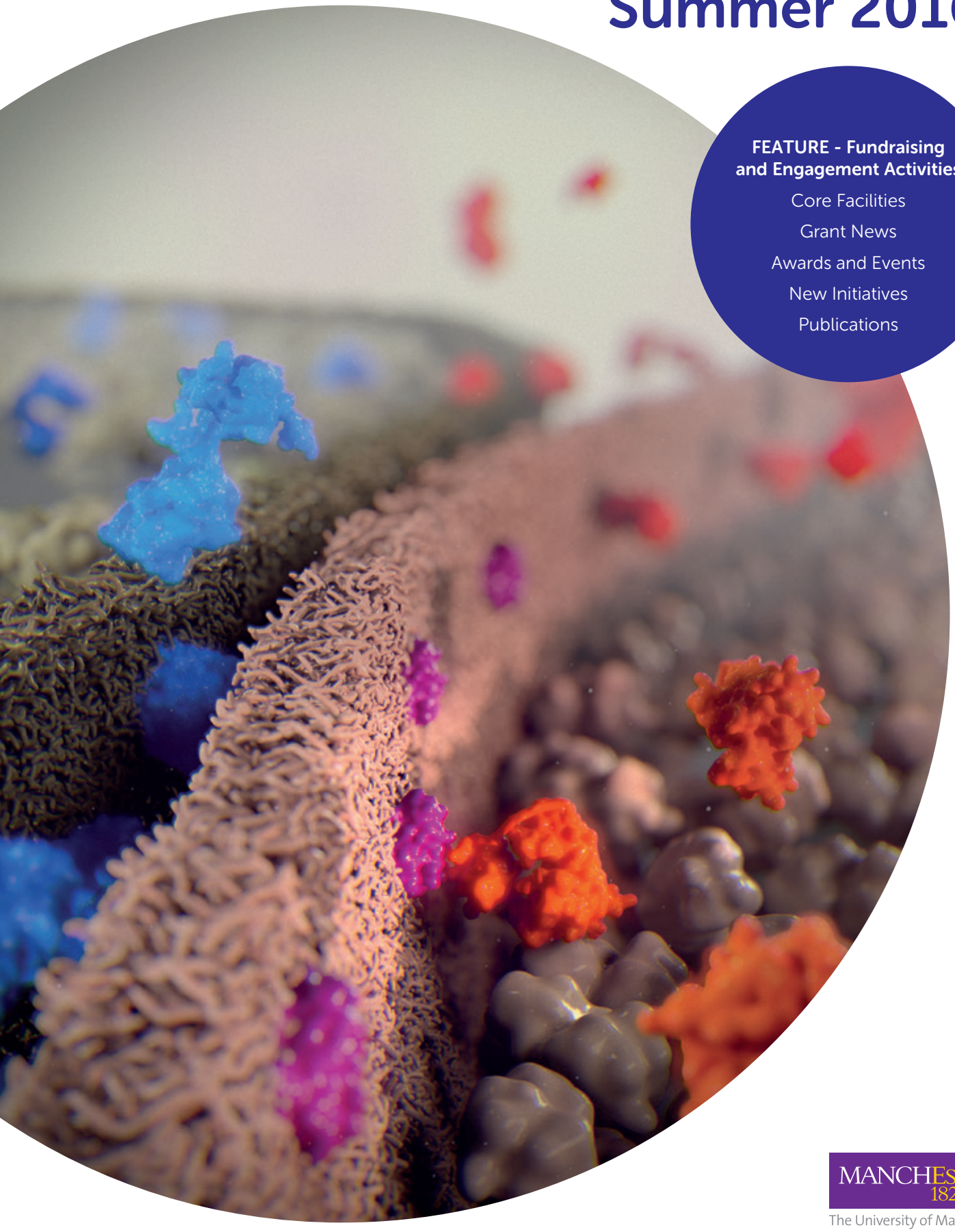
Newsletter

CANCER RESEARCH UK | MANCHESTER INSTITUTE

Summer 2016



FEATURE - Fundraising and Engagement Activities

Core Facilities

Grant News

Awards and Events

New Initiatives

Publications

MANCHESTER 1824
The University of Manchester

Director's Introduction

Welcome to the Spring edition of our newsletter. The front cover illustrates a ground-breaking study from our Systems Oncology group, led by Claus Jørgensen. Their work, published in the prestigious journal *Cell*, uncovers the communication between pancreatic adenocarcinoma cells and their neighbouring healthy cells. Their study revealed that cancer cells can co-opt adjacent tissue into releasing signals that further stimulate the growth of cancer, reinforcing the complexity that underpins many types of cancer. Claus has also obtained additional funding for his research through a successful grant application to the Pancreatic Cancer Research Fund.

There have been a number of other recent successful funding applications made by the Institute's scientists. Iain Hagan has received significant funding from the Wellcome Trust through his application for an Investigator Award that will enable him to expand his exciting work on understanding the temporal and environmental control of cell division. Extending the breadth of our work through external funding is critical to our research aims and so to this end, I have recently established a grants committee to oversee submission of our applications. Iain is utilising his extensive grant review experience by chairing the committee which consists of several Group Leaders and is ably supported by our Grants Advisor Gill Campbell.

Amaya Viros has been awarded a Clinician Scientist Fellowship from the Wellcome Trust. Amaya is currently a fellow in my group but will be establishing her own team from September to understand the biology behind ageing in skin, and specifically to determine why older patients are less likely to survive following a diagnosis of melanoma.

In April, a number of the Institute's scientists attended the American Association for Cancer Research meeting in New Orleans. It was exciting to see Caroline Dive chair and speak in a plenary session to present the work of the Clinical and Experimental Pharmacology group. This summer, it will be my privilege to chair the European Association for Cancer Research biannual meeting which will take place in Manchester. These meetings allow us to share ideas and foster new collaborations and I look forward to seeing many of you there. It is an excellent opportunity to showcase the city of Manchester and its science.

Finally, I would like to thank everyone who sponsored and encouraged me to ride the Fred Whitton Challenge. This is a 112-mile cycle ride across some of the toughest climbs in the Lake District which I took on in order to raise money in memory of my late friend and mentor, Chris Marshall. Chris was an outstanding scientist who devoted his life to studying cancer; he was also a talented cyclist who excelled on the hills, so the Fred Whitton was an appropriate challenge to tackle in his memory. A mechanical incident on the day of the race meant that I had to abandon halfway round but I returned just over two weeks later and finished the course. I more than doubled my fundraising target and raised £10,433 which will be divided between Cancer Research UK and The Institute of Cancer Research in London, where Chris spent most of his career.

Richard Marais
Director

Richard in action on his bike in the Lake District riding the Fred Whitton Challenge.

Cover Image: The cover image was generated by Dr Jeroen Claus, Phospho Biomedical Animation, based on the data in the Systems Oncology publication in Cell (further details on page 6). The image Illustrates reciprocal signalling between pancreatic cancer cells (right) and healthy stromal fibroblasts (left). The mutated KRAS signalling protein (purple) drives the growth of the cancer cells. In addition, the soluble signalling molecule SHH is released from the cancer cells (blue) to engage neighbouring healthy fibroblasts. These coerced cells in turn release signals for the receptor molecules in the cancer cells (red, background) ultimately changing their drug sensitivity, proliferation and metabolism.

Full animation available: https://www.youtube.com/watch?v=GU-QZp5FwM8

Fundraising and Engagement activities

By Sive Finlay

Lab tour highlights

We've had a busy couple of months welcoming a wide range of supporters, fundraisers and corporate partners to our labs.

Staff from local branches of TK Maxx visited in January to celebrate their long term support for CRUK having raised over £22 million for the charity since 2004. The company mainly raises funds by collecting donation bags for CRUK shops as part of their "Give Up Clothes for Good" campaign and also through staff fundraising and profits from their carrier bag levy. The visitors thoroughly enjoyed their afternoon in the labs, commenting that "the whole experience was truly worthwhile and an eye opener" and our research was "mind blowing in how clever it is"!

The Sandbach CRUK committee visited the Drug Discovery labs and MCRC Building to celebrate their 60th Anniversary year. The committee fundraised for the More Tomorrows Campaign and now give all their income directly to Manchester. As part of the afternoon, individual members were presented with their 40 year CRUK volunteering badges to mark their dedicated support for the charity.

Staff and volunteers from local CRUK shops visited in April to hear about our latest research. For many of them, this was their first opportunity to find out how the funds that the shops generate are spent so the afternoon was a lovely opportunity to bring different branches of the charity together.

Members of the Sandbach local fundraising committee proudly pointing out their name on the MCRC donor wall

Fundraising and research were combined when staff from AstraZeneca visited the Institute after spending their morning volunteering in local shops, an eye-opening experience for everyone involved. They were inspired by the dedication of the people they met, commenting that "the enthusiasm from everyone is infectious and motivating" and that they were "in awe of the work done here and the obvious passion of the people involved".

Combined with our Institute visits for the CRUK roadshow team, Race for Life interns, Stockport Relay for Life organisers, patient groups, door to door fundraisers and local corporate partners, these lab tours are an important way of thanking our supporters for all their hard work and demonstrating how we're putting their funds to good use. Thank you to everyone who helps to make these visits so successful.

Images left to right: Staff from TKMaxx after their recent lab tour at CRUK MI; Race for Life interns extracting DNA from strawberries with Genny Filiciotto; Staff from AstraZeneca touring our imaging facilities with Steve Bagley

Marathon News

If you passed by the CRUK tent at either the Manchester or London marathons you probably spotted a familiar face!

Marina Parry was featured as the host of CRUK MI's virtual reality lab tour, a great opportunity for runners and supporters alike to get an insight into how their donations are spent.

The virtual reality lab tour hosted by Marina Parry was a great attraction at the Manchester marathon.

Eve Hart celebrates with an alcohol-free, isotonic recovery beer after the Manchester marathon

Congratulations to Eve Hart, Senior Research Engagement Manager for CRUK for completing her first marathon in April.

She completed the course in a very commendable four hours and 45 minutes which was her target time. Eve's caught the running bug and is planning to do the Manchester Half marathon in October, get in touch if you would like to join!

Research café series

Our new research café series gives staff, patients and visitors an opportunity to find out more about our work through short, informal talks in the MCRC café.

Launched by Stephen Taylor on World Cancer Day, subsequent talks included James O'Connor's discussion about the role of clinical scientists and Rob Duncombe's insights into the role of the Christie NHS Foundation Trust's pharmacy team in running and administering clinical trials. Talks take place on Thursday mornings roughly every six weeks; look out for our flyers and emails for upcoming dates.

Staff and visitors getting up to date with our work at the research café series

Award winning open day

Our November 2015 Open Day won the "Best Storyteller" award at the CRUK national fundraising conference in Birmingham. CRUK's head of volunteer fundraising, Simon O'Leary praised the event for the impact it had on our supporters in the North West.

Our engaging activities, lab tours, demonstrations and chats about our work inspired people to create more fundraising events such as extra Relay for Life dates and to raise even more money for our research. The award is a fantastic recognition for all of our staff's hard work and support of our public events. A massive thank you to everyone involved!

World Cancer Day

On the 4th of February, we joined researchers, volunteers, patients and supporters across the world to celebrate World Cancer Day.

The new and improved unity bands proved to be a hit and dozens of staff from across the MCRC partners joined us for our #ADayToUnite photo on the staircase. Professor Stephen Taylor from The University of Manchester's Institute of Cancer Sciences, who is based in the MCRC Building, launched our new research café series with his talk on "Chromosomes, cancer and the quest for novel therapies" and the day was rounded off with a bake sale that raised over £100 for CRUK.

Images left to right: Some of the Drug Discovery group proudly displaying their World Cancer Day unity bands; Our #ADayToUnite photo on the MCRC stairs for world cancer day

Britain's Biggest Breakfast

On the 11th of March, we celebrated Britain's Biggest Breakfast in style with a sumptuous spread provided by the lovely people at Warburtons.

An array of toast, crumpets, pancakes and teacakes proved very popular and were soon snapped up, raising a fantastic £126 for CRUK. Warburtons sponsored the café space in the MCRC building so the morning was a great way to work with them again.

A selection of Warburtons' goodies proved very popular for Britain's Biggest Breakfast in March

Dates for your diary

17th June 2016
CRUK prostate cancer roadshow, showcasing how clinical research is improving treatments for prostate cancer

25th June 2016
CRUK/MCRC open day,
Celebrating 10 years of the MCRC

2nd - 3rd July 2016
Stockport Relay for Life,
Best of luck to our dedicated staff team

23rd July 2016
Soapbox Science
Come along to Piccadilly Gardens in Manchester to support our postdoctoral scientists Marina Parry and Alba Marques-Diaz

23rd - 29th July 2016
European City of Science Festival,
Look out for our exciting science/fashion collaboration!

Featured Publications

Cancer cells turn healthy cells to the 'dark side'

Dr Claus Jørgensen and the Systems Oncology group have shown that cancer cells use a mutant gene to coerce neighbouring healthy tissue into helping with the disease's growth and spread. Their study sheds light on how cancer cells and normal cells communicate with each other, and could open up new approaches to cancer treatment.

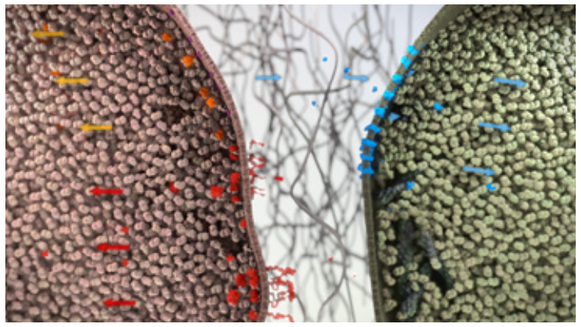
Working in collaboration with scientists at The Institute of Cancer Research in London they found that faulty versions of the KRAS gene – the most commonly mutated gene in cancer – can have an important effect on healthy tissue.

Normal KRAS makes occasional signals that tell a cell to divide, but when mutated the gene becomes hyperactive and helps drive cancer cells' rapid and uncontrolled growth.

In the new study, researchers found that mutated KRAS also plays an important role in turning healthy 'stromal cells' into cancer's allies.

The study showed for the first time that there is a communication loop with a cancer-causing gene controlling cancer via healthy stromal cells.

They studied communication networks in cells from a type of pancreatic cancer called pancreatic ductal adenocarcinoma – one of the most deadly forms of cancer responsible for around 9,000 deaths each year in the UK. KRAS is mutated in more than 90 per cent of pancreatic cancer, and in nearly 20 per cent of all cancers.



Tumour cell signalling capacity is expanded by co-opted fibroblasts. Tumour cells (left) with mutations in oncogenic KRAS (purple) engage RAF-MAPK signalling pathway (yellow arrow). In addition, oncogenic KRAS also enables the tumour cells to secrete growth morphogens such as SHH (blue arrow), which leads to co-option of neighbouring fibroblasts (right). These fibroblasts then elicit a reciprocal signal back to the tumour cells to activate the receptor tyrosine kinases IGF1R and AXL (red), which results in activation of the AKT signalling pathway (red arrow). *Image supplied by Dr Jeroen Claus, Phospho Biomedical Animation.*

The team studied thousands of different growth factors, proteins, and receptors across different pancreatic ductal adenocarcinoma cells to see how signals were being transmitted. They recognised well known pathways that KRAS uses to communicate with neighboring healthy cells but also noticed something unusual. By monitoring proteins in the two cells at the same time, they discovered that healthy cells were responding with a totally new message – a message that doubled the capacity for KRAS to drive malignant behavior in the cancer cells.

The paper, '**Oncogenic KRAS Regulates Tumor Cell Signaling via Stromal Reciprocation**', was published in the journal *Cell*. DOI: http://dx.doi.org/10.1016/j.cell.2016.03.029

Teasing apart the threads of blood cell creation story

Scientists from the Institute have revealed that two proteins play a critical role in the generation of blood cells – knowledge vital for the progress towards creating such cells in the lab.

A step-by-step process governs the development of blood cells during embryo growth; key to this is the creation of early blood cells from endothelial cells in the haemogenic endothelium (HE) through an endothelial-to-haematopoietic transition (EHT). Acting as 'master regulator' of EHT is the factor RUNX1 - when this gene is deleted, there is embryo death and a complete lack of blood-generating cells.

The teams from the Stem Cell Biology and Stem Cell Haematopoiesis groups have explored two targets of RUNX1 - GFI1 and GFI1B - in order to better understand the molecular mechanisms behind EHT.

It was already known that GFI1 and GFI1B are important players in the first wave of blood cell development.

The study, led by Drs Georges Lacaud and Valerie Kouskoff, found that this pair of proteins also played a prominent role in the second stage of this process. By knocking the two genes out, they prevented cells progressing through EHT.
They also revealed a set of 78 genes that were controlled by GFI1 and GFI1B during the transition. Their findings offer a wealth of leads for future studies into the processes behind blood cell development.

"**GFI1 proteins orchestrate the emergence of haematopoietic stem cells through the recruitment of LSD1**" R Thambyrajah et al. (2016) *Nature Cell Biology* 18(1):21-32.

Cancer test comes closer to home

Work by Institute scientists has brought the possibility of cancer patients being accurately monitored via blood tests nearer to reality.

There is much excitement over the potential of blood-based or 'liquid' biopsies – where a cancer patient's tumour can be profiled using a blood test without the need for surgery – to allow doctors to select appropriate treatments, and to detect response or relapse.

This test relies on the fact that tumours shed cells and DNA, which are then carried in the blood. These cancer fragments – known as circulating tumour cells (CTCs) and circulating tumour DNA (ctDNA) – can give insight into the genetic makeup of the tumour itself.

Detecting and tracking genetic mutations would allow medics to match patients with the right drug, and even pick up when a tumour has developed resistance to a particular therapy.

The Clinical and Experimental Pharmacology group, led by Professor Caroline Dive, are leading the way in developing technology and applications in this area.

Now the team has investigated whether using a special preservation tube could allow samples to be stored at room temperature before being sent away for analysis, meaning that patients could have their blood test taken at a local clinic.

They found that using the CellSave system they could isolate tumour cells and DNA from four-day-old patient blood samples and then successfully identify genetic alterations.

"**Genetic profiling of tumours using both circulating free DNA and circulating tumour cells isolated from the same preserved whole blood sample**" D G Rothwell et al. (2016) *Molecular Oncology* 10(4):566-74.

Illuminating one dark spot in the genetics of bowel cancer

Scientists in the Signalling Networks in Cancer group have explored the role of one particular cell signalling protein in bowel cancer, and found that its mutation promotes tumour growth.

Bowel cancer, also known as colorectal or colon cancer, is the fourth most common cancer in the UK, and the second most common cause of cancer death. While the disease is very treatable if caught early, survival is poor for those diagnosed at a late stage.

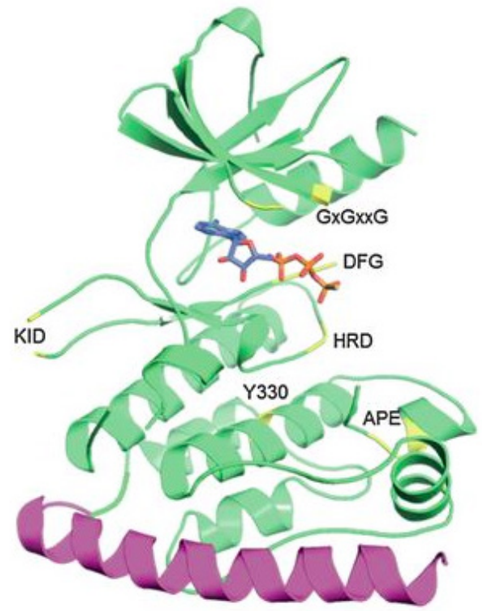
In order to fully understand the root of the disease, and to identify new ways to treat it, researchers need to tease apart the various genetic mistakes.

One gene of interest – MLK4 – is frequently mutated in bowel cancer, but until now scientists haven't fully studied the effects of such genetic changes.

Dr John Brognard's group has looked at the consequences of MLK4 mutations on the growth of colon cancer cells. The team showed that the majority of genetic faults in MLK4 made it stop working. When they restored its function in cancer cells, they saw slower growth and smaller tumours.

"Our results show that MLK4 subdues tumour growth, and that when it accumulates genetic mistakes, it loses that ability. Knowing more about MLK4 and other similar proteins is vital if we are to find new ways to treat cancer," added Dr Brognard.

"**Recurrent MLK4 Loss-of-Function Mutations Suppress JNK Signaling to Promote Colon Tumorigenesis**" A Marusiak et al. *Cancer Research* 2016 76(3):724-35.



"Cartoon depiction of MLK4 structure (4UYA)—the kinase domain (green) with highlighted features (yellow), bonds of ATPγS (light blue carbon atoms), putative LZ1 (magenta), and the protein section linking the C-terminus of the kinase domain with the N-terminus of LZ1 (green line)".

Researchers find a genetic new target for most common lung cancer

Research has identified mutations in lung cancer that are key to tumour growth, offering a new way to differentiate and treat some patients with the disease.

Non-small cell lung cancer (NSCLC) makes up around 8 in 10 cases of lung cancer but the outlook is bleak for many patients, who are often diagnosed at a late stage. For some there is the promise of targeted 'smart' drugs, but scientists have so far struggled to identify which targets to hit in the majority of patients.

Despite an ever-increasing amount of genetic data revealing a host of mutations in NSCLC cells, there is much work to do in order to pinpoint which are vital for tumour survival.

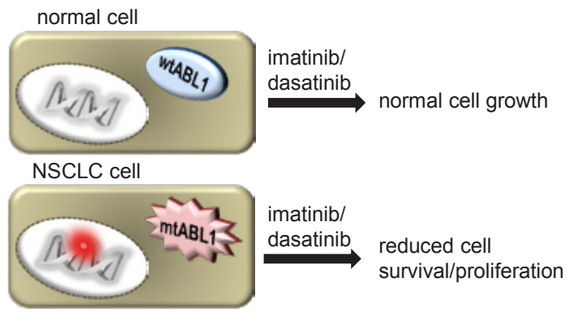
The Signalling Networks in Cancer group has focused on a pair of genes known as ABL1 and ABL2, which are mutated or amplified in up to 10% of lung cancer cases.

Drugs that block the activity of the ABL proteins have been used to successfully treat leukaemia patients, where ABL is overactive. However, until now, the role of ABL1 and ABL2 in other cancer types hasn't really been explored.

Dr John Brognard's team looked at lung cancer cells in the lab and showed that mutations in ABL1, but not ABL2, were necessary for their survival. By using an ABL inhibitor – imatinib – they could block tumour growth in cancer cells that harboured an ABL1 mutation.

Their findings give doctors an extra ready-made tool for the treatment of lung cancer in the form of an existing leukaemia drug.

"**Somatically mutated ABL1 is an actionable and essential NSCLC survival gene**" E Testoni et al. (2016) *EMBO Molecular Medicine* 8(2):105-16.



Somatically mutated ABL1 is defined as a novel druggable driver in NSCLC where mutant forms of ABL1 kinase promote increased survival and proliferation, altered localisation, and enhanced downstream pathway activation. Lung cancer cells harbouring ABL1 mutations are sensitive to ABL inhibitors, such as imatinib or dasatinib, suggesting NSCLC patients with ABL1 mutations could benefit from treatment with these clinically available inhibitors.

Revolutionary technique expanded to study other types of lung cancer

A cutting edge method of creating patient-specific laboratory models has now been replicated in a second type of lung cancer.

Patient relevant models of cancer are vital for scientists to investigate the genetic profile of individual cases and to develop and test new treatments. Previously, laboratory models were created in mice using tumour tissue samples taken from patients, but this process involves invasive surgery.

Researchers from the Institute's Clinical and Experimental Pharmacology group, led by Professor Caroline Dive, recently showed that they could instead create similar mouse models, which they named CDX, from a patient's blood sample. Such a blood sample contains so-called circulating tumour cells (CTCs) – cancer cells that have broken free from the original tumour and have passed into the bloodstream.

Their first study – published in 2014 – involved injecting the mice with samples from small cell lung cancer (SCLC), where many CTCs are generally found. The SCLC CDX tumour model they created closely matched the characteristics of the patient's tumour – including its appearance under a microscope and its genetic profile.

Now the team has looked to replicate this method in NSCLC, a disease with considerably lower CTC counts.

The group successfully generated a CDX using a blood sample taken from a patient diagnosed with NSCLC. This achievement paves the way for scientists to better understand non-small cell lung cancer (NSCLC) without the need for tissue samples.

The paper, **Tumourigenic non-small-cell lung cancer mesenchymal circulating tumour cells**: a clinical case study, by Morrow CJ et al. (2016) was published in the journal *Annals of Oncology*. [Epub ahead of print]

Blood test may give early warning of skin cancer relapse

A blood test may be able to sound early warning bells that patients with advanced melanoma skin cancer are relapsing.

Scientists from the Molecular Oncology group led by Professor Richard Marais, in collaboration with Professor Caroline Dive's Clinical and Experimental Pharmacology group, studied the DNA shed by tumours into the bloodstream – called circulating tumour DNA – in blood samples from seven advanced melanoma patients at The Christie NHS Foundation Trust.

In this early work they found they could see whether a patient was relapsing by tracking levels of circulating tumour DNA. And they found that new mutations in genes like NRAS and PI3K appeared, possibly causing the relapse by allowing the tumour to become resistant to treatment.

Around 14,500 people are diagnosed with melanoma and more than 2,100 people die from it every year in the UK. Most melanoma patients respond to treatment at first but their cancer can become resistant within a year. It is hoped that these approaches will allow doctors to use circulating tumour DNA to tailor treatment for individual patients to get the best result.

Around 40 to 50 per cent of melanoma patients have a faulty BRAF gene and they can be treated with the targeted drugs vemurafenib or dabrafenib. But for many of these patients the treatments don't work, or their tumours develop resistance after a relatively short time. When this happens these patients can be offered immunotherapy drugs including pembrolizumab, nivolumab and ipilimumab. Detecting this situation early could be key to improving their care and chances of survival.

"**Application of sequencing, liquid biopsies and patient-derived xenografts for personalized medicine in melanoma.**" MR Girotti et al. (2016) *Cancer Discovery* 6(3):286-99.

Twin blood cell growth proteins are not identical

Researchers at the Institute have shown that a pair of proteins involved in the development of blood cells may have different roles to play, with one apparently much more implicated in certain types of leukaemia.

RUNX1 is known as a 'master regulator' of blood cell development, primarily in action as an embryo grows. It also controls the accurate production of the various types of blood cells throughout adult life.

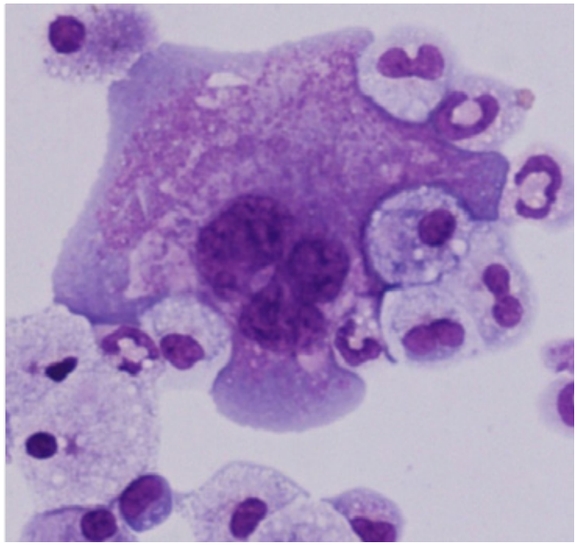
A significant number of leukaemia cases involve the mutation of RUNX1, but the fully functioning version of the gene is conversely required in some cases to maintain a leukaemic state.

Through the work of 'promoters', P1 and P2, RUNX1 is used to generate two different proteins: RUNX1C and RUNX1B respectively. The team from the Stem Cell Biology group, led by Dr Georges Lacaud, labelled the two promoters to trace their activities in adults.

The group showed that RUNX1C dominated – P1 was active throughout the bone marrow. On the other hand, P2 activity appeared to be restricted to only certain cell types, allowing differentiation between platelet-producing cells and red blood cells.

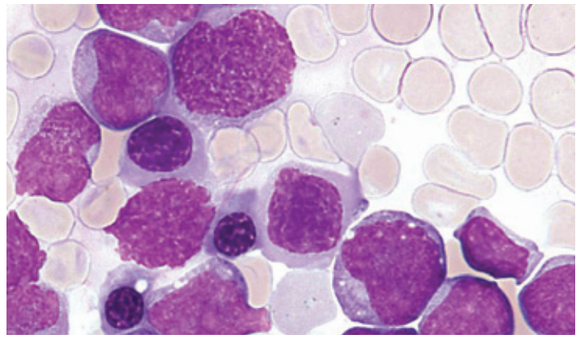
When the scientists removed activity of RUNX1C, they saw a reduction in the production of platelets – a similar situation, although less severe, to when RUNX1 as a whole was lost. Other cell types were less affected. However, when they investigated the effect of one particular leukaemia gene – AML1-ETO – they saw that it appeared to promote P2 over P1.

"**RUNX1B Expression Is Highly Heterogeneous and Distinguishes Megakaryocytic and Erythroid Lineage Fate in Adult Mouse Hematopoiesis**" JE Draper el al. (2016) *PLoS Genetics* 12(1):e1005814.



Picture of a platelet-producing multinucleated megakaryocyte, surrounded by smaller monocytes/macrophages and granulocytes. All of these white blood cells express both RUNX1 protein isoforms, whereas an absence of RUNX1B favours red blood cell production.

Institute scientists identify possible double whammy to attack leukaemia



Leukaemia cells

Scientists from the Molecular Oncology group have identified a potential double drug combination against B-cell acute lymphoblastic leukaemia by studying how two drugs called trametinib and ABT-263 work in cancer cells and mice.

Trametinib blocks the MEK/ERK signalling pathway to stop cancer cells from growing out of control. However, when the scientists studied B-cell acute lymphoblastic leukaemia cells in the laboratory, trametinib did not work as well as expected and did not stop cells growing.

The scientists found that this was because these cancer cells had high levels of some proteins that help the cells to survive and overcome the effects of the drug.

They therefore decided to test if another drug known as ABT-263 – which targets the survival proteins – could work alongside trametinib to counteract this problem.

Their laboratory experiments in cell lines and mice showed that when they combined these drugs and blocked both signalling pathways, the cells could not escape the effects of trametinib and died.

There are 820 new cases of acute lymphoblastic leukaemia each year in the UK and B-cell acute lymphoblastic leukaemia is the most common type of the disease. More than half of these cases are diagnosed in children.

These findings are the first step to finding a new effective drug combination for B-cell acute lymphoblastic leukaemia.

"**BIM mediates synergistic killing of B-cell acute lymphoblastic leukemia cells by BCL-2 and MEK inhibitors.**" K Korfi et al. (2016) *Cell Death & Disease* 7:e2177.

Cellular signalling 'tug-of-war' proteins identified

Institute scientists have explained some of the contradictory behaviour of a molecule known as Rac1 by showing that its activity depends on where its 'push' comes from.

Rac1 has previously been implicated in tumour formation and spread. In particular, it seems to have a role in controlling the movement of cells.

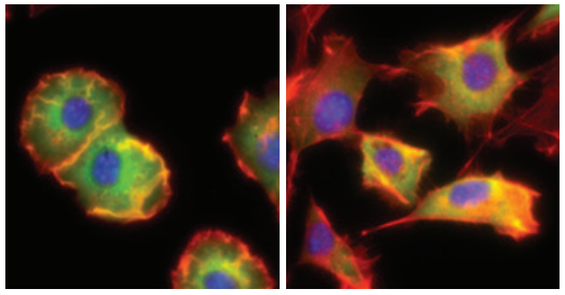
However, studies have shown that activation of Rac1 can cause opposing effects – sometimes leading to the formation of cell 'feet' or lamellipodia – to allow cells to migrate and invade, and at other times impeding such action.

The researchers from the Cell Signalling group, led by Dr Angeliki Malliri, have looked at two proteins – one at each end of this signalling tug-of-war – to find out more.

The group found a new signalling cascade, where the P-Rex1 and FLII proteins worked in conjunction with Rac1 to encourage cell migration. On the other hand, when Rac1 linked with a protein called Tiam1 it appeared to increase the stickiness of cells and reduce their movement.

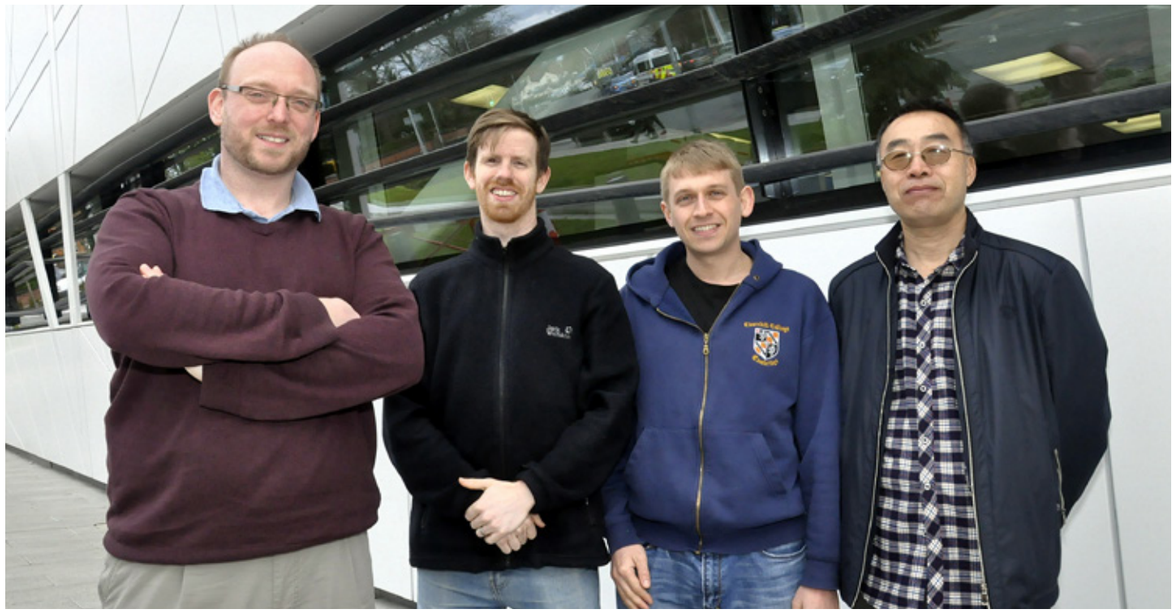
Their study reveals that the two factors – Tiam1 and P-Rex1 - have opposite actions when they each team up with Rac1.

"**Differential Rac1 signalling by guanine nucleotide exchange factors implicates FLII in regulating Rac1-driven cell migration**" H Marei et al. (2016) *Nature Communications* doi: 10.1038/ncomms10664



Left: Cells expressing Tiam1, which promotes their cell-cell adhesion/ aggregation and inhibits their migration. Right: Cells expressing P-Rex1 , which promotes membrane extensions/elongation and induces migration

Core Facilities Update



The SciCom team (L to R): Marek Dynowski, Chris Wirth, Chris Smowton, ZhiCheng Wang.

New Head of Scientific Computing

High Performance Computing (HPC) is an essential tool used in contemporary cancer research. It has become a pre-requisite for the proper exploitation of cancer research data, in part because of the high volumes of data produced by recent advances in deep sequencing, imaging, and tandem mass spectrometry technology.

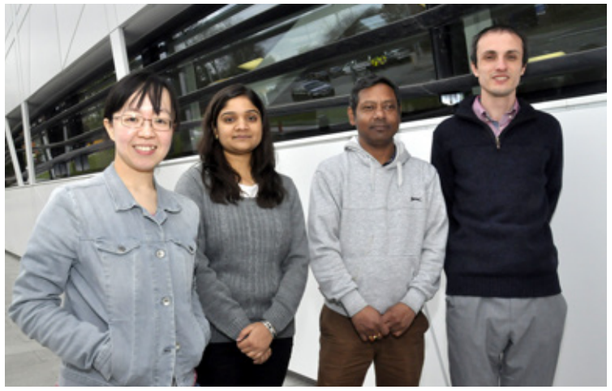
The Scientific Computing Team (SciCom) at the Institute offers services, infrastructure, technology and software for data processing, analysis, integration and archiving. These services are developed and operated in close co-operation both with the other research facilities at the Institute as well as the research groups that make use of the data.

A new team leader, Marek Dynowski joined the Institute in March to lead SciCom as it continues to apply the cutting edge computing approaches needed to support the breathtaking advances that are driving the field of cancer genomics forward so rapidly.

Marek gained a PhD in Molecular Biology at the University of Tübingen in Germany, during which he conducted intensive molecular dynamic simulations and other scientific calculations on various high performance computing systems. He then became a programmer and scientific consultant for HPC applications at the University of Freiburg data center. In 2012 he returned to Tübingen to build an HPC cluster and an HPC Competence Center for Bioinformatics and Astrophysics for the state of Baden-Württemberg, as well as planning and establishing an HPC system and associated virtualisation and storage infrastructure for the Bioinformatics Core Facility of the University.

In March he moved to Manchester and became the new head of SciCom, which comprises the senior HPC engineer ZhiCheng Wang and the programmers Chris Wirth and Chris Smowton. Currently the team operates HPC systems with a total of 1,780 compute cores and more than 30 terabytes of main memory, as well as various storage systems for data processing, backup and archiving with an overall capacity of 3.9 petabytes. The water-cooled machine room and the uninterruptable power supply enable SciCom to provide high availability services with great performance and in-house secure backup. In combination with a highly skilled and motivated team of programmers and due to the close co-operation with the Computational Biology Support team, the core facility is able to offer coherent bioinformatics solutions for high-throughput analysis and data management. In future, SciCom will further enhance the transition from basic into translational research by implementing scientific software and workflows over a virtualisation infrastructure, which is currently being established. It will provide a scalable and flexible platform for offering database and web services that need a tight integration into the local computing or data storage infrastructure.

Computational Biology Support Team



The Scientific Computing Support team (L to R): Hui Sun Leong, Shambhavi Srivastava, Sudhakar Sahoo, Sam Taylor

Recent advances in high-throughput technologies have resulted in an enormous amount of 'omics' data being gathered at steadily increasing rates.

Great strides in technological development is causing a shift in biological research from a traditionally hypothesis-driven to a data-driven approach. Given the size and complexity of these big data, scientists are in need of rigorous and scalable methods to unearth the exciting knowledge in the data. The Computational Biology Support (CBS) team is committed to help researchers within CRUK MI to meet this challenge.

The team was established in 2015 to address the growing demand for computational biology support for Next-Generation Sequencing (NGS). They combine biology, computer science and statistics to study and process high-throughput genomics and proteomics datasets.

Working closely with the Scientific Computing team, they have developed and implemented data analysis pipelines for the initial processing and analysis of diverse data types generated from our in-house NGS facilities, including RNA-seq, small RNA-seq, ChIP-seq, targeted re-sequencing, whole-exome and whole-genome sequencing data. In addition to using well-established methods, they are also actively trying to overcome the shortcomings of existing tools by refining or developing our own according to the requirements of projects. One such example is the development of a dedicated mutation-calling pipeline for detecting somatic mutations in circulating free DNA from patients' blood samples, which was performed in collaboration with members from the Clinical and Experimental Pharmacology and RNA Biology groups.

CBS provides different levels of support: they often undertake all the analysis component of a project; however, they also act in an advisory role to researchers who want to perform their own analysis and need input.

AACR Meeting 2016

By Steve Bagley

The American Association for Cancer Research was held in New Orleans and this year's theme was "Delivering Cures Through Cancer Science".

With over 4000 attendees and 6000 offered abstracts from researchers worldwide, it's a huge meeting and a great opportunity to present the latest discoveries. This year, there was a fantastic representation from the Institute with 25 of our scientists presenting their research or chairing sessions. Predominant themes across the meeting were tumour heterogeneity, stromal-tumour interactions, immunotherapy and single cell analysis.

I was invited to present a talk on 'Information Rich Systems' and discussed how microscopy and cytometry is moving to multiple signals, multiple sampling multi-parametric analysis and merging with other technologies such as molecular biology and MRI. The following debate centered around how we merge and collate data from a variety of data streams.

My lasting memory of the meeting was the staggering volume of research presented; it was impossible to attend all of the fascinating presentations that interest you with so many major and minor symposia going ahead simultaneously. Other memorable moments include a trade show that required a whole day to fully explore and the sheer number of scientists and clinicians who attended.

Steve Bagley just before his presentation at "The Ernest N. Morial Convention Center" in New Orleans

Grant News

Institute Grants Committee

The Institute has recently formed its own Grants Committee to further strengthen our grant applications and increase the chances of success.

The Committee, chaired by Professor Iain Hagan – who has extensive experience of sitting on grant and review committees for several funding bodies – will review thoroughly all grant applications and provide detailed feedback to help applicants secure funding. Although in its infancy, both applicants and reviewers alike are extremely positive about the approach and believe it will add an invaluable step to the highly competitive process of applying for grant funding.

Prostate Cancer UK PhD Studentship in Bioinformatics

Dr Crispin Miller and Dr Esther Baena have been awarded a Prostate Cancer UK funded PhD Studentship.

The Movember Foundation, through PCUK are funding researchers with expertise in both statistics/data analysis and prostate cancer.

The appointed student will study how noncoding RNAs are switched on and off in response to different drug treatments and ask whether similar patterns can be detected in patients' tumours; and whether this can be used to predict which drugs are likely to work best for each patient.

Iain Hagan wins Wellcome Trust Investigator Award

Professor Iain Hagan has been awarded a Wellcome Trust Investigator Award to study "Spatial and temporal control of mitotic commitment".

This highly competitive and prestigious award provides substantial funding for world-class researchers with a compelling long-term vision for their research.

This Investigator Award will allow Iain to address the challenging question of how the decision to trigger the switch that drives cells into division is taken. Based on his previous findings that the centrosome plays a key role in regulating the switch, Iain and his team will investigate how centrosomes control division timing in normal conditions and under stress to determine how and why switch regulation changes in different environmental contexts. Progress in the understanding of these fundamentally important aspects of cell cycle control will make a significant impact in the development of cancer therapies.

Institute researcher wins share of £1 million to investigate pancreatic cancer

Dr Claus Jørgensen, who leads the Institute's Systems Oncology group, is one of six scientists to have new research projects funded by Pancreatic Cancer Research Fund (PCRF). His three-year study is entitled "Targeting enzymes for stromal normalisation in pancreatic ductal adenocarcinoma".

Pancreatic tumours have a thick protective coating called the stroma, which contains certain types of cells hijacked from neighbouring tissues that have been forced to help the tumour survive and grow. Claus has discovered that blocking a particular enzyme in these hijacked cells returns them to their normal state. His project will investigate how this happens and whether interfering with this enzyme will make the tumour cells more vulnerable to chemotherapy.

Education News

Where are they now?

Our former PhD students tell us how they are getting on with their new lives in new countries.

Tim Somerville is now working at Cold Spring Harbor laboratories on Long Island, USA.

Tim Somerville

Following the completion of my PhD studies in Tim Somervaille's group at the CRUK Manchester Institute, I decided to leave the great city of Manchester where I have spent most of my life and head over the Atlantic to take up a postdoctoral position in the lab of Chris Vakoc at the Cold Spring Harbor Laboratory in New York. The opportunity to live and work in the U.S. and to join a fantastic laboratory in such an esteemed institution was one I felt I could not let pass me by. After six months of living here, I can report that I am thoroughly enjoying my new life on Long Island as well as the work in the lab. My project centres on identifying new therapeutic targets for the treatment of pancreatic cancer by employing a domain-focused CRISPR screening strategy. The nature of the work requires that I spend a lot of time in the lab, fortunately however, Cold Spring Harbor is ideally situated with great views of the water and surrounding wildlife making it a beautiful place to work.

Away from the lab, I am looking forward to my first summer on Long Island. I am particularly eager to visit the Hamptons in the east of the island as well as the south shore beaches. I also enjoy trips into New York City, which is less than an hour away by train, and I am planning trips slightly further afield to Boston and Washington DC. Finally, I have joined a local 'soccer' team, which has enabled me to meet new friends away from the lab and to escape all things scientific for a few hours of the week at least.

Timurs Maculins enjoying the Silverstone Circuit before moving to Frankfurt, Germany.

Timurs Maculins

I completed my PhD with Dr Karim Labib, who led the Cell Cycle laboratory at the Institute until autumn 2013. After a short stay following my PhD defence, I joined a postdoctoral programme at AstraZeneca on a collaborative project with Professor Ronald Hay to develop a novel screening platform for identification of chemical inhibitors of E3 ubiquitin ligases, an enzyme class that is implicated in cancer development. Following completion of this project, I returned to academic research in Frankfurt-am-Main, Germany where I am pursuing my scientific interests in ubiquitin biology in the laboratory of Professor Ivan Dikic on a postdoctoral fellowship from Human Frontier Science Programme.

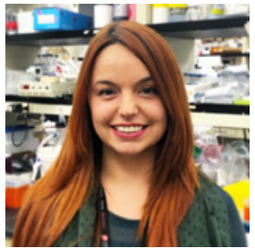
After more than seven years in the UK, I most enjoyed the Silverstone Circuit – what a ride that was!

Tim and Hadir enjoying Frankfurt together.

Hadir Marei

Following my PhD in the Cell Signalling group under the supervision of Dr Angeliki Malliri and my short stay after, I dared to undertake a new scientific adventure. This landed me in Frankfurt, Germany, where I'm currently a postdoctoral fellow in the Molecular Signalling group headed by Prof. Dr. Ivan Dikic at the Institute of Biochemistry II (IBCII). Expanding on my knowledge in the GTPases field, I am interested in understanding the role of regulators of Rab GTPases in modulating autophagy. Additionally, I'm also exploring the interplay between cytoskeletal regulators and the trafficking machinery, under normal and pathological conditions. Given my scientific background, I am also interested in identifying novel proteins that modulate the cytoskeleton, particularly following bacterial infection.

Coming from a very social environment at CRUK MI, it was very pleasant to see a similar collaborative spirit in IBCII. People, both in the institute and in the lab, are very helpful and friendly, making it very easy to settle in. Also, Frankfurt is a fantastic place to be, both on a scientific level as well as on a personal one.



Danielle in The Letai Lab at the Dana-Farber Cancer Institute.

Danielle Potter

I completed my PhD at the CRUK MI in the Clinical and Experimental Pharmacology group and graduated in December 2015. I am now working at the Dana-Farber Cancer Institute in Boston as a postdoctoral research fellow in a group led by Dr Anthony Letai. Previously in Professor Caroline Dive's lab, I worked on rational drug combinations in the treatment of colorectal and small cell lung cancer. Specifically I was focusing on apoptosis and mechanisms to increase the potency of BH3 mimetics, which are a class of drugs that target the intrinsic apoptotic pathway. I had long followed Dr Letai's research on BH3 profiling, so when the opportunity to work as a postdoc in his lab came up I grabbed it with both hands. I am interested in investigating whether BH3 profiling can be used to identify patient tumour heterogeneity and whether dynamic BH3 profiling on patient biopsies can be used to aid therapeutic decisions. Also I would like to investigate whether BH3 profiling is possible on circulating tumour cells and what this may reveal about the patient and possible treatment options.

I feel privileged and honoured to be a part of the Letai lab and look forward to making my mark within the group. I have only been in my new role for two months so I am still finding my feet, however so far Boston has been a fantastic city to live in. Being a part of Harvard University comes with many opportunities and I look forward to making the most of them.

Tim Somerville wins Dexter Award

Tim Somerville, a recent former PhD student, was the 2015 winner of the Institute's Dexter Award for Young Scientists.

The prize recognises the most impressive scientific achievement of the year across the building by a student, post-doc or scientific officer. The judging panel were highly impressed by Tim's achievements during his PhD studies in the Leukaemia Biology lab and felt that he was a very worthy winner. Tim joined the group in 2011 and started on a project that followed up a previous observation that FOXC1 transcripts are highly expressed in at least 20% of human Acute Myeloid Leukaemia cases. Tim subsequently discovered a completely novel oncogenic mechanism in AML, namely the tissue inappropriate de-repression of a mesenchymal transcription factor which leads to a differentiation block in myeloid lineage cells and inferior survival in patients. This work was published in *Cancer Cell* in September 2015 with Tim as first author. He is also a co-author on four other papers produced by the group which is a highly impressive output from his time here. Other success enjoyed by Tim during his PhD included winning an American Society of Hematology abstract achievement award and he also had his work selected for an oral presentation at the 8th International PhD Student Cancer Conference and at The University of Manchester's Postgraduate Summer Research Showcase. He is continuing his scientific career and his interest in cancer research having recently moved to Cold Spring Harbor to take up a post-doctoral position with Chris Vakoc.

Tim Somerville wins Manchester Doctoral College Best Outstanding Output Award

Tim's excellent contribution to scientific research made during his PhD was also recognised by The University of Manchester when they bestowed upon him their Doctoral College Award for the Best Outstanding Output for a PhD student in 2015. This award acknowledges research outputs of the highest quality associated with the Faculty of Medical and Human Sciences at the University.

Awards and Events

Cancer Research UK Lung Cancer Centre of Excellence Conference

John Brognard presenting his work to the meeting

The inaugural Cancer Research UK Lung Cancer Centre of Excellence meeting was held at the Midland Hotel Manchester at the end of 2015.

This ambitious meeting brought together world leaders in lung cancer, encompassing expertise from immunotherapy and tumour evolution through to medical imaging and clinical trials, to discuss the latest advances in lung cancer research and accelerate progress in understanding and treating the disease. The event included talks from biologists, geneticists, immunologists, physics experts and clinicians. Our own Director Professor Richard Marais opened the meeting and Joint Centre Lead Professor Caroline Dive spoke about the significance and impact of circulating biomarkers on lung cancer, while Joint Theme Lead for Basic Science, Dr John Brognard, gave a talk on the identification of novel oncogenic and tumour suppressing kinases as targeted therapies for non-small cell lung cancer.

The meeting highlighted the multidisciplinary approach being spearheaded at Lung Cancer Centre of Excellence to make a real difference to patients with lung cancer. This message was brought home both by an introductory video message from Sir Alex Ferguson, whose parents both died from lung cancer, and an emotional and inspiring talk from Tom Haswell, a patient survivor who works with CRUK giving real life perspective to the research being undertaken at the Centre. The meeting was a great success and attendance at future meetings is highly recommended to all those working in lung cancer.

Amaya Virós

Prestigious Fellowship for Clinician Scientist

Dr Amaya Virós, a clinician scientist based in the Molecular Oncology group, has been awarded a Wellcome Trust Intermediate Clinician Scientist Fellowship.

This highly competitive fellowship will allow Amaya to establish her own group to carry out research into why older patients are less likely to survive following a melanoma diagnosis.

Dr Virós is an academic dermatologist who splits her time between conducting research into skin cancer and seeing patients at Salford Royal NHS Foundation Trust. Most of her research so far has been undertaken within the group led by Professor Richard Marais, a world expert in melanoma research, and the Wellcome Trust award will now offer Amaya the opportunity to build her own team and answer new questions that aim to help melanoma patients. Over four years her team will explore how melanoma affects elderly patients.

She explained her project: "More than 80% of melanoma deaths occur in patients who are more than 50 years old, and mortality is specifically increasing in the elderly. Melanoma in the elderly is also more likely to progress. We will investigate why older people are more vulnerable to melanoma and if melanoma in the elderly is inherently more aggressive."

Alongside funding to cover salaries, expenses and laboratory costs, the fellowship includes mentoring support to guide Dr Virós as she develops an independent career in academic medicine.

Institute Director Professor Marais said: "This prestigious fellowship is an exciting opportunity for Amaya. The award by the Wellcome Trust is a reflection of her impressive achievements to date and her potential as a world-leading cancer researcher. We at the CRUK MI are very proud of her achievements."

Marie Curie Fellowship for Pedro Torres-Ayuso

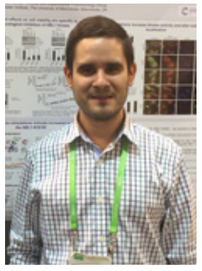
Congratulations to Dr Pedro Torres-Ayuso on his success in obtaining a prestigious Marie-Curie-Skłodowska Action Individual Fellowship.

The MSCA, funded through the European Commission, supports the best or most promising researchers to enhance career development and training towards establishing an independent position.

Pedro is a postdoctoral research fellow in the Signalling Networks in Cancer group, led by Dr John Brognard, where he is part-funded by a fellowship he secured from the Fundación Ramón Areces. Pedro will focus his two-year MSCA fellowship on developing a potential therapeutic target for the treatment of patients with lung squamous cell carcinoma, a cancer type where treatment options are still scarce.

This fellowship will enable Pedro to develop a wide range of new and transferable skills, and allow him to strengthen his expertise in the laboratory whilst broadening his management and communication competencies. Under the mentorship of John, this project will enable Pedro to achieve his long-term career goal of obtaining a leadership position in a competitive European Institute where he can establish his own research group.

AACR Scholar-in-Training Award for Pedro Torres-Ayuso



Pedro Torres-Ayuso presenting his poster in the 2016 AACR meeting'

Congratulations to Dr Pedro Torres-Ayuso, from the Signalling Networks in Cancer group, who won an American Association for Cancer Research (AACR) Scholar-in-Training Award sponsored by Abbvie.

Scholar-in-Training Awards recognise outstanding young investigators presenting meritorious proffered papers at the AACR Annual Meeting. They are highly competitive and are presented to fewer than 10% of applicants. The award consisted of US$2000 and supported Pedro's travel and accommodation expenses.

Pedro's poster, presented at the 2016 AACR meeting in New Orleans, was entitled "Mutant ABL1 is a genetic dependency in non-small cell lung cancer amenable to pharmacological intervention".

As one of the winners of this prize, Pedro was also invited to an Awardees reception to meet his sponsor. "I had the opportunity to network with other early-career scientists who got the same prize, as well as to meet and discuss my research with renowned scientists attending the event", says Pedro who also acknowledges the help and support of Dr John Brognard, his team leader: "Part of my success is thanks to him".

Romina Girotti is honoured in Biochemical Society Awards

Romina Girotti

Romina Girotti has been awarded The Biochemical Society Early Career Research Award in Signalling.

The Biochemical Society's Awards allow the work of high calibre scientists at all stages of their careers to be recognised and rewarded. The 2017 Award lecture series will showcase the outstanding contributions to molecular bioscience that the winners have made during their careers.

Romina joined the Molecular Oncology group in 2012 and has specialised in translational medicine in melanoma. Under the mentorship of Institute Director Professor Richard Marais, she achieved an outstanding track record of publications in high impact factor journals.

Her work has provided crucial insights into the molecular mechanisms underlying resistance to targeted therapies in melanoma, the development of new therapeutics to treat resistant patients in collaboration with the Institute of Cancer Research and new technologies for personalised medicine in melanoma patients. As a result of this research, a Phase-I clinical trial started in April 2015 at The Royal Marsden NHS Foundation Trust and at The Christie NHS Foundation Trust.

Romina was thrilled to receive this award and acknowledges Richard Marais for nominating her and for being an amazing mentor.

The Awards ceremony will take place in 2017 and all winners are invited to submit an article to a Society-owned publication. Romina has submitted her article to The Biochemist, one of the most highly-respected life-science association magazines in the country.

Kate Hogan takes her research to Parliament


Kate Hogan

Kate Hogan, who recently completed her PhD at the Institute, attended Parliament to present her research to a range of politicians and a panel of expert judges, as part of SET for Britain in March. She was shortlisted from hundreds of applicants to appear in Parliament.

Her poster on research about the role of ultraviolet light in melanoma was judged against dozens of other scientists' research in the only national competition of its kind.

On presenting her research in Parliament, Kate said: "I applied to take part in SET for Britain because I think it's very important for scientists to share their research with politicians. Not only does this build bridges between researchers and policy makers, but also it is through these sorts of discussions that discoveries in the lab can benefit the wider community".

Stephen Metcalfe MP, Chairman of the Parliamentary and Scientific Committee, said: "This annual competition is an important date in the parliamentary calendar because it gives MPs an opportunity to speak to a wide range of the country's best young researchers.

"These early career engineers, mathematicians and scientists are the architects of our future and SET for Britain is politicians' best opportunity to meet them and understand their work."

The Parliamentary and Scientific Committee runs the event in collaboration with the Royal Society of Biology, the Royal Academy of Engineering, the Royal Society of Chemistry, the Institute of Physics, The Physiological Society and the Council for Mathematical Sciences, with financial support from Essar, the Clay Mathematics Institute, Warwick Manufacturing Group (WMG), the Institute of Biomedical Science, the Bank of England and the Society of Chemical Industry.

Dominic Rothwell wins BACR travel award

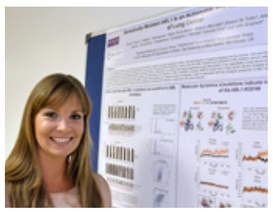
Dominic Rothwell was awarded a British Association for Cancer Research (BACR) travel award following selection to give an oral presentation at the 16th World Conference on Lung Cancer, Denver, in September 2015.

Dominic works as a Research Fellow in the Clinical and Experimental Pharmacology group, within the Nucleic Acids Biomarkers team.

At the conference Dominic talked about the *'Molecular characterisation of small cell lung cancer using both circulating tumour DNA and circulating tumour cells isolated from the same whole blood sample'* and described how they have demonstrated that preserved blood samples can be used for the isolation and molecular analysis of both circulating cell-free DNA and circulating tumour cells. These are two clinically important biomarkers that enable us to determine the genetic status of a patients' tumour from a simple blood sample, bypassing the requirement for an intrusive biopsy and facilitating the analysis of longitudinal samples. Both of these biomarkers are starting to be used extensively in clinical trials and showing that their analysis is feasible from preserved blood samples expands the use of these valuable biomarkers into multi-site clinical trials.

The meeting was highly informative, allowing Dominic to broaden both his scientific and clinical knowledge of lung cancer, which has been extremely valuable in a number of projects within CEP. It also provided him with the opportunity to meet world leaders in the field of lung cancer research including Charles Rudin (Memorial Sloan-Kettering) and Roman Thomas (Cologne).

Best Poster Prize winner


Ewelina with her poster

Ewelina Testoni received the Best Poster Prize at the Lung Cancer Centre of Excellence Conference that took place in Manchester last December.

Ewelina is a PhD student working in the Signalling Networks in Cancer group, led by Dr John Brognard. She was awarded Best Poster Prize for her research showing that for the first time somatically mutated ABL1 represents a novel driver in non-small cell lung cancer (NSCLC). Her poster described how mutated ABL1 kinases are required to maintain lung cancer cell survival and proliferation. ABL1 mutations identified either in lung cancer cell lines or in primary lung tumours can alter kinase structure, increase kinase activity or promote cytosolic retention. Importantly, this study suggests that NSCLC patients presenting with ABL1 mutations could benefit from treatment with imatinib.

Honor Fell Travel Award winner

Congratulations to Alice Lallo who was recently awarded an Honor Fell Travel Award to attend a European Molecular Biology Organisation (EMBO) Conference in May this year.

The awards are sponsored by the Company of Biologists (the publishers of *The Journal of Cell Science and Development*) and they provide financial support for British Society for Cell Biology members at the beginning of their research careers to attend meetings.

Alice is a PhD Student in the Clinical and Experimental Pharmacology group and she will use the funding to attend the EMBO Conference focusing on "Cellular signalling and Cancer therapy" held in Croatia. The aim of this meeting is to share new insights in the understanding of cancer and how they provide novel strategies for cancer treatment, and brings together leading experts from different scientific disciplines. This conference will be an important experience for Alice, where she will present a poster about her project looking at the mechanisms of resistance to standard chemotherapies in small cell lung cancer patients using circulating tumour cell (CTC) and CTC-derived xenograft (CDX) models.

Melanie Galvin wins Steve Moore Memorial Poster Prize

At the Institute of Animal Technology (IAT) North West Branch meeting held on 14 April, Melanie Galvin was awarded the Steve Moore Memorial Poster Prize for her outstanding poster on the "Refinement of Tumour Passage by Optimisation of the Tissue Disaggregation Protocol".

The IAT is an organisation dedicated to animal welfare in science and promotes approaches to replace, refine and reduce their use for scientific purposes.

Melanie is a Senior Scientific Officer in the Clinical and Experimental Pharmacology group, where she manages the pre-clinical pharmacology in vivo team, a role that sees her co-ordinating all of the in vivo activity for the Clinical and Experimental Pharmacology group. Winning such a prestigious award is an impressive achievement which includes an all-expenses paid trip to the American Association for Laboratory Animal Science National Annual Meeting – the largest Animal Technology conference in the world – this year held in North Carolina. Attendance at this meeting will provide Melanie with the opportunity to showcase her vital work and importantly share the techniques internationally to help promote the 3Rs (Replacement, Reduction and Refinement) and better animal welfare.

CRUK MI shows 'genuine commitment' to the 3Rs


Winners of the CRUKMI 2015 3Rs' Poster Prize, Alice Lallo of CEP (left) and Kate Hogan of Molecular Oncology (centre) with Vicky Robinson, CEO of the NC3Rs.

The Institute held its first 3Rs poster and prize event in November 2015. In a buzzing lunchtime event in the Coffee Room, thirteen groups of poster authors described how they had replaced, reduced or refined the use of mice in their research during the last few years.

Judging the entries, Dr Vicky Robinson, CEO of the National Centre for the 3Rs (NC3Rs) remarked on the teamwork and enthusiasm shown by scientists and technicians and said it demonstrated 'genuine commitment' to the 3Rs.

Two prizes of £250 were awarded: to Alice Lallo from the Clinical and Experimental Pharmacology group, who had developed an 'ex vivo' method using small cell lung cancer explant tissue that had reduced the need for 'in vivo' studies; and to Kate Hogan of the Molecular Oncology group who had refined protocols in melanoma studies to minimise the effects of UV exposure on mice.


Denis Alferez, 3Rs Network Lead with Vicky Robinson, CEO of the NC3Rs.

The event was organised by the CRUK MI 3Rs Network, led by Denis Alferez from The University of Manchester's Institute of Cancer Sciences' Breast Biology group, who will soon be calling for entries for the 2016 prize.

CRUK Travel Award for Romina Girotti

Romina Girotti of the Molecular Oncology group successfully applied for a Cancer Research UK travel award, allowing her to work in Argentina for three months.

"It was a great experience, and I feel very honoured to have received this competitive CRUK award. I had the opportunity to work on and learn about immunology and its related techniques from an expert in the immunology field, Prof Gabriel Rabinovich and his team at the IBYME (Institute of Biology and Experimental Medicine)", says Romina.

The IBYME is part of the Argentinean National Council Research and the University of Buenos Aires and was founded by the Nobel Prize winner Bernardo Houssay in 1944. Professor Rabinovich's group works at the interface of immunology, tumour biology and glycobiology, using in vitro and in vivo approaches to understand how the molecular interactions between endogenous lectins and their glycosylated ligands can mediate cellular processes relevant to immunity, inflammation and angiogenesis. For more than 20 years the group has investigated the role of glycan-binding proteins in mediating cellular processes central to immune regulation and human diseases.

This travel award allowed me to start a collaboration between our group in Manchester led by Professor Richard Marais and the Immunopathology Lab in Argentina", concludes Romina.

Romina (in the floral dress) with Prof Rabinovich's group on World Cancer Day

Science and policymaking: Marina Parry's experience in Parliament

By Marina Parry


Marina with MP Liz NcInnes

In November last year, I spent four days in Parliament thanks to the Royal Society's Pairing Scheme. Its aim is to pair a scientist with a UK parliamentarian or a civil servant in order for each of them to discover, or better appreciate, each other's worlds.

I was paired with Liz McInnes, MP for Heywood and Middleton, herself a former NHS employee. I shadowed her for two days, following her from meetings about her party's response to immigration, to report launches and to prize-giving ceremonies organised by charities. I was also fortunate enough to watch MPs in action, from within the House of Commons debating intervention in Syria, and also the famous Prime Minister's Questions (PMQs), to the Science and Technology Select Committee questioning the government's response to Ebola in West Africa. Together with others on the scheme, we were also given the opportunity to learn about the actual political process and meet policymakers who have the most interaction with scientists: members of the Government Office for Science and POST (Parliamentary Office of Science and Technology). We learnt how they work with scientists on briefing or policy documents and also how we could become involved with them.

I often complain that there isn't enough science in government, but heard the converse from them: there aren't enough scientists getting involved with policymakers! It was a fascinating few days and for those interested in the process of shaping government policy, this scheme is a great way to get started.

A "Scientists' Choice" Award for the Institute

At this year's AACR meeting, on behalf of the Institute Allan Jordan, from the Drug Discovery Unit, received "The Scientists' Choice Award for Most Successful Video" from SelectScience, a website which offers reviews of scientific equipment.

In the winning video, Allan discusses how acoustic liquid dispensing is helping to accelerate compound screening at the Institute, reducing the volume of compound required for each experiment, thus enabling compounds to last longer and more data to be produced. This is an Institute-wide initiative, which was funded by a grant from the UKRPIF.

To watch the video, follow this link: http://bit.ly/1QwSHGE.

New Initiatives

Athena Swan Team

By Caroline Wilkinson

The Equality Challenge Unit's Athena SWAN Charter was established in 2005 to encourage and recognise commitment to advancing the careers of women in the scientific areas of technology, engineering, maths and medicine (STEMM) in higher education and research.

More recently, the charter has been expanded to recognise work undertaken in other areas including the humanities, business and law and to encompass professional and support roles, and transgender staff and students. The charter now recognises work undertaken to address gender equality more broadly, and not just barriers to progression that affect women.

Institutions can apply for a bronze, silver or gold award to acknowledge their commitment to these issues. We are in the process of making an application which involves the formation of a self-assessment team from staff members across the different grades and categories. The team is then tasked with assessing various data, policies and the culture that exists across the Institute, with a view to compiling an action plan which will result in the development of initiatives that will benefit all staff. The team is co-chaired by Caroline Dive and Caroline Wilkinson (Deputy Director and Chief Operating Officer respectively) and comprises 21 staff members who held their first meeting in March. The current focus is on analysing staff data and various policies as well as planning events, surveys and outreach activities covering Athena SWAN related issues. Work towards the application will continue in the coming months with the aim of submitting an application in 2017. Further details of the team's work can be found on the Institute's intranet.


Some of the members of the CRUK MI Athena Swan self-assessment team

STAy – Science Take-away

By Andrew Porter and Marina Parry


STAy committee members

Postdocs and PhD students at the Institute have been running monthly meetings, called P3 (for Postdocs, PhD Students and Pizza) for a number of years.

What started out as informal lab meetings evolved to incorporate journal clubs and short poster-style presentations. More recently, a new committee with wider representation from the Institute was formed, and the brief expanded to include topics ranging from the use of social media to alternative medicine and presentation skills. To reflect this broadening range, and to enable Scientific Officers to join these meetings, the committee became known as 'STAy', short for 'Scientific Takeaway'. Our goal is for researchers at the Institute to stay up-to-date with ideas in science; stay connected to one another and the wider scientific community; and ultimately to help each other stay in science.

One highly successful meeting comprised a panel of speakers from academia and industry with experience of medical writing and clinical trials, who helpfully talked about their career paths. We aim for our meetings to become an integral part of the Institute calendar, where new (and not so new!) staff and students can socialise, debate and learn, but also engage and be stimulated. In addition, we have links to seminars discussing the 3Rs – Replacement, Reduction and Refinement in animal research; Seiques project, which is a Manchester-based group that holds creativity in science events; the Research Staff Forum; and the Athena Swan team.

If you are a postdoc, PhD student or Scientific Officer, feel free to attend one of our meetings and get to know some of your colleagues better, gain some new skills, and possibly a new perspective. You can check out our page on the Institute's intranet.

Staff News

Babies!

Miere Tang

Haoran Tang, from the Molecular Oncology Lab, and Jing Bi, from the RNA Biology Group, celebrated the birth of their first baby girl, Miere, in February. Impossible not to melt with the smile of this little bumblebee!

Luca taking a nap

Michela Garofalo, team leader of our Transcriptional Networks in Lung Cancer group, and Gianpiero Di Leva, former post-doc in Molecular Oncology who is now a lecturer at Salford University, welcomed their baby boy Luca in January.

Wedding bells

Congratulations to James and Samantha Hitchin, who got married in April.

For their big day, the happy couple swapped Manchester for the paradisiac island of Jamaica. James and Samantha met in the Drug Discovery Unit, where they both work and which witnessed every stage of their romance.

James and Samantha, a love that was born in the DDU

Diploma success

Congratulations to Denise Owen, who recently completed her National Vocational Qualification (NVQ) in Supply Chain Management.

This gives her full membership status of the Chartered Institute of Procurement and Supply (MCIPS), which is an internationally recognised gold standard of achievement for procurement professionals.

Denise Owen

Conferences

John Castle, based with the CEP Group, attended the ICTHIC conference in Bergamo, Italy during April, with The University of Manchester's Cancer and Thrombosis group, led by Cliona Kirwan.

They gave oral and poster presentations on a range of preclinical and clinical data from their breast and colorectal cancer studies, including the upcoming TIP Trial.

From left to right: John Castle, Adam Rees, Cliona Kirwan, Hud Shaker and Hamish Clouston.

Keswick to Barrow - A day out in the park

By Gillian Campbell

Esther, Colin, Andrew and Crispin

Natalie, Esther and Gill enjoying the Lake District sun!

On Saturday 7th May, nine plucky members of the Institute took on the challenge of walking from Keswick to Barrow in the Lake District National Park in a single day.

This annual event has tested many intrepid members of our Institute over the years. 2016 marks the 50th anniversary for the "K2B" and our scientists wanted to help celebrate in the only way they know how – to walk those long miles again in aid of charity. Historically, the K2B has been billed as a 40 mile walk, but in reality it was always a mile or so further. An important distinction to make if you have ever walked that far! This year it was even further, clocking in at 42.7 miles; the increase due to changes to the route as a result of damage caused by the devastating floods that hit the region earlier this year.

Despite the early rise, having been picked up by 'Happy Buses' at 03:25 to take us to the start, spirits were high as we began the walk in clear, dry conditions; a phenomenon rarely enjoyed even by seasoned K2B walkers.

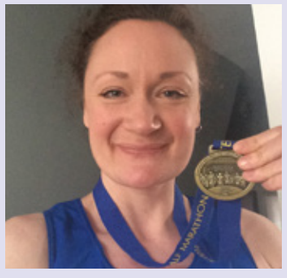
The extended part of the route took us through St John's in the Vale before we approached peaceful Thirlmere and on to the first checkpoint at Grasmere, 12.9 miles down. It was then on to Elterwater (15.7 miles) lying in the jaws of the Great Langdale valley. From here the route changed again, following a delightful cycleway towards Tilberthwaite before arriving at Coniston, having now past the half way mark at 21.5 miles. We continued alongside picturesque Coniston Water and towards Lowick, pausing only to dine at a much appreciated burger van. The final slog up Kirby Moor, a long and relentless climb that leads down to the villages of Marton and Dalton and our goal in Barrow, tested our mettle but on we pushed. Here the support and offers of jelly babies from the locals were very welcome and gave us weary walkers a final boost to the finish line.

Special mention goes to Kiran Batta who was the quickest in our group finishing in 10 hours 11 minutes. This time was closely followed by stalwart Andrew Renehan, taking 10 hours 45 minutes. Unfortunately, Esther Baena suffered a painful knee injury and after 26 miles had to stop. It was a gloriously sunny day and despite the increased distance and elevation, everyone enjoyed themselves and many were already talking of participating next year!

All our walkers thank those who supported us on the day and our sponsors who helped raise over £800 for Prostate Cancer UK and local Cumbrian charities.

Walker	Finish time (in hours & minutes)
Esther Baena	Injured out at 26.36 miles (9:66)
Kiran Batta	10:11
Gillian Campbell	14:34
Colin Hutton	11:48
Alice Lallo	12:14
Crispin Miller	11:30
Andrew Renehan	10:45
Darren Roberts	12:02
Natalie Stephenson	14:36

Half Marathon



Gill with her medal after completing the half marathon

Our Grants Advisor and Research Integrity Officer, Gillian Campbell, completed the Waters Wilmslow half marathon and raised £215 for the Christie Charity.

"It was my first half marathon and I was very pleased with my time (01:58:17). The event was well organised, everyone was really friendly and the local folks were very supportive and cheered us on – it is a big annual event in Wilmslow", says Gill, who also comments that "it was quite a warm, sunny day and the course was very picturesque, with a few challenging inclines".

In the spotlight with Esther Baena

Esther Baena leads the Prostate Oncobiology group that is working to understand cancer signalling pathways and identify tumour-initiating cells in prostate cancer. Originally from Seville in Spain, Esther completed her PhD at the University Autonoma of Madrid, Spain before embarking on a post-doctoral research position at Harvard Medical School in Boston. From there, she joined the CRUK Manchester Institute to establish her own research team in 2014.

1. **What is your favourite part of the UK?**
   Among the places I've visited so far, I'll pick Wales, I really like the beaches around Tywyn.

2. **What was your best ever holiday and why?**
   My first long trip ever as a teenager, I won a scholarship/trip to Central America and we travelled by ship from Spain to Honduras for about 10 days, and then through the forest of Guatemala and Mexico. It did reset my perspective on life and the world and experienced for the first time that the world has no boundaries. I still have many good friends from that trip.

3. **Which website do you always check, and why?**
   El Pais, a Spanish newspaper, I guess I like to keep the Spanish connection.

4. **What is your favourite film?**
   "Black cat, white cat" by Kusturica.

5. **What is your favourite band/singer?**
   U2

6. **If you had to change careers tomorrow, what would you do?**
   Chef, I love cooking

7. **What is the most important lesson that you have learnt from life?**
   YOLO (you only live once)

8. **Name three things you would take with you to a desert island?**
   A solar-power iPad with loads of music and ebooks, my other half and a snorkel-mask set

9. **What is your greatest fear?**
   Global extremist terrorism, it makes everybody vulnerable and I cannot imagine a way to stop the spiral.

10. **How would you like to be remembered?**
    Career based definitely I would like my research to contribute to new cancer treatments, and personally as a happy memory.

11. **If you could change one thing in your past what would it be?**
    Actually I will not change much that will change my current self and life, quite happy with my experiences so far.

12. **What is your signature dish to cook?**
    Seafood rice (not Paella!)

13. **You've just won the lottery and have £5 million pounds to spend. What do you buy first?**
    I would travel the world changing hemispheres to live in summer for a year. I would invest in an educational program to support universal access to higher education. I guess I would need to invest some time in a business plan to ensure sustainability. I would also buy a house and a boat by the sea.

14. **What is your idea of perfect happiness?**
    Sharing good food and wine with friends/beloved ones.

15. **What keeps you awake at night?**
    My noisy party-neighbours.

Editorial Team:
Steve Bagley
Gillian Campbell
Belen Conti
Sive Finlay
Katy Holliday
Ruth Perkins
Steve Royle
Caroline Wilkinson

Cancer Research UK Manchester Institute
The University of Manchester
Wilmslow Road
Manchester
M20 4BX

t: 0161 446 3156
www.cruk.manchester.ac.uk

Design and Layout:
cornerstone design & marketing
www.cornerstonedm.co.uk

The University of Manchester
Royal Charter Number: RC000797