# Newsletter



# Spring 2015

### FEATURE - Fundraising and Engagement Activities

Meetings Round-Up Grant Awards Recent Prizes and Events Latest Publications All Change in MBCF Staff News



The University of Manchester

# **Director's** Introduction

First, I would like to congratulate Caroline Dive on two well-deserved honours which she has recently received in recognition of her pioneering work on minimally invasive cancer biomarkers. In March, Caroline was presented with an International Women's Day Award for Breaking Through in Science and Technology at the Manchester Town Hall to mark International Women's Day.

In May, Caroline was elected a Fellow of the Academy of Medical Sciences, in recognition of her excellence in medical research and her commitment to developing the next generation of cancer research scientists.

More broadly, I am delighted that the Institute has already had an extremely successful start to 2015 with several high profile publications, many of which are featured in this issue and which included a particularly elegant study by the Cell Division group, led by Iain Hagan, which was published in Nature, describing a novel mechanism controlling mitotic progression and exit. We also saw a highly fruitful collaboration between the Signalling Networks in Cancer group, led by John Brognard, with scientists at University of California San Diego (UCSD) which has overturned a long-held view in cancer biology about the role of a key signalling molecule Protein Kinase C and was published in Cell. During the last few weeks, clinical trials of new drugs to treat melanoma and acute myeloid leukaemia have begun as a result of studies from the Molecular Oncology and Leukaemia Biology groups respectively. It is exciting to see how the Institute's work is having a major impact across the cancer research spectrum and I look forward to us building on this success over the coming months.

All of these achievements are underpinned by our research facilities and supporting infrastructure. Over the last three years, there has been significant investment into our research services through £8.7m of funding obtained from the UK Research Partnership Investment Fund. Co-ordinating the purchases of this equipment has been a significant and complex undertaking which has recently been completed by Stuart Pepper, who was ably supported by both other members of the research facilities team and by the Institute's finance team. Many other members of the Institute's operational staff have been participating in preparations for the opening of the Manchester Cancer Research Centre Building and I thank them all for their hard work.

The coming weeks will see members of the Institute participate in several exciting activities that will allow us to share our research with the public. First, there is a programme of events to mark the opening of the new Manchester Cancer Research Centre Building which also offers us a chance to convey our thanks to many of the donors and fundraisers who have made this project possible. Towards the end of June, the Clinical and Experimental Pharmacology group will showcase their work on identification of circulating tumour cells in lung cancer at an exhibit at the Royal Society Summer Science Exhibition in London. This highly prestigious event attracts several thousand participants and has a significant media presence so offers a tremendous opportunity to engage the public in our research. The process leading to acceptance of an exhibition at this event is extremely competitive so I would like to congratulate all involved for this achievement and look forward to hearing about its impact.

**Richard Marais** Director

## **Coming Soon FLS/CRUK Manchester Institute Away Day** 2015

In 2013, the inaugural CRUK Manchester Institute/Faculty of Life Sciences away day took place with researchers from both institutions giving presentations about their latest research.

Following the success of this event, another away day has been arranged. This will take place in Manchester at the King's House Conference Centre on September 3rd.

Cover Image: Professor Caroline Dive, Deputy Director of the Cancer Research UK Manchester Institute and head of the CEP group, with her International Women's Dav award.

# **Fundraising and Engagement activities**

## **Cancer Research UK Ambassadors' Visit**

In March, MPs voted in favour of introducing standardised packaging for cigarettes in the UK. Cancer Research UK Ambassadors are groups of volunteers that help the charity lobby the government on campaigning issues like this, and they played a vital role in the success of this plain packaging campaign.

The day after the vote on standardised packaging, some Ambassadors from the North West visited the Institute to celebrate! Stuart Pepper took them behind-the-scenes in MBCF for a sneak peak at the new drug screening automation robot, and Steve Bagley gave them a guided tour of Advanced Imaging.

They also received some communications' training, which gave them the skills they need to confidently champion our local research when they're talking to councillors and MPs. They had the chance to speak to Nikki March (an Ambassador herself!), Marina Parry and Steve Lyons about their research.

## **Cancer Research UK Fundraising Conference**



One of the delegates at the conference left a 'hero card'

about John Brognard

The Volunteer Fundraising team at Cancer Research UK helped to raise over £30million for the charity last year. The team - all 180 of them! recently got together in Chester for their annual conference, and John Brognard went along for the day. During his presentation, he inspired the audience with his pioneering research into lung cancer, and guests were particularly touched when he shared his personal motivations for being a cancer researcher.



Corporate supporters of Cancer Research UK visiting the Institute

### **Visiting Local Schools**

Steve Lyons and Mel Galvin have both recently visited some local schools, to talk to children about science and cancer research. Armed with CRUK lab coats and a special presentation featuring characters from the Lego Movie and Frozen, they spoke to the children about careers in science and helped them extract DNA from strawberries.

Mel said 'It was great! The kids were brilliant and I think we all got a lot out of it. I'd definitely do it again'. Steve commented, 'I loved it. The kids were absolutely great - very enthusiastic and put me on the spot with loads of great questions.' The schools were incredibly appreciative too - apparently the children couldn't stop talking about it for days!

## **CRUK Trustees**

Back in December, we welcomed an important group of Cancer Research UK Trustees to the Institute. After lunch with Richard Marais, the group visited the Molecular Biology Core Facility to see our state of the art DNA sequencing technology and discuss how this technology benefits cancer research. They had the opportunity to measure the concentration of DNA in biological samples and perform a standard quality control run on an agarose gel. The tour also visited our Advanced Imaging facility and the Drug Discovery Unit, where they were pitted against each other in a compound purification challenge.

Images Left to right: Mel and Stuart from CEP, wearing their unity bands on World Cancer Day; Allan Jordan, dressed as Gwen the Gorilla, ready to take on the Morrisons Manchester 10k; David's Lucky Dip raised nearly £300

### We Will Unite

On 4th February, World Cancer Day, people across the country united in their fight against cancer. Staff at the Institute wore 'unity bands' in support of the campaign, and helped raise hundreds of pounds for Cancer Research UK with a delicious cake sale

### Manchester 10k

Three of our scientists took part in the Morrison's Manchester 10k run. Allan Jordan from Drug Discovery took to the streets dressed as the Race for Life mascot, Gwen the gorilla. David Jenkins also took part, and had yet another fantastic fundraising day, supported by Roche Diagnostics. He held a raffle, cake sale, and his famous 'David's Lucky Dip', raising nearly £300 for Cancer Research UK. Crispin Miller also completed the run just a few days after he ran the London marathon.

## **Research on film: Behind** the scenes in CEP

The Multimedia team from Cancer Research UK recently visited the Institute. They wanted to film a video about CEP's lung cancer research for the CRUK's YouTube channel. This kind of virtual access to our research is so important, as it means that anyone, anywhere, is able to engage with our pioneering science.

First to step in front of the camera was Caroline Dive, who spoke about the challenges of detecting lung cancer at an early stage, and the urgent need to develop better drugs that actually have a more curative effect rather than just delaying the progression of the disease.

Things then took a slightly more unusual turn, as some willing volunteers from the CEP team donned Go-Pro Action Cameras to capture activity in the lab from their point of view. Filming followed a blood sample's journey from the 'clinic' (actually the Phlebotomy room on the second floor) right through to the lab.

The Multimedia team were really pleased with all the footage they captured. The final video will be available to view on Cancer Research UK's YouTube channel soon.

### Football **Shirt Friday**

Staff at the Institute also took part in Football Shirt Friday, wearing their football shirts to work with pride, to raise money for the Bobby Moore Fund.



Dan from CEP supporting Football Shirt Friday

### **Coming Soon** in 2015

15<sup>th</sup> – 20<sup>th</sup> June MCRC opening week celebrations

3<sup>rd</sup> October Institute Open Day

22<sup>nd</sup> October - 1<sup>st</sup> November Manchester Science Festival

## **Stockport Relay for Life**



Last year, a team of scientists from the Institute helped Stockport Relay for Life raise over £50,000 for Cancer Research UK. This is the only Relay for Life across the UK that has a team made up of researchers, and the organisers are rightly very proud of this fact.

Some of the Relay for Life team at their plant sale

With a successful plant sale under their belt, and cake sales and raffles still to come, the team are sure to raise a fantastic amount of money this year. For information about joining the team, please speak to Steve Lyons.

### **Patient Engagement Event**

Patients are at the heart of Cancer Research UK, and their voice helps to shape the strategic direction of the charity. It's important that we build on this and involve them as much as possible in what we do. We were delighted, therefore, to hold a patient engagement event at the Institute, to tell them about our research and campaigns, and to ask them for their ideas on how we can best give them a say in our work.

Patients were interested to hear about Cancer Research UK's strategy, and were especially keen to learn more about the research taking place here in Manchester. They also enjoyed being able to share their stories and experiences, and there were some great discussions on the day.

## Lab tours: a record breaking year



We've welcomed a record breaking number of quests through our doors for lab tours over the past 12 months over 500 people joined us for 42 lab tours. Supporters love having the chance to go behind the scenes in our labs.

Fantastic fundraisers visiting us for lab tours

and to get 'hands on' with science, so huge thanks must go out to everyone who has taken part in a lab tour this year. These events are a really effective way to thank and motivate supporters, increase donations and ultimately fund more research, so if you'd like to get more involved in the Institute's lab tour programme, please speak to Hannah Leaton, the Research Engagement Manager.

### International Women's Day

We also celebrated International Women's Day on March 8<sup>th</sup>. We used social media to share photos of some of the inspirational female scientists here at the Institute.



Alex Stowell on International Women's Day



Esther Baena speaks about her research for International Women's Day

# **Meetings' Round-Up**

## AACR 2015



Biology group, explains how

analysis of single cells can help

elucidate tumour heterogeneity.

The American Association for Cancer Research (AACR) is the world's oldest and largest professional association related to cancer research. It was founded in 1907 by a small group of physicians and scientists but now has now has more than 34,000 members in over 90 countries.

The AACR focuses on all aspects of cancer research, including basic, clinical, and translational research into the etiology, prevention, diagnosis, and treatment of

cancer. It holds an Annual Meeting which is a major forum to present and discuss cancer-related research. The meeting is held in various locations across the US and attracts more than 18,000 attendees from around the world. This year the meeting took place in Philadelphia, the home of the AACR, and had the theme of "Bringing Cancer Discoveries to Patients". It comprised more than 5000 abstracts and over 250 invited talks on significant discoveries in basic, clinical, and translational cancer research. These presentations were complemented by scientific award lectures, grant writing workshops, networking events, and educational sessions.

There was plenty of representation from the Institute including nine talks and six poster presentations from the Institute's staff with four sessions being chaired by CRUK MI Group Leaders. This offered an amazing opportunity to promote the Institute and showcase our research. The meeting was also notable as it marked Richard Marais starting his tenure on the AACR's Board of Directors.



Outside Independence Hall, Philadelphia

### Micro-sampling: The smallest things add the greatest value

Congratulations to Ben Acton for winning the Steve Moore Memorial Poster Competition at the Institute of Animal Technology North West Branch.

The IAT exists to advance and promote excellence in the care of animals used in research and the event on 23<sup>rd</sup> April was for members to present a poster based on animal welfare.

Ben is the in vivo scientist in DDU and is responsible for all in vivo testing of compounds in the Institute. During the development of new drugs, nonclinical safety studies are carried out in mice to identify and characterise adverse effects and facilitate risk assessment for clinical studies. His poster illustrating the application of blood microsampling alongside preliminary toleration studies drew the attention of the judges. They were looking for the biggest impact on the 3Rs (replacement, reduction, refinement) of animals in research and were impressed with Ben's studies highlighting the benefits of micro-sampling and how this technique can provide early insight into compound behaviour while reducing the number of animals being used and the severity of procedures undertaken. The judges, from industry and academia, particularly commended the potential wide reaching influence Ben's studies have on other groups that are now starting to adopt this technique in their in vivo studies.

Ben was awarded first prize, which includes an allexpenses paid trip to the American Association for Laboratory Animal Science National Annual Meeting in Phoenix, Arizona – the largest Animal Technology conference in the world with some 1000 plus attendees.

## **Poster Prize for CEP Group**

Jonathan Tugwood, of the Clinical and Experimental Pharmacology group, attended the British Thoracic Oncology Group (BTOG) 2015 meeting in Dublin in January, where he presented a poster based on the ground-breaking research from CEP that was published in Nature Medicine last year.

The poster describes the generation and early evaluation of CTC-Derived Xenograft mouse models, obtained by implanting Circulating Tumour Cells from Small Cell Lung Cancer patients into immune-compromised mice. The various models accurately reflect the profile of the patients from whom they were derived with respect to responses to standard-of care therapies, and represent

## CRUK Manchester Institute researcher takes her science to Parliament



Romina Girotti presents her poster in Parliament.

Congratulations to Dr Romina Girotti, a postdoctoral research fellow with Professor Richard Marais in the Molecular Oncology group, who earned the fantastic opportunity to attend Parliament to present her science to a range of politicians and a panel of expert judges, as part of SET for Britain in March. the first demonstration that the implanted cells from lung cancer patients are tumour forming.

Therefore, these mouse models represent an exciting opportunity for evaluation of novel lung cancer therapies.

Although the BTOG meeting was mainly attended by clinicians rather than researchers, all major pharmaceutical companies were represented and the poster generated considerable interest. Significantly, the poster was allocated poster board #1 and won one of the runner-up prizes.

Romina was shortlisted from hundreds of applicants to appear in Parliament. Her poster on research about new drugs to treat melanoma patients resistant to particular treatments was presented alongside dozens of other scientists' research before an array of MPs and Society Presidents.

On presenting her science in Parliament, she said, "I applied to this fantastic competition as I thought it would be a wonderful opportunity for me to share with the UK public the important findings of my scientific research in relation to the development of new drugs for the treatment of melanoma patients. We are very excited to start a clinical trial with the new drugs in April this year. The SET for BRITAIN competition is the perfect environment to describe our discoveries and enthuse MPs and the public about them."

She added that it was a great experience being inside Parliament and that there was an atmosphere of excitement throughout the whole event. She especially enjoyed presenting her work to a lay audience and taking this unique opportunity to inform politicians about the importance of her research.

Dr Mark Downs, chief executive of the Society of Biology, said, "Scientists and politicians both have major roles in addressing some of society's biggest challenges, from climate change to food security.

"It is important that MPs make policy decisions informed by evidence, and a greater mutual understanding between MPs and scientists will improve this. This is a message that is even more important just ahead of a General Election. The next Government needs to ensure the UK continues to lead the world in biological research where we have enormous strength".

### **Travel award for Romina Girotti**





for Cancer, held in March in Luxembourg. Romina presented recent findings from a productive collaboration between Molecular Oncology, Clinical and Experimental Pharmacology and the Christie NHS Foundation Trust. She described the powerful combination of complementary techniques that they have used to provide personalised therapy for melanoma patients. She also discussed the challenges and limitations of implementing these novel technologies in the clinical management of patients.

We also congratulate Dr Romina Girotti

for being awarded a **Participation Grant** 

(European Association for Cancer Research

Institutes) Conference

on Precision Medicine

 Organisation of **European Cancer** 

to present a talk at the EACR-OECI

Participation Grants support full attendance at the conference and are used to assist with the cost of accommodation, travel and registration.

### **Richard Marais** elected to AACR **Board of Directors**

We are delighted to announce that our Director, Professor Richard Marais, has been elected to the Board of Directors of the American Association for Cancer Research for the 2015-18 term.

The term of office began at the AACR Annual Meeting in Philadelphia in April, Richard is one of only two members of the board who work outside of the US. The position is a great honour and Richard hopes that it will result in a strengthening of the links between the AACR and European cancer scientists and clinicians. This will be a great advantage to research and cancer patients both in Europe and the US.

## Funding for novel drug development in head and neck cancer

Congratulations to Dr John Brognard for his success in obtaining a Drug Discovery Project Award from Cancer Research UK. John, who leads the Signalling Networks in Cancer group, will use the funding to focus on a novel target for therapeutic intervention in head and neck squamous cell carcinoma (HNSCC).

HNSCC develops from the mucosal linings of the upper aero-digestive tract. Squamous cell carcinoma is the most frequent malignant tumour of the head and neck region and HNSCC is the sixth leading cancer by incidence worldwide. There are approximately 400,000 deaths per year, a figure which has remained unchanged for several decades. Thus there is a clear unmet need for targeted therapeutics for HNSCC patients. LZK, an enzyme that activates key pathways associated with cancer in humans and mice, has strong potential for novel inhibitor development. This support will allow John and his group to continue important validation of this novel therapeutic target that could lead to new treatments for head and neck squamous cell carcinoma patients.



John Brognard

### Major CRT Pioneer Fund investment to develop lung cancer drugs at the Cancer Research UK **Manchester Institute**



From Left to Right: Allan Jordan (Head of Chemistry, DDU), Donald Ogilvie (Head of the DDU) and Ian Waddell (Head of Biology, DDU).

The Drug Discovery Unit (DDU), led by Dr Donald Ogilvie, have secured significant funding from the Cancer Research Technology Pioneer Fund (CPF) to develop a promising class of drugs called RET inhibitors to treat cancer.

Cancer Research Technology (CRT), Cancer Research UK's commercial arm, and the European Investment Fund (EIF) launched the £50M CPF in 2012 to bridge the UK funding gap between cancer drug discovery and early drug development. Sixth Element Capital was appointed to manage the fund.

Building on research by our scientists, this investment will enable the DDU to accelerate the development of RET inhibitors and fund early clinical trials of potential drugs developed through the collaboration. The RET (rearranged during transfection) gene plays a critical role in the development of medullary thyroid cancer, although it was recently found that some non-small cell lung adenocarcinomas have RET mutations. The goal of the project is to discover novel compounds that will specifically focus on the RET gene in patients with non-small cell lung cancer. RET may also be involved in other cancers including breast and chronic myelomonocytic leukaemia (CMML) and potentially lead to broader therapeutic applications in the future.

Donald said: "We're extremely pleased to work with the CRT Pioneer Fund to help accelerate progress on the exciting RET inhibitors discovered by Cancer Research UK scientists at our Institute. Lung cancer remains a significant clinical challenge. As part of the Cancer Research UK Centre of Excellence on Lung Cancer, we are determined to deliver new treatments into the clinic for this disease and this programme offers the potential to improve the outlook for cancer patients".



Nicola Hamilton working at the Echo access station

### **Prestigious ERC Advanced Grant for Richard Marais**



**Professor Richard** Marais, Director of the Institute and leader of the Molecular Oncology group, who has been awarded a prestigious European **Research Council** Advanced Grant to elucidate the role of ultraviolet radiation in melanoma.

**Congratulations to** 

Richard Marai

Melanoma is a potentially deadly skin cancer. In the UK, this disease affects over 12,000 people and sadly causes over 2,000 premature deaths each year. Worryingly melanoma rates continue to increase in most European countries and,

in many countries, the rate is almost doubling every decade. Compared to other cancers, melanoma disproportionately affects young people, causing a significant loss in life-years in those affected. Ultraviolet light or ultraviolet radiation (UVR) is the only environmental risk factor in melanoma, but the underlying genetic makeup of the individual also plays an important role. However, our knowledge of the gene-gene and gene-environment interactions in the development of melanoma is still very limited. Professor Richard Marais and Dr Amaya Viros, Senior Clinical Scientist in his group, propose to use this significant funding – €2.5 million – to investigate the role of UVR in melanoma initiation and progression.

Forming the basis of this study is their ground-breaking discovery – published in *Nature* last year – that tumours grown in mice exposed to UVR had a significantly higher number of mutations than mice that had not been exposed. They plan to integrate knowledge from these crucial animal experiments with epidemiological, histopathological, clinical, and genetic features of human tumours to determine how UVR exposure affects melanoma development. This work aims to improve stratification of human melanoma and thereby assist clinical management of melanoma and help develop effective public health campaigns for individuals at risk of this deadly disease across the UK and Europe.

### **Manchester Institute** joins European consortium to develop liquid biopsies

**Professor Caroline Dive from the Cancer Research** UK Manchester Institute will participate in CANCER-ID, an international project to validate blood-based biomarkers for cancer.



Blood-based biomarkers such as circulating tumour cells (CTCs), circulating free tumour DNA (cfDNA) and microRNAs (miRNAs)

are potential tools to assess the tumour burden of cancer patients in a minimally-invasive manner. They offer an invaluable tool for modern cancer medicine: in addition to allowing biopsies of tumour tissue that is otherwise inaccessible, blood-based tests may aid follow-up of disease, allowing doctors to monitor the efficacy of treatment and potentially improve decisions regarding therapy.

CANCER-ID is a newly formed European consortium funded by the Innovative Medicines Initiative (IMI) with currently 33 partners from 13 countries aiming to establish standard protocols for clinical validation of blood-based biomarkers. It brings together experts from academic and clinical research, innovative small-tomedium sized enterprises (SMEs), diagnostics companies and the pharmaceutical industry, thus providing a unique setting for establishing clinical utility of 'liquid biopsies'.

Coordinating the international consortium, with a total budget of €14.5 million, are Professor Klaus Pantel from University Medical Center Hamburg-Eppendorf, Professor Leon Terstappen from University of Twente, together with Bayer HealthCare and Silicon Biosystems. Joining them are researchers from the Clinical and Experimental Pharmacology group led by Professor Caroline Dive, who will be contributing expertise in liquid biopsies and CTCs.

Professor Dive said: "We have a strong reputation in research into circulating tumour cells. We are excited to join this impressive European consortium and look forward to contributing to the establishment of bloodbased biomarkers into routine clinical practice."

# **Recent Prizes and Events**

## **Caroline Dive is** elected to the **Academy of Medical Sciences**

Professor Caroline Dive has joined the ranks of eminent UK scientists and become a Fellow of the prestigious Academy of Medical Sciences.

Founded in 1998, the Academy of Medical Sciences is the independent body in the UK that represents the diverse spectrum of medical science - from basic research through clinical application to healthcare delivery.

Academy fellows are recognised for their exceptional contribution to and excellence in medical research. Fellowship of the Academy acknowledges original discoveries and innovative application of scientific knowledge that brings about advances in human health and welfare.

Professor Dive, who leads the Clinical and Experimental Pharmacology group, was awarded the Fellowship in recognition of her contributions to advancing medical science. She is internationally renowned for pioneering circulating biomarker research, particularly with circulating tumour cells (CTCs) in lung cancer, and transforming early clinical trial activities. The Academy also acknowledged Caroline's commitment to nurturing the next generation of clinical researchers, having designed and led a Clinical Pharmacology Fellowship Scheme that prepares young medical oncologists for the challenges of personalised medicine for cancer treatment. Furthermore, she has played a pivotal role in establishing powerful alliances between academia, the pharmaceutical industry and the NHS that are key to the advancement of medical science.

Caroline says that she is honoured and absolutely delighted to accept this prestigious Fellowship. Alongside other newly appointed Fellows, she will be formally admitted to the Academy at a ceremony in London later this year.

Breaking Through was Manchester's theme for this year's International Women's Day, representing the achievements of women who have succeeded against the odds.

Caroline, head of Clinical and Experimental Pharmacology, earned her award for Breaking through in Business or Legal or Science and Technology. She says that she is thrilled to have been awarded this prize and extends her gratitude to Professor Richard Marais, who nominated her for this award.

Important to Caroline is the message this award sends to young women that they can succeed in science. She is delighted that she can be a role model and encourage young women to push their careers in cancer research. The award also recognised the vital work she does promoting science to girls at local schools.

Of her own experience, Caroline says that she has always worked hard and been driven by her passion to make a difference to the way cancer patients are treated. She acknowledges the difficulty of balancing work with family but believes it is manageable - and her triumphs certainly prove that success and family are possible.



## **Caroline Dive receives International Women's Day Award**

There was further success for Professor Caroline Dive, who received an International Women's Day Award in recognition of her pioneering work on circulating biomarkers and the development of minimally invasive biopsies for cancer patients.

Manchester City Council celebrated inspirational women by recognising their achievements and valuable contributions to the city at a ceremony at the Manchester Town Hall in March.

Professor Caroline Dive receives her award from Lucy Powell MP

### Marie Curie Fellowship for Anne Largeot

Congratulations to Dr Anne Largeot on her success in obtaining a prestigious Marie-Curie-Skłodowska Action Individual Fellowship. The MSCA, funded through the European Commission, supports the most promising researchers in order to enhance their career development and training towards establishing an independent position.

Anne, a postdoctoral research fellow in the Stem Cell Biology group, led by Dr Georges Lacaud, will start her two-year Individual Fellowship in September, focusing on the global role of the Histone Acetyl Transferase MOZ, a critical player in the haematopoietic system, and a target of translocations in Acute Myeloblastic Leukaemia. She was both surprised and delighted to learn that she had been awarded this fellowship which is a great opportunity for her to expand the project she established with Georges. In addition to the strength of her project, she believes the quality and reputation of the Institute was crucial to the success of the application, and reinforces her decision to move here to progress her career.



Anne Largeot

This fellowship represents an important step towards establishing her future career. Having such a fellowship will augment her CV and make her a very attractive candidate for further funding. Anne strongly encourages other postdoctoral fellows to apply for the Marie-Curie-Skłodowska Action Individual Fellowship. She hopes to ultimately become an independent researcher and set up her own research group in a world leading research institute somewhere in Europe.

## Basic research is translated to patient benefit in phase I clinical trial

A consortium, including the CRUK Manchester Institute has entered an agreement with the biopharmaceutical company Basilea Pharmaceutica Ltd to progress a new family of cancer drugs designed to block several key cancer-causing proteins at once.

The new drug class, called panRAF inhibitors, originated from a research collaboration between Richard Marais' Molecular Oncology group and Professor Caroline Springer's team at The Institute of Cancer Research (ICR) which is funded by the Wellcome Trust and Cancer Research UK.

The drugs have the potential to be used where a patient's tumour has developed resistance to existing drugs targeting the BRAF protein, which is mutated in a range of cancers including 50% of melanomas and 10% of bowel cancers.

The new drugs target both BRAF and the growth pathways that the cells come to rely on when they become resistant. It is hoped that the new drugs could be effective in patients who have developed drug resistance and exhausted all other available treatments.

A phase I clinical trial of the drugs is underway at The Christie NHS Foundation Trust and The Royal Marsden NHS Foundation Trust in London. The first patients have already begun treatment. The trial will recruit around 25 patients with advanced, solid tumours – focusing on advanced melanoma - with the aim of establishing the safe maximum dose for a planned phase II clinical trial.

Professor Marais is delighted with the announcement; "This agreement represents the culmination of over 10 years of academic research and we are pleased to see our basic research studies being translated into patient benefit. It is an important milestone in efforts to tackle resistance to existing cancer therapies and provide new options for cancer patients. Melanoma is a devastating disease that kills over 2,000 people each year in the UK and we hope that these new drugs will provide new lines of treatment."



Nikki March promotes the Cross Cancer Out campaign in Piccadilly Gardens, Manchester.

## **Campaigns Ambassador** helps influence change

We are proud to highlight the important role that Nikki March has undertaken as a Cancer Research UK Cancer Campaigns Ambassador. Nikki is a Senior Bioscientist in the Drug Discovery Unit and has been working tirelessly over several months to communicate the importance of her research in order to facilitate policy change.

In December last year, Nikki went on a tour of the Francis Crick Institute in London- which opens its doors next month - with Vicky Ford, MEP for East of England. During this visit, Nikki spoke to Vicky about her research, focusing on big data - an area of interest for the MEP - and its role in the identification of new drug targets. Nikki also relayed her personal experiences of cancer as a motivating factor behind her campaign and stressed the need for political action if we are to beat cancer sooner.

Late last year, Nikki met with her own MP, Stephen O'Brien of the Eddisbury constituency to discuss early diagnosis and access to innovative treatments for cancer patients, as well as the standardised tobacco packaging campaign. Thanks to Nikki's involvement, Stephen subsequently voted in favour of the legislation, which is a great result.

You might have seen Nikki out in Manchester in February last year when she took part in a stunt in Piccadilly Gardens to raise public awareness of the Cross Cancer Out campaign.

She also encouraged members of the public to contact their local election candidates about the campaign. In the lead-up to the general election, Nikki has been lobbying the candidates in her constituency to sign up to the Cross Cancer Out campaign.



Nikki March and Vicky Ford MEP tour the Francis Crick Institute.

### Dexter Award Winner for 2014



Romina Girotti receiving her award from Institute Director Richard Marais

Romina Girotti has been selected as the winner of the Institute's Dexter Award for Young Scientists for 2014. The prize recognises the most impressive scientific achievement of the year across the building.

The judging panel felt that Romina has achieved an extraordinary amount, not only during 2014, but also throughout her four years in the Molecular Oncology group which is reflected in an impressive set of publications in high quality journals. In particular her work in understanding the mechanisms of resistance in melanoma, and the development of a technology platform for personalised medicine in this type of cancer, represents significant advances in this field. Romina received her award from the Institute's Director, Professor Richard Marais, at his annual Director's address.

BRAF is mutated in about half of human melanomas and drugs that target mutant BRAF improve overall survival in BRAF mutant patients. However, most patients eventually fail on treatment and the focus of Romina's studies is to understand their mechanisms of resistance and develop a technology platform for personalised medicine in melanoma. In 2013, Romina published a paper in *Cancer Discovery* in which she revealed that resistance can be mediated by the EGF receptor (EGFR) signalling through SRC family kinases (SFK). She validated these findings in clinical samples and showed that a combination of BRAF plus SFK inhibitors could block the growth of resistance and identifying an effective drug combination for second-line treatment of these patients.

Romina went on to show that novel panRAF inhibitors (blocking both BRAF and CRAF) that also inhibit the SFK are very effective in resistant tumours. She demonstrated that activation of SFK was coincident with ERK pathway reactivation in resistant tumours and that the new drugs inhibited the growth of patient-derived xenografts (PDX) from resistant patients. By blocking BRAF, CRAF and SFK, she found that the drugs work in tumours where resistance is mediated by NRAS, because it signals through CRAF, and when resistance is mediated by receptor tyrosine kinases, because they signal through SFK. She also showed that these drugs are effective in tumours that are resistant to a BRAF/MEK inhibitor combination. Her work reveals that the new drugs could provide first-line treatment for treatment-naïve BRAF mutant melanoma patients and second-line treatment for patients who develop resistance to BRAF inhibitors. This work was recently published in *Cancer Cell* and the drugs have recently started clinical trials at the Christie and Royal Marsden NHS Foundation Trusts.

Romina has established analysis of circulating tumour DNA (together with Dominic Rothwell in the CEP group) and is currently working to establish analysis of circulating tumour cells. In addition to the two first author papers mentioned above, Romina has published two authoritative reviews and co-authored four more papers (in *Science Signalling, Nature Communications, Cancer Cell and Nature*). She has also been the recipient of four external poster prizes and travel awards during her time in the Molecular Oncology group as well as winning the Institute Colloquium Poster Prize in 2013.

### PhD place success for Rob Sloane



As a scientific officer in Caroline Dive's Clinical and Experimental Pharmacology group, Rob Sloane has had the opportunity to work on many ground breaking clinical and pre-clinical projects leading to nine (and counting) publications.

With this valuable research experience, he recently successfully competed for a PhD studentship on the Experimental Therapeutics program at the MD Anderson Cancer Centre, in Houston, Texas.

The MD Anderson is the largest cancer centre in the United States and is regarded as one of the top cancer centres in the world. On the Experimental Therapeutics program, Rob will receive a year of intensive teaching and training including lectures and lab rotations. Beyond this, he will conduct his own research for approximately four years using a rational approach to developing novel and personalised cancer therapies. We wish Rob all the very best in this new phase of his life.

# **Featured Publications**

## Molecular tag team revealed to control cell division

Scientists from the Cell Division group have explored the role of three molecules in controlling the process of cell division in a bid to gain new insight into the transmission of vital signals from a cell's exterior to its interior. In a ground-breaking paper published in *Nature*, they show that the three protein complexes act in relay to regulate cell division: reactivation of one leads to the second becoming active. Scientists from the Cell Division group have explored the role of molecule's activation and its control of cellular activity. They act in opposition to kinases, which add phosphate groups and are known to be over-active in some cancers. PP1 and PP2A account for 95% of all of the phosphatase activity of a human cell and had previously been assumed to be unlinked enzymes with a discrete set of functions. The group looked at

Cells rely on control systems to make sure that each aspect of the cell division cycle occurs in the correct order. Following successful segregation of the genomes in mitosis, each must return to its pre-division state in a process called mitotic exit. Mitotic exit is irreversible for all multicellular organisms. Loss of cell cycle control during this process – leading to unregulated and abnormal growth – is a key characteristic of cancer cells.

The researchers, led by Professor Iain Hagan, investigated the regulation of mitotic exit in yeast cells, in particular, the role played by three molecules, known as Protein Phosphatase 1, 2A-B55 and 2A-B56. Phosphatases are enzymes that remove phosphate groups from molecules, leading to a change in the

# Blood test could help bowel cancer patients avoid drug side-effects

Researchers from the Clinical and Experimental Pharmacology group have provided early evidence to suggest that a blood test could be used to identify bowel cancer patients that may benefit from more intensive chemotherapy.

Colorectal, or bowel, cancer is the second biggest cancer killer in Europe. It is most commonly treated with a combination of chemotherapy agents, and outcome can be improved by using additional drugs. However, this multi-drug approach can increase side-effects such as hair loss, low white blood cell count, diarrhoea and damage to the peripheral nervous system.

Professor Caroline Dive, who jointly led the study, said: "Here in Manchester we are interested in detecting cancer cells that have been shed from a patient's tumour and are circulating in their blood. In this study we wanted to see if the number of tumour cells in a blood sample could be linked to how well patients respond to intensive chemotherapy."

The group looked at patients with advanced colorectal cancer who received a four-drug combination treatment, and counted tumour cells in each patient's blood sample to explore whether PP1 and PP2A account for 95% of all of the phosphatase activity of a human cell and had previously been assumed to be unlinked enzymes with a discrete set of functions. The group looked at the activity of the three phosphatases and found that PP1 was the master regulator that controlled the timing of the successive activation of each PP2A. This molecular 'tag team' coordinated the yeast cell's progression through the different steps in mitosis.

"Much of this process is conserved throughout all mammalian cells, which means that our studies in yeast will give us greater insight into cell division, and indeed overall cellular communication, in humans," added Professor Hagan.

Grallert A, Boke E, Hagting A, Hodgson B, Connolly Y, Griffiths JR, Smith DL, Pines J, Hagan IM. (2015) A PP1/PP2A phosphatase relay controls mitotic progression. *Nature*, Jan 1;517(7532):94-8.

it could be used to predict who might benefit most. They confirmed that those patients with three or more circulating tumour cells (CTCs) in their blood sample had a lower overall survival, compared with those patients who had fewer than three CTCs.

The team also presented data that suggested that patients with a higher CTC count before treatment could benefit more from this more intensive treatment regimen. These initial results suggest that this test could prove useful for patient selection and our scientists are now looking to validate it in further larger trials of new treatments for bowel cancer.

Krebs MG, Renehan AG, Backen A, Gollins S, Chau I, Hasan J, Valle JW, Morris K, Beech J, Ashcroft L, Saunders MP, Dive C. Circulating Tumor Cell Enumeration in a Phase II Trial of a Four-Drug Regimen in Advanced Colorectal Cancer. (2014) *Clin Colorectal Cancer*, published online: Dec 31.

## Understanding of cell enzyme flipped on its head

Researchers from the Signalling Networks in Cancer group, working with scientists in California, have found that certain molecules long thought to promote cancer growth, in fact suppress tumours, suggesting that therapeutic approaches should aim to restore, rather than block, their activity.

The protein kinase C (PKC) family of molecules are enzymes that facilitate a range of cellular processes, including cell survival, proliferation, migration and death. In the 1980s it was found that PKCs were activated by cancer-causing phorbol esters, and led to the conclusion that PKCs themselves induced the development of tumours. However, attempts to develop new treatments that prevent tumour cell growth by blocking the activity of PKCs have had little success.

Dr John Brognard's group collaborated with a team from the University of California, San Diego, to analyse PKC mutations in human cancer cells and to explore the effect of mutations on tumour growth. They found that most were 'loss of function' mutations, meaning that the genetic changes stopped PKC from working. When they corrected these mutations in bowel cancer cells, they saw a reduction in tumour growth, meaning that contrary to our previous understanding, PKC normally acts to block cancer.

"Clinical trials have so far been working on the incorrect assumption that PKC enzymes cause cancer growth. This new insight from our studies has turned current thinking on its head. Looking ahead, instead of blocking PKC activity, new therapies

should instead be targeting mechanisms to restore its activity," added Dr Brognard.

Antal CE, Hudson AM, Kang E, Zanca C, Wirth C, Stephenson NL, Trotter EW, Gallegos LL, Miller CJ, Furnari FB, Hunter T, Brognard J, Newton AC. (2015) Cell, Jan 29;160(3):489-502.



Loss-of-function protein kinase C mutation



Figure 1: Model illustrating role of Protein Kinase C in normal versus cancer cells

### Scientists zero in on how lung cancer spreads

Scientists from the Cell Signalling group have taken microscopic images revealing that the protein ties tethering cells together are severed in lung cancer cells – meaning they can break loose and spread. They have discovered that the ties which lash cells together – controlled by a protein called TIAM1 – are chopped up when cell maintenance work goes wrong.

Healthy cells routinely scrap old cell parts so they can be broken down and used again. But this process spirals out of control in lung cancer cells, which scrap too many TIAM1 ties, because there is an excess of a protein, called HUWE1, which is in charge of scrapping TIAM1. Targeting this recycling process could stop lung cancer from spreading by keeping the cells stuck firmly together.

Dr Angeliki Malliri, head of the Cell Signalling group who led the study, said: "This important research shows for the first time how lung cancer cells sever ties with their neighbours and start to spread around the body, by hijacking the cells' recycling process and sending it into overdrive. Targeting this flaw could help block cancer spread."

Vaughan L, Tan CT, Chapman A, Nonaka D, Mack NA, Smith D, Booton R, Hurlstone AF, Malliri A. (2015) HUWE1 ubiquitylates and degrades the Rac activator TIAM1 promoting cell-cell adhesion disassembly, migration and invasion. Cell Reports, Jan 6;10(1):88-102.



Figure 1: Normal cells (left) compared to when the cell ties are broken down (right)]

### New targeted drugs could treat drug-resistant skin cancer

A brand new family of cancer drugs designed to block several key cancer-causing proteins at once could potentially treat incurable skin cancers.

The complex research involved the teams designing and Existing drugs target faulty versions of a protein called BRAF synthesising molecules shaped to overcome major drug which drives about half of all melanomas, but while initially resistance cell signalling pathways in melanoma, testing the very effective, the cancers almost always become resistant to molecules in cultures of melanoma cells and in mice, and treatment within a year. The new drugs – called panRAF inhibitors studying of the compounds using drug-resistant tumours - could be effective in patients with melanoma who have from patients grown in mice. The studies established that for developed resistance to BRAF inhibitors. both drugs, a dose of 20mg per kg per day – which when translated to humans would be achievable by taking in pill form -The study, published in the journal Cancer Cell, was jointly caused tumours to regress without significant side-effects.

led by scientists from the Molecular Oncology group and the Institute of Cancer Research in London, led by Professor "The next step is testing this family of drugs in clinical trials to Caroline Springer. The researchers showed that the new drugs establish that they are both safe and effective in cancer patients, - provisionally named CCT196969 and CCT241161 - stopped potentially providing urgently-needed new treatments for the growth of BRAF-driven melanomas, including those that had patients who have run out of options. The trial is set to open stopped responding to currently available BRAF-targeted drugs. soon and we await the results with great interest," added In addition, the new drugs halted tumour growth in cancers in Professor Marais. which BRAF-targeted drugs had never worked in the first place - which happens in around 20% of cases. The team showed Girotti MR, Lopes F, Preece N, Niculescu-Duvaz D, Zambon that these new drugs work because they target both BRAF and A, Davies L, Whittaker S, Saturno G, Viros A, Pedersen M, the growth pathways that the cells come to rely on when they Suijkerbuijk BM, Menard D, McLeary R, Johnson L, Fish L, Ejiama become resistant. S, Sanchez-Laorden B, Hohloch J, Carragher N, Macleod K, Ashton G, Marusiak AA, Fusi A, Brognard J, Frame M, Lorigan P, Marais R, Springer C. (2015) Paradox-breaking RAF inhibitors that also target SRC are effective in drug-resistant BRAF mutant melanoma. Cancer Cell, 27(1):85-96.

Study co-leader Professor Richard Marais said: "Our laboratory study showed that these new drugs deliver multiple blows to cancer by hitting several cell survival routes at once. It's a step on

## New insights into blood formation

Scientists from the Stem Cell Biology and Stem Cell Haematopoiesis groups have gained a deeper understanding of the formation of early blood cells and demonstrated a more reproducible and efficient method for their generation. Their work paves the way towards a limitless supply for blood transplantation to treat leukaemia and auto immune diseases.

Using stem cells to generate blood and other cells could offer an alternative to using tissue donors. The field of stem cell-based regenerative medicine has been studied for around 30 years with limited success, and existing approaches have proven inefficient and lacking in reproducibility.

The teams from the Manchester Institute have developed a serum-free culture - an environment in which the stem cells can grow that is much easier for other laboratories to replicate. They have also identified the point at which the stem cells become early blood cells and are ready for use in transplantation.

Pearson S, Cuvertino S, Fleury M, Lacaud G, Kouskoff V. (2015) In vivo repopulating activity emerges at the onset of from the drugs that are currently available which can't multitask in this way."

hematopoietic specification during embryonic stem cell differentiation. Stem Cell Reports, 10;4(3):431-44.



Figure 1: Embryonic stem cell-derived haemogenic endothelium undergoing endothelium to haematopoietic transition

### A more personalised strategy for the treatment of leukaemia

A collaborative study by scientists from the Molecular Oncology and Leukaemia Biology groups has revealed the potential of a personalised approach to treating chronic leukaemia.

Survival rates for chronic myeloid leukaemia (CML) have improved significantly over the last few years thanks to the introduction of new drugs, known as tyrosine kinase inhibitors (TKIs), which block the activity of enzymes controlling cancer cell growth. However, CML patients often acquire additional gene mutations, meaning they become resistant to many existing TKIs. Therefore, in order to try and identify alternative treatment strategies, researchers from the Institute have profiled the genetic make-up of one patient's disease.

Study leader Professor Richard Marais said: "When cancer-driving mutations combine, doctors struggle to overcome treatment resistance and it's a real clinical challenge."

The team used whole genome sequencing to explore the cause of resistance in a CML patient who had previously received treatment using three different TKIs. They found that there was duplication of the BCL2 gene, and it is known that damage to this gene causes both cancer development and treatment resistance. By using an experimental drug designed to block activity of the Bcl-2 protein, in combination with an established anti-cancer agent, they were able to stop growth of the patient's leukaemia cells in the lab.

"Unfortunately in this instance, this new drug is not yet licensed for use in the clinic, so we were unable to translate our findings to benefit the individual patient. Nevertheless, it is an encouraging approach that may help us to find new combination treatments for patients who have failed all other options," added Professor Marais.

Korfi K, Mandal A, Furney SJ, Wiseman D, Somervaille TC, Marais R. (2015) A personalised medicine approach for ponatinib-resistant chronic myeloid leukaemia. Annals of Oncology Feb 23.

# **Staff News**

### **Crispin: The Marathon Man**

This April, Crispin Miller (RNA Biology & Computational Biology Senior Group Leader) ran his second marathon. His first marathon was in Manchester last year, and this year Crispin took part in the London Marathon, saying 'I've always wanted to run it ever since I first saw it on TV - I thought the atmosphere looked amazing'.

How does he train for a marathon you wonder? 'I run all year round, but started training for the marathon about 18 weeks before.' And although he says he found it difficult to get all the runs in this year, Crispin completed the marathon in 3 hours and 45 minutes, just a few minutes outside his personal best. This time was particularly amazing considering he had been in Philadelphia at the busiest cancer conference in the world, the AACR, just a few days before and was still suffering from jetlag.

Crispin 'absolutely loved' the marathon, saying afterwards 'it is a fantastic experience - and the support is brilliant - parts of the course are quite enclosed with tall buildings and you just get hit by a wall of sound. As you know, I ran it for CRUK - and the support from the charity volunteers was great as well they had cheering points around the course, and it really does give you a lift."

He enjoyed the experience so much he said he would 'do it again tomorrow if [his] legs could stand it!' Instead, he has already run the Manchester 10k - exactly 2 weeks after finishing the London marathon; and is planning to run his next marathon in the Autumn.

We congratulate Crispin on his incredible achievement, and in turn, Crispin would to say thank you to everybody who sponsored him and to the fantastic supporters in London.



Crispin Miller with his finishers T-shirt and medal

### **Baby news**



Leo Sebastian with his parents

Dan Wiseman (Leukaemia Biology) and his wife Beth welcomed a beautiful baby boy, Leo Sebastian Wiseman, into their family on the 4th April 2015



Neve Alice sitting up by herself!

Congratulations to Kate Smith (DDU) and husband Chris on the birth of their baby girl, Neve Alice who was born on the 28th November 2014



2 month old Anou Niamh has already been to Germany & Ireland

Meet Anou Niamh Baenke, Fraziska Baenke and Garry Lyons' baby girl who was born on the 1st March 2015

Last month, former CRUK MI Postdoctoral Researcher Shameem Fawdar was named Best Young Mauritian Scientist 2015 at an award ceremony organised by the Ministry of Technology, Communication and Innovation and the Mauritius Research Council (MRC). The award recognises the efforts of young Mauritian scientists and researchers, and Shameem won the prize to recognise her dedication to advancing cancer research.

Her award included a cash prize of RS100,000 (£1800) and RS50,000 (£900) to attend a conference of her choosing.

Lisa Waters, CEP Administrator, is a qualified yoga teacher (British Wheel of Yoga) and pilates instructor (Pilates Foundation) with years of experience of yoga and pilates. Lisa has recently started a lunchtime yoga session for staff. Yoga is an ancient form of exercise and focuses on strength, flexibility and breathing to improve physical and mental wellbeing. The sessions have been a great success and enjoyed by many people across the building.

### **Best Young Mauritian Scientist Award**



Shameem Fawdar receiving her award cheque.

Shameem worked for three years in the Signalling Networks in Cancer group, led by John Brognard, where she performed a genetic decency screen to identify novel targets for therapeutic intervention in lung cancer. During her time in the Brognard Group, Shameem had a first author paper in PNAS and a first author editorial in Oncotarget, among other publications. She is currently setting up a project on the genetic background of breast cancer, with Professor Theeshan Bahorun in Mauritius.

### **Yoga with Lisa Waters**

The class is held on Thursday at 12:30pm in the Holt Major. There's no charge but donations to CRUK are accepted.

# All change in MBCF



After 13 years as head of the Molecular Biology Core Facility, Stuart Pepper is handing over the reins in order to concentrate on his role as Chief Laboratory Officer, a position which includes oversight of all of the core research facilities. Here we take a look back at the facility since its formation and also consider what lies ahead.

Stuart Pepper

The Molecular Biology Core Facility (MBCF) was created during the Summer of 2001 when Stuart Pepper was tasked with the job of converting an area that had been the Institute's mechanical workshop into a modern core research facility. Originally the facility was known as the 'Equipment Park' but this was changed to MBCF once the service was up and running.

The first major purchase was an ABI 3100 at a cost of £97,000. This instrument has proved itself to be highly reliable - thirteen years later it still provides the daily Sanger sequencing service. From a relatively modest beginning, providing just Sanger sequencing and qPCR support, the facility grew rapidly. Within five years MBCF had established a national microarray service for CRUK, added mass spectrometry to its portfolio (though this was later moved to become a separate facility) and added other screening services. MBCF was involved in setting up an in house genotyping service which for many years has provided a fast turnaround for murine genotyping. Further screening services were also added - first of all for mycoplasma and then cell line authentication. These services have enabled research groups to have confidence in cell lines used around the Institute.



Chris Clark operating the Echo550



Next Generation Sequencing platforms

This expansion was also associated with an increase in the size of the team. The facility was originally set up by Stuart Pepper and Yvonne Connolly, with Yvonne Hey joining almost immediately to create the Affymetrix microarray service. From this point the ethos has been to recruit graduate technicians and train staff in house. The first recruit was Gill Newton who has moved from genotyping and sequencing to microarrays to Next Generation Sequencing. At its peak, the facility had ten staff, including two bioinformaticians. Now with Mass Spectrometry and Bioinformatics services managed separately, the team comprises seven members.

In addition to the introduction of major new technologies, Stuart has also looked to introduce small-scale innovations which nevertheless have had a big impact. They were the first microarray facility in the UK to buy a Nanodrop which, when it arrived, was by far the best spectrophotometer available for measuring DNA. Initially this was the only one in the Institute but as word spread, we gradually acquired several more for other groups to use.

The team were also one of the very first groups in Europe to buy an Epmotion automation platform. This allowed more efficient use of the quantitative PCR instruments as it became possible to move from 96 to 384 well plates without buying a new instrument – effectively quadrupling the throughput of the service for a modest outlay.

Over the last few years, Next Generation Sequencing has been a major focus of the facility with the Illumina HiSeq and NextSeq500 becoming the core of the sequence service. Over the last couple of years these instruments have generated a large amount of sequence data that has contributed to several exciting publications.

Having started with an empty room 13 years ago, Stuart is stepping away from this role and leaving a world-class research facility in the capable hands of Wolfgang Breitwieser.

## New head of MBCF

By Wolfgang Breitwieser



Technology in Molecular Biology is developing at a lightning pace. Scientific equipment that delivers increasingly faster throughput, more content, and higher precision is helping scientists to tackle ever more elusive problems in biology. The Manchester Institute's Molecular Biology Core Facility was developed

Wolfgang Breitwieser

to fulfil just this task and has earned a formidable reputation for cutting-edge services and its ability to adapt to the fast changing pace of research.

Against this backdrop I took on the role as new Head of the MBCF just over four months ago - so no pressure there! But how else to step up to the mark than to take stock and look into the future. Our Institute hosts world leaders in a variety of areas of cancer biology, who excel in unravelling seemingly intractable complexities in cancer biology. It is the Facility's task to support our scientists with the latest technologies and applications. We are in a genome age and massive parallel sequencing offers many of the solutions to these challenges.

## Echo550 - a "sound" investment

**By Wolfgang Breitwieser** 

It is hard to avoid a pun when describing instrumentation that is based on acoustic technology. The MBCF already boasts a select set of automated liquid handling platforms, but its newest acquisition is a breed apart. The theory behind the Echo550 technology is based on the automated transfer of liquids via acoustic pulses.

The instrument creates precisely sized droplets that travel small distances through air from a source into a microplate. This type of liquid handling therefore dispenses with plastic tips, with the benefit of reducing waste, saving costs and eliminating contamination.

The Echo550 transfers liquids in multiples of nanolitre droplets, allowing compounds to be handled in the minutest of quantities - these being log scales lower compared with pipette tip based platforms. The instrument's emphasis is

While our current crop of next generation sequencing platforms has a strong foothold in the services we offer, our scientist colleagues challenge us to tackle samples from ever smaller sources, and of ever more diminished quality. For example, nucleic acid analysis from fixed tissue blocks was a no-go area not long ago, but the expectation is there for it to be tackled and it will soon become the norm. Along similar lines, high throughput screening used to be the domain of big pharma or dedicated specialists. Recent investment into the service has enabled us to provide high throughput compound handling, but it will be crucial that we look beyond our own lab benches and link up with the other state of the art services the Institute boasts to create efficient work flows. The service's biggest asset, however, is the skilled and dedicated people that have made me welcome in the team and who see it as their mission to deliver a first rate job.

I have been known to spend a bit of my spare time on my bike lately, and I believe I share this particular passion for cycling with other Institute colleagues. It hasn't happened yet, but I expect it won't be long before I will be huffing and puffing up the winding roads of the Snake Pass or Holme Moss only to get caught up by the Director enquiring about what the service can deliver next. There is a saying popular among cyclists which I guess, is also true for science: it's not getting easier, you're just getting faster.

on precision and high throughput and a design for a flexible management of 96, 384, or 1536-well microplates. The Echo is incorporated into the Access robotic platform that manages plate handling, sealing, and centrifugation, in a "programme and walk away" design.

Jointly with the Institute's Drug Discovery Unit, the MBCF also supports an annotated compound library (MIDaS, approximately 10,000 compounds), as well as small, targeted libraries of known chemical inhibitors. The aim is to meet the needs of our Institute's researchers for compound screening by providing highly automated workflows. A critical aspect of this will be the link up with the high content cell analysis platform that is operated by the Advanced Imaging Facility. Of course, to make this a successful service we will rely heavily on the expertise of the imaging specialists as well as the chemists and drug screeners down the corridor.

As an added bonus, with its flashing lights and robotic arm whizzing about, the platform has become a popular destination for lab tours. It is great to demonstrate to donors and fundraisers how we are moving forward.

# **New Building set to herald** a new era for cancer research in Manchester



Inside the building - laboratory space for cancer research scientists

Finishing touches are being made to the new Manchester Cancer Research Centre (MCRC) building and it will soon be ready for scientists to move in.

Providing over 6,000 m<sup>3</sup> of space for expansion of cancer research activity in Manchester, the laboratories in the new building will be home to nearly 150 scientists focused on understanding how cancer starts, develops and progresses. Joining them are around 100 clinical academics and R&D staff from The Christie.

The building layout is designed to foster interaction and collaboration between researchers - several groups will share each laboratory and work together in an open-plan office space. Breakout spaces on each floor and a publicaccess café provide further opportunities for informal discussion between researchers. Various environmentallyfriendly features have been incorporated, such as rainwater harvesting, solar panels and high-tech aluminium cladding that has a special self-cleaning coating that uses UV radiation from the sun to break down pollutants.

Construction work began in November 2012 and by January 2014 the building was weather-tight. Throughout last year, internal fit out works took place, including installation of electrical cables, pipework, ceiling, doors and flooring. Over the last few months there has been delivery of furniture, printers and IT systems alongside some of the specialist laboratory equipment. In May 2015, some office-based staff moved in, whilst laboratory scientists will begin to move in later in the year. The final decision on who will occupy each of the five labs is still being considered.

Outside, landscaping of the 'green swathe' area along Kinnaird Road is now complete and focus has turned to the redevelopment of Withington Green, to create a new high-quality public space. Local residents and councillors worked with the landscape architects to incorporate the preferred options for seating, planting and paving, to allow the design to meet the needs of both the building users and the local community.

To mark completion of the project, the MCRC is holding a week of soft opening events in June to thank donors and fundraisers and to recognise the contribution of those who have been involved in the project from its initiation. There will also be the chance for staff and members of the public to tour the building.

#### Timeline

March 2012	Planning approval obtained
May 2012	Enabling works on site started
November 2012	Breaking the ground event marks start of construction
November 2013	Topping Out ceremony marks completion of the highest point of the building
January 2014	Building weather-tight enabling internal works to progress
June 2014	Completion of the building façade
February 2015	Re-landscaping of Withington Green commences
Spring 2015	Building completed and ready for use



The 'green swathe' alongside the MCRC building

# **Operational News**

### Improvements to our **IT** infrastructure

Our Senior IT Administrator, Steve Royle, updates us on some improvements that will be made to our IT infrastructure that will benefit everyone in the Institute.

There are two elements to the improvements that will be made in the Institute; one is the network and the other is the file servers. You may be aware that the network is comprised of miles of copper wires and fibre optic cables, not unlike the circulatory system in humans. There is the 'core' of the network, which would be the organs through which most of the traffic passes, and there is the 'edge', akin to the fingertips and toes where the data points and desktop PCs and Macs are located. Within the network, the legacy hardware will be replaced at both the core and edge with state of the art equipment that has greater capacity and speed. Single points of failure will be removed by inserting dual redundant links, providing an alternative route. Legacy equipment at the edge will be replaced with new switches. Overall, these changes will increase the speed of the core

### Rolling out the intranet



Tom Bolton is our web developer and the Institute has been keeping him busy from the moment he started here in the summer of 2013. There have been many changes since his arrival and his role to replace websites and applications in need of updating - designing new ones where necessary has been challenging.

Tom Bolton is looking forward to a wellearned break

Tom is a joint appointment with the MCRC and after completing a project to re-develop the Manchester Cancer Research Centre (MCRC) website, he moved on to rebrand the old Paterson Institute website to coincide with our name change to the CRUK Manchester Institute. He then built new sites for the CRUK Lung Cancer Centre and the CRUK and EPSRC Cancer Imaging Centre.

Finally, it was agreed last year that the existing Institute intranet, cheerfully called PICRBoo, was long overdue replacement. It was decided that Tom would design and build our own application to our exact specifications.

network by a factor of 20 and improve data transfer between instruments.

The current 'farm' of servers, which includes email servers. file servers, web servers, and intranet servers, has reached capacity and will be replaced with a new server farm with a vastly increased speed and capacity. This will improve connectivity between the network and file servers. Our Institute members will see a noticeable difference in response time with internal servers - most definitely more 'click and go'! The upgrade will also increase resilience to failures by increasing redundancy, thus removing most of the single points of failure.

We anticipate that the projects will start this summer and take approximately two months over the summer period. Downtime to services will be kept to a minimum and will take place outside of normal working hours where possible.

Ultimately, these two projects will create an IT infrastructure to support both our general IT needs as well as the High Performance Computing requirements of the Institute for the foreseeable future.

Settling on the name 'The Hub' seemed appropriate; we wanted the new intranet to act as a central resource for research facilities, as well as providing information about operations and support services.

With the inaugural MCRC building due to open soon, The Hub needs to encompass staff in both buildings. Simply deciding what to put where was a lengthy process, and a long time was spent deliberating over a suitable layout.

The list of requirements to incorporate was daunting. We needed a staff directory, an overhaul of the Porters' store, a brand new room-booking calendar, and a range of essential HR functions. On top of this, the system needed to be easy to navigate and secure.

Armed with the final piece of advice - "as long as it's not green" – Tom sat down and designed an application from scratch that included all the necessary specifications. With invaluable help from many staff at the Institute, the information and functionality within PICRboo has been completely rebuilt to become The Hub. The whole system is currently undergoing a final tweaking and testing and we hope to launch it over the next few weeks.

# In the spotlight with John Brognard

John Brognard leads the Signalling Networks in Cancer group that focuses on novel oncogenic and tumour suppressing kinases. He is originally from Maryland in the USA and completed his PhD at the University of California, San Diego. As a result, he proudly owns a PhD certificate signed by Arnold Schwarzenegger in his previous role as the governor of California. Following a period of postdoctoral research with Dr Tony Hunter at the Salk Institute in San Diego, John arrived in Manchester as

a Junior Group Leader in 2010. The last year has seen John enjoy a good deal of success with the publication of several significant papers and the award of two research grants.

#### 1. What is your favourite part of the UK?

I really enjoy the Lake District and North Wales, but nothing beats Formby for a day out with my sons at the beach.

#### 2. What was your best ever holiday and why?

A two week trip with my family where we travelled to Corsica first then Tuscany – a relaxing week at the beach followed by some great hiking in wine country.

- 3. Which website do you always check, and why? Washington Post to stay informed.
- 4. What is your favourite film? Life is Beautiful.
- What is your favourite band/singer?
  Probably the Beastie Boys, but I should not admit that.

## 6. If you had to change careers tomorrow, what would you do?

Become a fishing guide in the summer and ski instructor in the winter.

## 7. What is the most important lesson that you have learnt from life?

Pursue your passion in life to achieve some level of daily happiness.

8. Name three things you would take with you to a desert island?

I would challenge myself and opt for the minimalist option and try to survive without any additional items.

#### 9. What is your greatest fear?

At this stage in my life, having one exciting on-going project in the lab get scooped!

#### 10. How would you like to be remembered?

As someone who expanded our basic knowledge of fundamental biology and ultimately delivered discoveries that improved the outcome and survival rate for individuals diagnosed with cancer. Also as a good father and husband.

## 11. If you could change one thing in your past what would it be?

Some of our biggest mistakes shape who we are today, so I would not change anything.

#### 12. What is your signature dish to cook?

Sausages on the Grill – not known for my culinary skills.

## 13. You've just won the lottery and have £5 million pounds to spend. What do you buy first?

To clear my conscience I would have to dedicate at least £1 million to charity (including CRUK!), then buy my wife a place where she could have a bed and breakfast.

#### 14. What is your idea of perfect happiness?

I love flying down a ski slope at high speeds, I connect with nature and can fully experience the moment. I imagine experiencing this with my sons in the future will be a moment of "perfect happiness".

#### 15. What keeps you awake at night?

Science

#### Editorial Team:

Ekram Aidaros Steve Bagley Gillian Campbell Katy Holliday Hannah Leaton 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

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