitting under a parasol with a plate of buffet food on a desert island after an afternoon of jet skiing.

15. What keeps you awake at night?
    Ghosts.