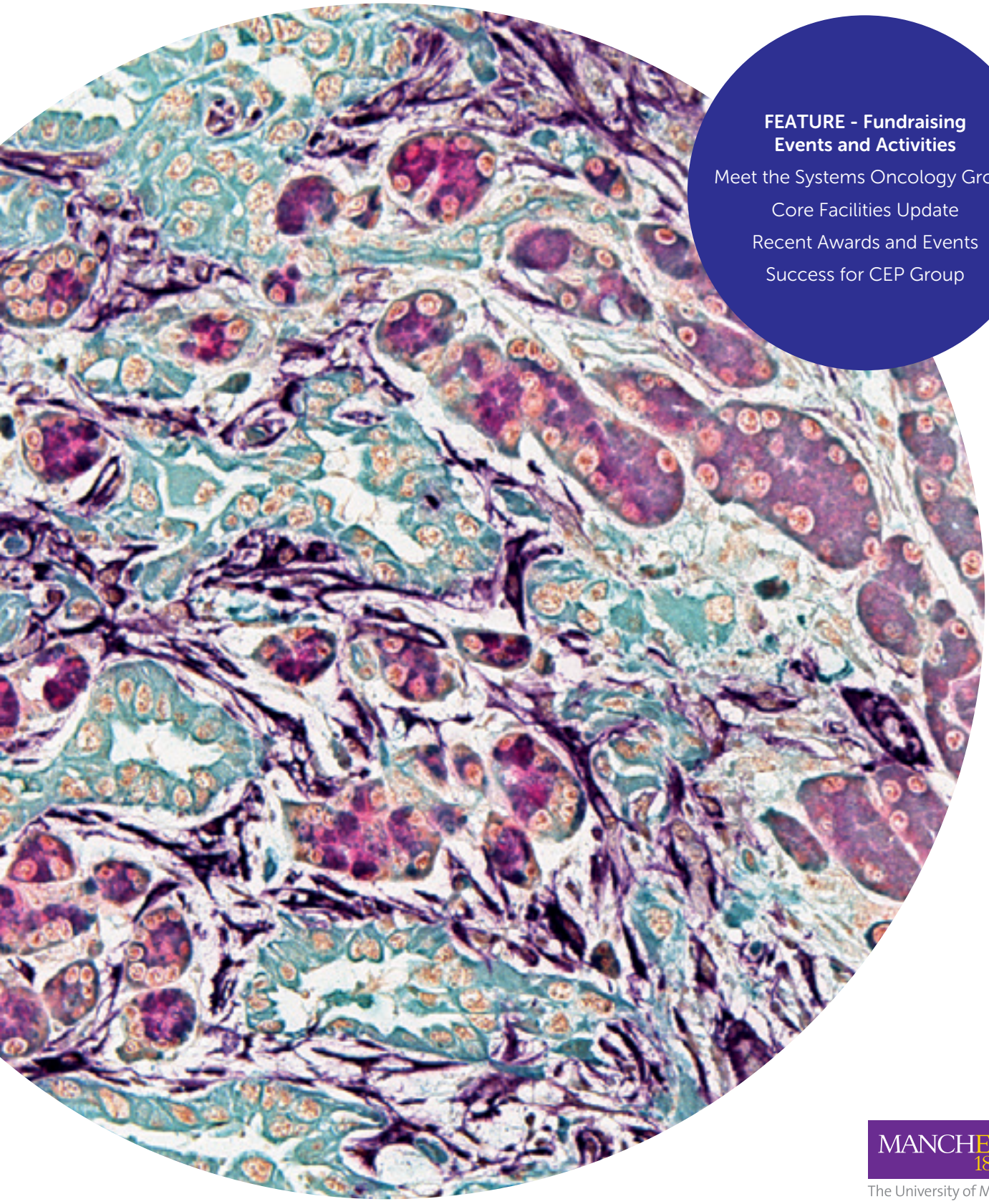
Newsletter

Featuring news from around the Paterson Building

CANCER RESEARCH UK | MANCHESTER INSTITUTE

Spring 2014



FEATURE - Fundraising Events and Activities

Meet the Systems Oncology Group

Core Facilities Update

Recent Awards and Events

Success for CEP Group

MANCHESTER 1824

The University of Manchester

Director's Introduction

It's been a busy few months at the Institute with some exciting new initiatives and an extremely successful quinquennial review for the Clinical and Experimental Pharmacology Group.

The work of the CEP team, led by Caroline Dive, was assessed at the end of 2013 by an international panel of experts who rated their output as outstanding. This is a fantastic achievement and a strong endorsement of the quality and critical nature of their work in developing and validating circulating biomarkers to aid in the decision-making processes for the treatment of cancer patients. I would like to take this opportunity to congratulate Caroline, her Deputy Ged Brady, and the whole team for their efforts and look forward to their continued progress in this essential and exciting field. Both Caroline and Ged have also played an instrumental role in two recent centre awards.

In collaboration with Queen's University, Belfast we have been selected to establish a *Prostate Cancer UK Movember Centre of Excellence*. This award came in response to a call from Prostate Cancer UK and in collaboration with MCRC expertise in this area from Noel Clarke, a member of the University's Institute of Cancer Sciences (ICS). The programme is worth £5m over five years (split equally between the two sites) with the aim of improving prostate cancer survival rates via personalised delivery of DNA-damage based therapy. This programme is a good strategic fit with the personalised medicine agenda that runs through all of our priority areas and recruitment for the associated posts is underway.
As part of the centre's programme for this year, we shall be organising a one day prostate cancer workshop and public lecture, both in Manchester, later on this year. As part of our focus on this area, Esther Baena has recently joined the Institute and will complement the activities of the Centre of Excellence by studying the role of certain transcription factors that are pivotal in this disease.

Our continued focus on lung cancer has been strengthened with the creation of the CRUK Manchester-UCL Lung Cancer Centre of Excellence in collaboration with colleagues within the ICS. The corresponding £2.5 million of funding will allow us to play a key role in coordinating lung cancer research across the UK. The aim is to improve outcomes for lung cancer patients through a better understanding of the biology and genetics of lung tumours and the mechanisms underpinning adaptation to treatment.

Lung cancer is a major priority for CRUK, as outlined in the charity's recent new research strategy, as survival rates remain extremely low in this area. We are continuing to build on our strong platform of lung research at the Institute and in July, we will welcome Michela Garofalo, a new Junior Group Leader who will study the role played by micro-RNAs in modulating the response of lung cancer to treatment. Another CRUK priority area is pancreatic cancer where outcomes are also currently very poor. Claus Jorgensen joined the Institute in January and will study the interaction between pancreatic cancer cells and their surrounding stromal environment. He will be working closely with ICS colleague Juan Valle and you can find out more about the aims of his research in this issue.

The on-going development of the core research facilities is progressing well with new technological platforms added recently through funding from the recent UKRPIF award. The Histology Facility has expanded considerably in recent months under the excellent leadership of Garry Ashton who features in this issue along with his team.

Research engagement continues to be extremely well supported by members of the Institute so I would like to thank everyone for their participation in these vital activities. In particular, the recent Open day in March was a tremendous success. Congratulations to all the Keswick to Barrow walkers (and runners) and participants in the Relay and Race for Life events.

In the last few months we have said goodbye to some long-serving members of the Institute. Nullin Divecha has taken up a post at the University of Southpamton and we wish him all the best in his continuing research efforts there. I would like to pay particular tribute to David Broadbent, Martin Greaves and Fran Hockin who between them have worked at the Institute for over 100 years. On behalf of everyone here, I would like to thank them for their many years of excellent service and wish them all the very best for their retirement.

Richard Marais
Director

The team of scientists, captained by Steve Lyons, who took part in the Stockport Relay for Life to raise money for the More Tomorrows campaign which will support the new MCRC building.

Cover Image: Triplex immunohistochemical staining of orthotopic pancreatic tumours showing acinar cells in magenta, alphaSMA positive myofibroblasts in deep purple and cytokeratin positive epithelial cells in green

Fundraising Events and Activities

By Hannah Leaton

Scientists for a Day

The chance to be a 'Scientist for the Day' at the Institute was auctioned at a CRUK fundraising ball, and the lucky winners recently came in to claim their prize. They isolated compounds from plasma and stained cells in Drug Discovery, used PCRs and loaded samples onto gels in the Molecular Biology Core Facility and learnt about Circulating Tumour Cells with CEP. A huge thank you to everyone who helped make this day so special for our guests.

Manchester Histories Festival

The Institute hosted two walking tours as part of the Manchester Histories Festival. More than 20 participants came to explore Manchester's rich history of cancer research. They discovered the origins of the Christie hospital, learnt about the treatments pioneered by Ralston and Edith Paterson and explored the future of cancer research by visiting the site of the new MCRC building.

Research on Film

Caroline Dive stepped in front of the camera to talk about her research into lung cancer. Look out for her on twitter. This virtual access to our research is so important, as it ensures that anyone, anywhere, has the opportunity to interact with the Institute's pioneering science.

Corporate Lab Tours

The Institute opened its doors to 60 representatives from local companies who were considering making CRUK their charity partner. They enjoyed lab tours, some hands on science and a trip to the MCRC Visitors' Centre. The event was a huge success, and CRUK has already been announced as the charity partner for several of the organisations who joined us!

CRUK supporters getting hands on with science at the Institute Open Day

Open Day

In March around 120 CRUK supporters attended an inspiring Open Day at the Cancer Research UK Manchester Institute. After a welcome from Professor Caroline Dive, guests got the chance to go behind the scenes and see the impact that their fundraising is having on cancer research.

They learnt about some of the Institute's recent successes, tried their hand at pipetting and took part in other hands-on science activities, including strawberry DNA extraction. They also visited the new Manchester Cancer Research Centre building.

Images Left to right: Allan Jordan from the Drug Discovery Unit presenting the Schofield family with a CRUK Certificate of Appreciation, after they raised a fantastic £60,000 for the More Tomorrows campaign; some of the CEP team taking part in Football Shirt Friday in support of the Bobby Moore Fund; John Weightman from the Molecular Biology Core Facility explaining genome sequencing to the new Race for Life interns; some of our researchers taking their #makeupselfie

Images Left to right: Bruno Simoes, Ricardo Gândara and Adam Mitchell; Darren Roberts and his daughter Heather; Courtney Thwaites, Anna Marusiak, Kelly Brooks and Gabriela Gremel

Keswick to Barrow: A Walk in the Park

By Gillian Campbell

On 10 May 2014, 23 brave members of the Institute took on the challenge of walking or running 40 miles from Keswick to Barrow in the Lake District National Park. Here is their story:

Predictably, the rain was pouring down from the beginning, to be punctuated only by heavier downpours. It was an inauspicious start, but not unexpected as the night before we had hopelessly searched for a favourable forecast only to discover rain was the unanimous report. Having been unceremoniously deposited by various Happy Buses, our team of intrepid walkers (and runners) started between the uncivilised hours of 05:30 and 06:30 – depending on how enthusiastically one leapt from the warmth of bed. The first part of the route took in Thirlmere and its wondrously wild atmosphere, heightened by swirling mists and gushing waterfalls. Having unsuccessfully navigated flooded paths and earning soggy feet, we made it to the first checkpoint at Grasmere, 10 miles done. It was then on to Elterwater under the Langdales via the notoriously steep Red Bank Road. The skies may have cleared briefly at one point to reveal the Langdales glowing beautifully red in the sunshine. Moving ever forwards and it was on to Coniston next and more rain, body and soul-nourishing hot food and another change of socks. The route then went alongside picturesque Coniston Water towards Lowick and the final slog up Kirby Moor, a long and relentless climb that leads down to the villages of Marton and Dalton towards the final destination of Barrow. The generosity and support of the locals (cheers and offers of chocolate) was very welcome and gave us weary walkers a final boost to the finish line.

Everyone completed the walk and did fantastically well, despite miserable conditions yet again (many of us participated last year in the wettest recorded walk – but it did not deter us!). Special mention goes to Robert Metcalf who ran the 40 miles from Keswick to Barrow in the fantastic time of 6 hours 47 minutes (he came 88th out of the 2157 participants on the day). Many repeat walkers took on the additional challenge of beating their time from last year and succeeded in smashing their times. Andrew Renehan powered through all checkpoints and arrived in 9 hours 38 minutes, more than an hour quicker than last year.

All the walkers would like to express gratitude to those who supported us on the day. We would also like to thank those who sponsored us and helped raise over £3000 which will be divided between Cancer Research UK and The Christie charity.

Name	Time	Position
Robert Metcalf	06:47:36	88
Adam Whitworth	06:47:40	89
Kiran Batta	07:44:25	234
James Wall	07:49:51	251
Andrew Renehan	09:38:15	588
Bruno Simoes	09:41:12	606
Adam Mitchell	09:41:25	608
Ricardo Gândara	09:41:26	609
Gillian Campbell	10:01:23	714
Anna Marusiak	10:37:55	931
Darren Roberts	10:46:08	980
Tim Somerville	10:56:12	1040
Dan Wiseman	10:56:15	1042
Rebecca Foulger	10:56:16	1045
Filippo Ciceri	10:59:13	1056
Emma Williams	11:02:44	1084
Adam Prest	11:02:44	1085
Yaoyong Li	11:25:38	1238
Kenneth Oguejiofor	11:26:17	1245
Gabriela Gremel	11:32:09	1287
Kelly Brooks	11:32:10	1288
Nitin Rustogi	12:40:34	1722
Courtney Thwaites	12:56:17	1790
Shraddha Agashe	13:07:04	1837
Amit Mandal	14:12:51	2056

Hannah Leaton

Research Engagement Manager - Meet Hannah:

Hannah Leaton joined the Institute in January 2014 as Cancer Research UK's Research Engagement Manager, while Eve Hart is on maternity leave. Prior to joining CRUK, Hannah was working as a fundraiser for a much smaller cancer charity in London. But she's very pleased to be back in Manchester!

Hannah's office is shared with the More Tomorrows fundraising team, and is the last door on the left before the stairs down to the basement. She has a brand new 'menu' of public engagement opportunities, along with a never ending supply of CRUK branded t-shirts and labcoats, so if you'd like to get involved with the charity in any way, please come in and say hello!

Caroline Wilkinson and CRUK supporters at the top of Scafell Pike

CRUK does Scafell Pike

This year CRUK was asked by Buckingham Palace to be one of four charities to fly the Commonwealth Flag at the peaks of the four highest mountains in the United Kingdom to celebrate Commonwealth Day. CRUK MI's Chief Operating Officer Caroline Wilkinson joined 16 CRUK supporters in a scale up Scafell Pike in the Lake District. The weather was perfect and it was a very special day for everyone involved.

Juliet Mitchell and Richard Marais

Duerr's Donation for More Tomorrows

Duerr's, Britain's oldest family run jam and marmalade makers, have donated £30,000 to the 'More Tomorrows' fundraising campaign for the construction of the new Manchester Cancer Research Centre (MCRC) building.

The money was raised at Duerr's Russian themed 'Jamski' charity ball, held at The Monastery, Manchester in November 2013.

Mark Duerr, Managing Director of Duerr's said: "Our annual ball was a brilliant success and we're now delighted to hand over £30,000 on behalf of our guests who dug deep for such a deserving cause. The MCRC's aim is to revolutionise the treatment of cancer – a disease which affects 36 people in Manchester every single day."

Juliet Mitchell, cousin to Mark and Richard Duerr, who has previously been treated at The Christie, presented the cheque to Professor Richard Marais in a fun and rather sticky fashion, filling a conical flask with Duerr's delicious strawberry jam!

Coming up

14th June
Ideas of Life, Manchester Museum

20th June
Cancer Research UK Strategy Launch Event

17th - 19th September
Institute Colloquium

Featured Publications

"Liquid Biopsy" Offers New Way to Track Lung Cancer

The CEP team have shown how a lung cancer patient's blood sample could be used to monitor and predict their response to treatment – paving the way for personalised medicine for the disease. The recent study also offers a method to test new therapies in the lab and to better understand how tumours become resistant to drugs.

Small cell lung cancer (SCLC) is an aggressive disease with poor survival and new treatments are desperately needed. In many cases the tumour is inoperable and biopsies are difficult to obtain, giving scientists few samples with which to study the disease.

Now research carried out by the Institute's Clinical and Experimental Pharmacology Group has looked at the potential of using circulating tumour cells (CTCs) – cells that have broken off from the tumour and are circulating in the blood – to investigate a patient's disease in a minimally invasive manner.

The researchers, working closely with lung specialist and Medical Oncologist Dr Fiona Blackhall at The Christie NHS Foundation Trust, found that patients with SCLC had many more CTCs in a small sample of their blood than patients with other types of cancer. Importantly, the number of CTCs for each patient was related to their survival – patients with fewer CTCs in their blood lived longer.

Professor Caroline Dive, who led the study, said: "Access to sufficient tumour tissue is a major barrier to us fully understanding the biology of SCLC. This liquid biopsy is straightforward and not invasive so can be easily repeated and will allow us to study the genetics of each lung cancer patient's individual tumour. It also means that we may have a feasible way of monitoring patient response to therapy, hopefully allowing us to personalise and tailor individual treatment plans to each patient."

In addition, the team were able to use these CTCs to grow tumour models in mice, which they termed CTC-derived explants (CDXs). When they treated these mice with the same chemotherapy drugs as the SCLC patients, they showed that the CDXs responded in the same way as each donor patient.

"We can use these models to help us understand why so many SCLC patients acquire resistance to chemotherapy and to search for and test potential new targeted treatments," added Professor Dive.

Hodgkinson, CL et al. (2014). Tumorigenicity and genetic profiling of circulating tumor cells in small-cell lung cancer. *Nature Medicine*. doi: 10.1038/nm.3600.

Exploring Drug Resistance in Metastatic Melanoma

Melanoma is a form of cancer that develops from melanocytes – the pigment-producing cells in skin. Advanced metastatic melanoma – where the cancer has spread throughout the body – is associated with poor survival, so new treatments are urgently needed. In around 40% of melanoma cases, the tumour contains a mutation in a gene known as BRAF. Drugs that target BRAF, such as vemurafenib, have increased survival in patients with this mutation. However, many of these patients go on to develop resistance to treatment and their disease returns. Now a study by the Molecular Oncology group has looked at what happens in melanoma once the tumour has stopped responding to treatment. They showed how the BRAF-targeting drug makes certain melanoma cells change shape and become more invasive. Their findings suggest that using a combination of drugs may be the best approach for patients.

It is already known that BRAF inhibitors such as vemurafenib have different effects in BRAF mutant cells depending on the additional presence of RAS mutations. Recent work at the Institute has further explored the effect of both genetic and pharmacological inhibition of BRAF on RAS mutant melanoma cells. The team saw increases in ERK-interleukin 8 mediated signalling and secretion of extracellular proteases, leading to invasion in vitro and metastasis in vivo. In addition, the dominant morphology of the tumour cells switched from rounded to spindle-shaped cells. This behaviour also occurred in cells that were resistant to BRAF inhibitors. Finally, they were able to block this invasion and metastasis using MEK inhibition. Their results support the use of BRAF and MEK inhibitors in combination in the clinic.

Sanchez-Laorden B, Viros A, Girotti MR, Pedersen M, Saturno G, Zambon A, Niculescu-Duvaz D, Turajlic S, Hayes A, Gore M, Larkin J, Lorigan P, Cook M, Springer C, Marais R (2014). BRAF inhibitors induce metastasis in RAS mutant or inhibitor-resistant melanoma cells by reactivating MEK and ERK signaling. *Science Signaling*, 7(318):ra30

Potential Therapeutic Target for AML

A critical biological and therapeutic entity in acute myeloid leukaemia (AML) is the leukaemia stem cell (LSC), which has the ability to self-renew and therefore maintain and expand the disease. Understanding the biology of disordered LSCs in comparison with normal haematopoietic stem or progenitor cells (HSPCs) is central to the identification of new genes and cellular pathways critical for LSC function, which can be targeted by novel therapies. There is a substantial unmet need for novel therapies in AML because currently fewer than 25% of patients are cured. Application of knockdown screening and high throughput sequencing has made significant progress in understanding the biology of AML and its potential treatment.

Tim Somervaille and his group in Leukaemia Biology focus their research on disordered epigenetic regulation, a key feature of the pathology of AML. They recently reported the results of a targeted knockdown (KD) screen of chromatin regulatory genes that led to the identification of Enhancer of Polycomb genes EPC1 and EPC2. EPC is conserved from humans to yeast and its gene product forms part of the EP400 chromatin regulatory complex. Crucially, their studies revealed that AML cells, but not normal HSPCs, are selectively sensitive to EPC KD. It was observed that apoptosis of AML cells (largely due to acute accumulation of the oncoprotein MYC) followed KD of EPC1 and EPC2 and they further demonstrated that this accumulation of MYC contributed to apoptosis. That EPC1 or EPC2 prevent accumulation of MYC and thereby inhibit AML cell death and sustain its oncogenic potential, suggests the EPC/EP400 complex is an important therapeutic target.

Although it remains unclear why MYC accumulates following EPC KD in AML cells, elucidation of the differences in the structure and function of chromatin between normal HSPC and leukaemic cells may provide an explanation as well as an important approach to the identification of candidate therapeutic targets and strategies.

X Huang, G J Spencer, J T Lynch, F Ciceri, T D D Somerville and T C P Somervaille (2013). Enhancers of Polycomb EPC1 and EPC2 sustain the oncogenic potential of MLL leukemia stem cells. *Leukemia*, 1–11.

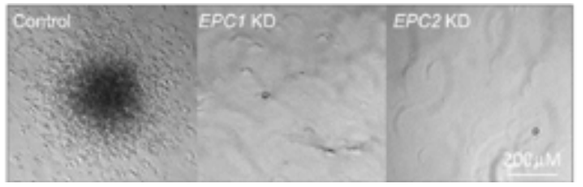


***Figure 1**: Images show EPC1 and EPC2 knockdown abolishes the clonogenic potential of primary human AML cells from a patient with a t(9;11) translocation. Primary AML cells from a patient with a t(9;11) were infected with lentiviruses targeting EPC for knockdown, or a non-targeting control (NTC), with GFP as the selectable marker.*

Greater Understanding of Processes Involved in the Control of Blood Cell Growth

The Stem Cell Biology and Stem Cell Haematopoiesis groups have recently published a study in the journal *Stem Cells* that explored what makes blood stem cells stop replicating. Replication of stem cells is a key process in maintaining normal tissue structure and function. Stem cells divide rapidly and there are certain defence mechanisms in place in case there are mistakes in these new cells – to hopefully stop the uncontrolled growth at the heart of cancer development.

In normal cells, one way of controlling replication is through senescence, when the cell enters a resting phase and no longer divides. In contrast, in acute myeloid leukaemia, there is abnormal growth and proliferation of white blood cells – these collect in the bone marrow and prevent the production of normal blood cells. Scientists have previously seen that in animals without a protein known as MOZ, which regulates the creation of blood stem cells, there is increased cell senescence. This new work shows that without MOZ, both blood and neural stem cells and progenitors stop replicating and enter senescence.

The group also found that MOZ binds to a key tumour suppressor molecule, p16-INK4a, and regulates its activity. In the absence of MOZ, expression of p16-INK4a was up-regulated in progenitor and stem cells and the proliferative capacity of these cells was dramatically impaired. Genetic deletion of p16-INK4a reversed this proliferative defect.

It is hoped that this new insight could lead to MOZ being a potential treatment target for leukaemia.

Perez-Campo FM, Costa G, Lie-A-Ling M, Stifani S, Kouskoff V, Lacaud G (2013). MOZ-mediated repression of p16INK4a is critical for the self-renewal of neural and hematopoietic stem cells. *Stem Cells*, Dec 4. [Epub ahead of print]

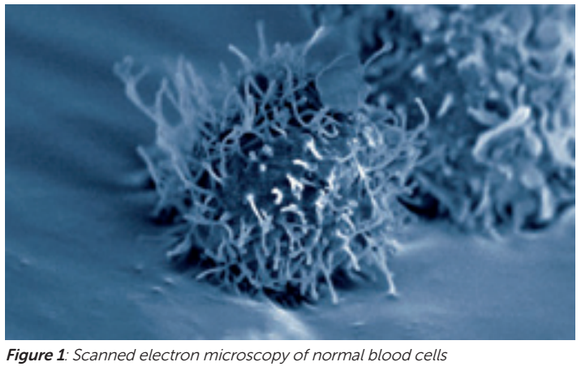


***Figure 1**: Scanned electron microscopy of normal blood cells*

Targeting Tdp2

The magic of medicinal chemistry design of drugs is finely balanced by potency, drug delivery into living systems, efficacy and toxicity. This article demonstrates how all these key factors can complement and oppose one another. The biological target is a DNA protein and the DDU chemistry-designed inhibitor compounds are called deazaflavins. To the best of our abilities we drove this drug discovery programme to a poignant decision point and has since been successfully handed over to our collaborators at Sussex University.

Topoisomerases are nuclear enzymes involved in the movement of DNA within the nucleus or in the opening of the double helix. These enzymes generate reversible breaks in DNA thereby allowing DNA decatenation. In order to carry out its critical physiological functions, topoisomerase generates transient topoisomerase-DNA cleavage complexes, so-called cleavable complexes, in DNA. Oxidation, ionising radiation or chemotherapeutic agents can stabilise this complex and prevent the enzyme from resealing the DNA break it creates, resulting in topoisomerase enzyme-mediated DNA damage. Topoisomerase II (Topo II) poisons, such as etoposide, can induce abortive DNA strand breaks in which Topo II remains covalently bound to a 5' DNA strand terminus via a phosphotyrosyl linker. It has been proposed that TDP2 may remove degraded Topo II peptides covalently linked to the 5' terminus, thus playing a central role in maintaining normal DNA topology in cells. Cellular depletion of TDP2 has been shown to result in an increased susceptibility and sensitivity of cells to Topo II-induced DNA double-strand breaks, thereby suggesting that TDP2 is a potentially attractive anticancer target. Following a high throughout screen (HTS) carried out at the Cancer Research Technologies Discovery Laboratories (CRT-DL), two distinct chemical series were identified as the first reported sub-micromolar and selective inhibitors of this enzyme. The first series, toxoflavins, appeared to exhibit clear structure activity relationships (SAR) for TDP2 enzymatic inhibition. However, we observed a key redox liability of this series, and unfortunately this, alongside early in vitro drug metabolism pharmacokinetics (DMPK) issues, precluded further exploration. The second series, deazaflavins, were developed from a singleton HTS hit, and although they showed distinct SAR and did not display redox activity, low cell permeability proved to be a challenge.

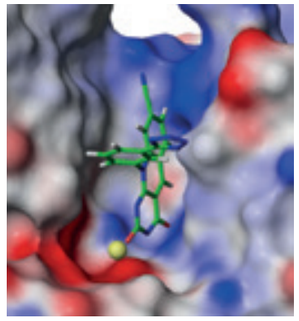


***Figure 1**: A model illustrating how one of the lead compounds might be interacting with the enzyme's active site.*

As part of the collaborative deal, the successful project handover to the Caldecott group at Sussex University was implemented and in recent months they have described a hit-to-lead deazaflavin compound, originally designed by DDU, in the human TDP2 crystal structure to aid future drug design.

Raoof A, Depledge P, Hamilton NM, Hamilton NS, Hitchin JR, Hopkins GV, Jordan AM, Maguire LA, McGonagle AE, Mould DP, Rushbrooke M, Small HF, Smith KM, Thomson GJ, Turlais F, Waddell ID, Waszkowycz B, Watson AJ, Ogilvie DJ (2013). Toxoflavins and deazaflavins as the first reported selective small molecule inhibitors of tyrosyl-DNA phosphodiesterase II. *Journal of Medicinal Chemistry*, 56(16):6352-70.

Institute Appoints New Cancer Research Group Leaders

Two new group leaders are set to join the Institute this summer. Research into two disease areas – lung cancer and prostate cancer – will be strengthened through the appointment of Dr Michela Garofalo and Dr Esther Baena as junior group leaders.

Dr Garofalo joins the Institute from Ohio State University in Columbus in the United States. Her work looks at potential treatment approaches in lung cancer and the importance of microRNAs – small molecules that prevent the expression of individual genes – in sensitising tumour cells to chemotherapy drugs.

Also moving from the US, Dr Baena comes to Manchester from the Dana-Farber Cancer Institute in Boston. Her research is focused on prostate cancer, and mechanisms involved in progression and treatment resistance. In particular, she is interested in certain transcription factors – proteins that control the flow of genetic information - and the role they play in tumour growth.

Michela Garofalo

Esther Baena

Professor Richard Marais said: "These are very exciting appointments for the Institute and for Manchester as a whole. It allows us to further develop these two important areas of cancer research."

Meet the Systems Oncology Group

The Systems Oncology team: Claus Jorgensen, Emma Newsham, Jonathon Worboys and Kelly Broster

Claus Jorgensen joined the Institute in early 2014. Below, he describes the approaches that his research team, the Systems Oncology group, will be undertaking to understand the complex interactions between malignant and normal cells, with a particular interest in pancreatic cancer.

Currently the team includes Emma Newsham, Kelly Broster and Jonathan Worboys. In addition, Brian Lee will be joining us shortly from the Garvan Institute as well as Ida Norrie and Marie Locard-Paulet who will be relocating from The ICR during the summer. Finally, Amy McCarthy will be starting her PhD this autumn.

The aim of the Systems Oncology group is to describe how oncogenic mutations affect cellular signal transduction and in particular how this translates to a multicellular environment. Specifically, we are investigating how malignant cells recruit and co-opt stromal cells to support tumour growth, metastasis and therapeutic resistance with an emphasis on pancreatic cancer.

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

We are currently working to identify and characterise signals that recruit and confer stromal cells with tumour-promoting activities, as well as their effect on therapeutic resistance. To model the multicellular microenvironment of the tumour we develop and employ co-cultures for biochemical and functional analysis. One challenge to global biochemical analysis of signalling networks in co-cultures is that information of the origin of individual molecules is lost during cell lysis and protein extraction. To overcome this, we label individual cell populations with non-radioactive isotopomeric versions of amino acids prior to their co-culture. As these amino acids are incorporated into the proteome in a cell specific manner, the cellular origin of individual peptides and proteins can be determined when samples are analysed using mass spectrometry. As such, we can identify and quantify the exchanged signalling molecules between tumour and stromal cells, as well as their regulatory effect on cellular signal transduction, in a cell-specific manner.

More recently, we have further developed our workflow and can now label cells in a cell-specific manner for up to ten days of co-culture. This therefore allows us to study how the tumour-stroma signalling evolves following drug administration. Furthermore, using a semi-automatic workflow for quantitative phosphorylation analysis we can evaluate thousands of regulatory events with high reproducibility. Together, these developments will facilitate the generation of hypothesis generating models of stromal activation in PDA. Subsequently, our goal is to evaluate whether any of the regulated proteins in the tumour stroma are viable therapeutic targets and we are currently developing novel models to assess these effects.

Major Success for Clinical and Experimental Pharmacology

Professor Caroline Dive

Professor Caroline Dive and her team in CEP have been highly successful over the last five years, culminating in December 2013 with an outstanding Quinquennial Review, securing CRUK funding for the next five years.

Professor Dive is a world leader in the study and development of circulating biomarkers, with a strong focus on circulating tumour cells (CTC) particularly in small cell lung cancer (SCLC). She has now established a world-class unit, with the depth and breadth of expertise to deliver biomarkers as a part of clinical trials. The last five years has seen the publication of 65 research papers, many in high impact journals, as well as recognition in terms of international prizes, most notably the CRUK Translational Research Prize in 2011 and the Pasteur-Weizmann/Servier International Prize in 2012 for minimally invasive biomarkers to aid management of cancer patients. The ultimate aim of CEP has been to facilitate delivery of personalised medicine by examining circulating biomarkers, working towards establishing CEP as a national biomarker hub. Whilst the group is predominantly focused on lung cancer, it is also interested in melanoma (linking with the work of Professor Richard Marais), pancreatic cancer (linking with the work of Dr Claus Jorgensen), early diagnosis and personalised medicine.

Lung Cancer

SCLC accounts for approximately 15% of lung cancer cases and is the most aggressive form of lung cancer, resulting in rapid tumour growth and early metastatic spread. Consequently, effective treatment opportunities are limited and with acquired resistance to treatment, the five-year survival is 5%, a statistic that has not changed over the last forty years.

The most exciting achievement for CEP has been the development of patient derived in vivo models of SCLC using CTCs from SCLC patients that can be used to test targeted therapeutics (*Nature Medicine, 2014*). They have demonstrated for the first time that CTCs from SCLC patients can form tumours in mice and resultant CTC derived explants (CDX) mirror the donor patient's response to chemotherapy. Significantly, they have shown that CTC molecular analysis based on a simple blood biopsy could facilitate delivery of personalised medicine for SCLC patients. This is particularly relevant in a disease where repeat tumour biopsies are rarely obtained.

In addition, Professor Dive has provided significant input to the successful bids for the CRUK Cambridge-Manchester Molecular Imaging Centre, the TRACERx consortium and the CRUK Manchester-UCL Lung Cancer Centre of Excellence. CEP has also joined the flagship TRACERx consortium, in collaboration with Professor Charlie Swanton (University College London), focusing on the evolution of non-small cell lung cancer and hosting its first CTC Biobank.

Translational Biomarker Hub

CEP has developed a comprehensive translational biomarker hub over the past five years, with the aim of evaluating potential non-invasive biomarkers in clinical trials and identifying ways to improve clinical outcomes. Their key achievement has been the discovery of angiogenic biomarkers for ovarian cancer and the development of robust biostatistical support for biomarker analysis.

Added Value across The CRUK Manchester Institute

CEP has a number of collaborations with the wider research community both within CRUK MI and externally. These projects are highly exciting and include supporting biomarker research in melanoma (Marais) and pancreatic cancer (Jorgensen). Professor Dive also works with the Drug Discovery Unit supporting the development of important parallel biomarkers for candidate drugs.

The Future

Looking forward to the next five years, CEP will focus on expanding and developing lung cancer research at CRUK MI, with the aim of making it an internationally leading Institute in this field. CEP will continue to work on CTCs, not only in lung cancer but also with its collaborative projects in melanoma and pancreatic cancer.

A Fond Farewell

Martin Greaves (centre) with Deputy Director and Head of CEP Caroline Dive and CRUK MI Director Richard Marais.

This spring, the Institute said farewell to one of its longest serving members, Martin Greaves. For the last decade, Martin has been a stalwart of the CEP group and has played a key role in coordinating activities in this large and highly successful team. Here Martin reflects on his path to the Institute and the varied roles he has undertaken. He will be greatly missed.

Back in 1976, when I was working in the Immunology department at the University of Manchester, I decided that I really wanted to work at the Christie Hospital and Holt Radium Institute, as it was known then, in order to advance my career and gain further experience at the cutting edge of cancer research. After sending a covering letter of application for a non-existent job, I was fortunate to be offered a technical position in the Molecular Experimental Pharmacology Group under Dr Margaret Fox. The work was mainly mammalian cell culture which was in its relative infancy. All culturing was undertaken in glass bottles on the open bench in culture rooms without air conditioning, using Bunsen burners and ethanol; as you can imagine, this was a lethal combination, and with 1976 being a scorching hot summer conditions were not ideal. The cells were incubated in gas boxes either in dry incubators or hot rooms.

In the early eighties, molecular techniques were introduced and I remember many a happy hour spent transferring eppendorf tubes between water baths to set up PCR reactions. I spent 17 very happy years with this group at a time when everyone seemed to know everyone else. A social highlight of the year was the Christmas Paterson Revue, held at the staff club where the MCRC Building now stands. Following the retirement of Dr Fox, I joined the Cancer Genetics group led by Dr Jenny Varley. This was a very exciting time as our research focused on cancer families, specifically Lie-Fraumeni syndrome and p53 mutation suppression genes. My technical expertise expanded to include in situ hybridisation techniques and sequencing.

Following the promotion of Dr Varley to Assistant Director, Cancer Genetics ceased to exist but I was lucky enough to be offered a promotion to enable me to work with Dr Raj Chopra investigating telomere length and cancer. In December 2003 Dr Chopra left the Institute but I was again very lucky to be shortlisted for a position in Professor Caroline Dive's new laboratory and the rest as they say is history. For me this has been the most exciting and challenging period of my career at the Institute and one that I have been extremely proud to be part of. To work in, and contribute to, such a dynamic group has been an absolute delight and I am very sorry to leave especially after Caroline's recent achievement at the Quinquennial Review.

However after 38 years at the Institute, and with a movement disorder that is making everyday life more difficult for me, it has been time to say farewell. I feel very privileged and proud to say that I have been employed for such a long time in cancer research at the Institute and of having the opportunity to be able to work alongside top international scientists and fantastic staff all trying to defeat our common enemy. I would not have changed a minute of it.

Nucleic Acid Biomarkers - By Ged Brady

Ged Brady

The development of molecular biology based platforms to detect cancer specific genetic aberrations now plays an increasingly important role in biomarker discovery to facilitate drug selection and to enable the monitoring of drug response.

Dr Ged Brady joined CEP as deputy leader in 2011 to establish and head a nucleic acids biomarker (NAB) group to detect and characterise tumour derived nucleic acids present in cancer patient blood samples. This represents an enormous challenge since a blood collection tube containing 7.5ml of blood from a cancer patient will contain approximately 7.5 x 10^7 peripheral blood mononucleated cells (PBMCs), 0-1000 circulating tumour cells (CTCs), 20-1000ng total circulating free DNA (cfDNA), of which about 0.2-100ng is tumour derived. Furthermore, each isolated single CTC will only contain around 6.66pg genomic DNA, representing two genomic copies of each gene (apart from rare exceptions such as X and Y linked genes and cancer associated DNA changes) and around 10-30pg of RNA representing approximately 5x10^5 mRNA molecules. To overcome these challenges, the NAB team has established a "one size fits all" blood collection process, allowing collection, transport and storage of whole blood at room temperature for four days in a format which is compatible with combined CTC and cfDNA isolation and molecular characterisation. Using this approach, genomic profiling of Small Cell Lung Cancer (SCLC) patient CTCs has established a striking similarity to the corresponding CTC derived explants (CDX) and has identified changes potentially linked to drug response (Nature Medicine, 2014). Circulating miRNAs have appealing features for biomarker research; they are highly stable with a wide dynamic range in levels, and since there are relatively few miRNAs (compared to mRNAs), global expression profiling is made relatively easy. For improved analysis of plasma derived miRNAs, the NAB group have developed a robust microscale assay which can be applied to both pre-clinical and clinical samples. In preclinical models, the miRNA assay has been used to monitor growth of CDX tumours from 10 – 20µl tail vein plasma and in clinical samples the assay is capable of distinguishing plasma from healthy volunteers and a range of cancer patients. The NAB group have also established single cell RNA profiling and will use this to identify biomarker signatures in prostate CTCs as part of the recently awarded Belfast/Manchester Prostate Cancer Centre of Excellence. In the coming years, the challenge of the NAB group will be to establish routine clinical use of this "molecular toolset" with the ultimate aim of cancer patient benefit.

Leukaemia Biology

Tim Somervaille

Dr Tim Somervaille heads the Leukaemia Biology Group, which investigates human haematological malignancies. He was recently promoted to Senior Group Leader, following a successful review of his accomplishments since 2007. Below, he describes the aims of his research.

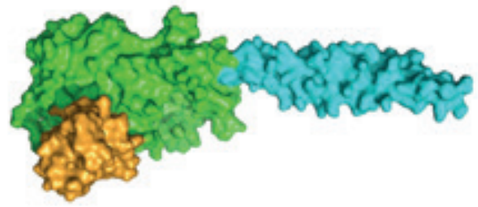
The focus of our laboratory's work is the identification of genes and cellular pathways critical for the function of myeloid leukaemia stem cells but not normal haematopoietic stem cells. Leukaemia stem cells are the cells which drive progression of leukaemia. They have to be eradicated in order to cure patients. An excellent example of the bench-to-bedside approach we take in the lab is our recent work on LSD1.

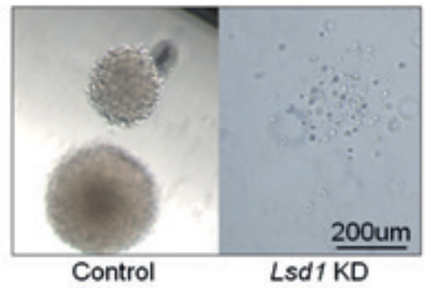
We first observed that expression of the gene coding for the lysine-specific histone demethylase LSD1 correlated with the frequency of leukaemia stem cells in bone marrow cell populations. Knockdown experiments confirmed that LSD1 was required to maintain both the proliferative potential and differentiation block of myeloid leukaemia stem cells, an observation which was of interest because the activity of LSD1 could potentially be targeted pharmacologically. In the first instance, we made use of tranylcypromine, which is a licensed anti-depressant and monoamine oxidase inhibitor which inhibits LSD1 with relatively low potency and specificity. The drug mimicked our knockdown findings, promoting loss of proliferation and induction of differentiation of myeloid leukaemia cells. However, in view of its deficiencies in terms of selectivity and potency, tranylcypromine is unlikely to be of therapeutic value in myeloid cancers. To address this, in collaboration with

The Leukaemia Biology Group: Tim Somervaille, Dan Wiseman, Gary Spencer, Emma Williams, Xu Huang and Tim Somerville

the Drug Discovery Unit, we identified from the patent literature and synthesised a novel tranylcypromine-derivative with much greater potency and specificity versus LSD1. This induced differentiation of murine and human *MLL* translocated AML cells, including patient cells, at concentrations in the low nanomolar range. Confirmatory data were obtained from in vitro and in vivo experimental systems. Critically, the functional potential of both murine and human normal haematopoietic stem cells was spared by both knockdown and pharmacological inhibition of LSD1, indicating its selective requirement in leukaemia stem cells versus normal haematopoietic stem cells and providing evidence for a therapeutic window. These discoveries, which we published in *Cancer Cell* in 2012, have had additional impact because they have led to a key collaboration with Oryzon Genomics, the Spanish biotechnology company which filed the patents for the tranylcypromine-derivative molecule used in our study. Oryzon has an advanced lead compound (ORY1001) ready for early phase clinical trials and, as a result of our data, has now commenced a first-into-man first-in-class phase 1 study in patients with relapsed acute leukaemia, with The Christie NHS Foundation Trust as one of five international study sites.

Moving forward, we plan to continue our research into the epigenetics of leukaemia with a firm emphasis on patient benefit. We were delighted with the recent successful outcome of the lab's tenureship review process which gives us the opportunity to continue and expand our translational research programme. Unfortunately the lab has recently had to say farewell to valued members as they move on to new opportunities. William Harris (PhD – graduated 2012) is now at the University of Warwick Medical School; Brigit Greystoke (PhD – graduated 2013) is a Senior Clinical Fellow in Haematopathology in Newcastle; and Filippo Ciceri and James Lynch are commencing periods of postdoctoral research in industry at Oryzon Genomics in Barcelona and AstraZeneca in Alderley Park respectively. We will also shortly be losing Xu Huang to the University of Glasgow where he will be starting up his own laboratory. We wish them all the very best for the future. In their place, we look forward to welcoming new postdoctoral researchers Alba Maiques Diaz from the CNIO in Madrid and Gauri Deb from the Indian Institute of Technology in Guwahati.





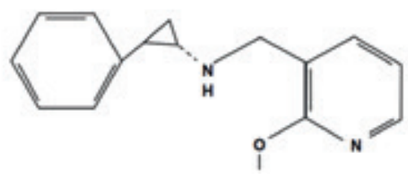


Figure: Therapeutic targeting of LSD1. (Top) Structure of LSD1 showing SWIRM domain (orange), amine oxidase domain (green) and tower domain (blue). LSD1 demethylates histone H3K4 and H3K9 Me1 & Me2, as well as non-histone targets such as TP53 and DNMT1. (Middle) Mouse leukaemia cells were infected with Lsd1 knockdown lentiviruses, or a non-targeting control vector. Image shows typical control AML colonies (containing predominantly myeloblasts) and Lsd1 KD colonies (containing predominantly terminally differentiated macrophages), enumerated after six days of culture. (Bottom) Structure of trans-N-((2-methoxypyridin-3-yl)methyl)-2-phenylcyclopropan-1-amine, termed Compound B in Harris et al., 2012, Cancer Cell.

Core Facilities Update

The past few months has seen some exciting developments in the Core Facilities, with the addition of several cutting-edge technology platforms and expansion of services. The latest additions are described below.

Facilities go to the Cloud

By Steve Bagley

Histology, Imaging and Cytometry, Biological Mass Spectrometry and Molecular Biology, will be moving to a cloud based calendar system, which will go live and replace the current system in July this year.

The new system has been designed with greater transparency to allow users to plan their work across the facilities more efficiently; group leaders will be able to assess usage statistics and costs, and staff in the facility will be able to organise resources more effectively.

The system, which is based on five secure commercial servers, will allow booking of equipment time and services on and off-site and will have greater emphasis on risk assessment of samples. Sample details will be electronically attached to a booking system (sample IDs and how they are to be processed) so that staff in the facilities have a more robust record.

The system has been tested on Linux, Mac, WinX, iOS and Android operating systems, and Chrome, Firefox, Opera and Safari browsers. The system is now live for registration and will be in use across the facilities in July.

Molecular Biology Moves to Lab on a Chip

By Chris Clark

Chris Clark from the Molecular Biology Core Facility

There is a pressing requirement within the laboratory to be able to provide high throughput of samples with reproducibility, sensitivity and importantly at a reduced cost. In response, the Molecular Biology Core Facility has put in place a BioMark and a C1 Single-Cell Auto Prep system (both Fluidigm) to facilitate these demands.

The BioMark system is a high-throughput qPCR instrument that uses microfluidic circuits for applications such as measuring gene expression, SNP genotyping, copy number variation, targeted re-sequencing and single cell genomic analysis.

The system utilises integrated micro-fluidic circuits known as dynamic and digital arrays, which permit parallel processing of multiple samples and many thousands of reactions per array plate; for example, it is possible to process 96 samples with 96 assays so that a staggering 9216 reactions are numerated. This high level of throughput permits "tried-and-true" techniques, such as TaqMan assays to be scaled up so to achieve a high fidelity of data in addition to the added advantage of cost and time savings.

With as little as 10 picograms of starting material, far more data is generated per sample compared to traditional molecular biology techniques and can describe not only the population but also the level of the single cell.

When considering a cell population, in addition to studying the whole, it is vital to be able to examine gene expression at the individual cell level, as within a population there is a large cell-to-cell variation both in a resting state and when exposed to stimuli. There is a necessity to statistically test the variation in a standard population and to examine the outliers; subsequently a method to handle, collect individual cells and isolate the strong stochastic element from gene expression is required. To enable researchers to achieve this aim, the laboratory has the C1 Single-Cell Auto Prep system in place, which allows the rapid isolation, processing, and profiling of individual cells for genomic analysis.

The system can be applied to a number of applications, including studies into cell differentiation, measurement of individual cell responses to stimuli, verification of disease biomarkers, validation of RNAi knockdowns and drug screens. With an optimised protocol, pre-formulated reagent kit, and disposable fluidics chips, we will be able to achieve the analysis of individual assays on single cells which, in the case of mRNA measurements, requires characterisation of femtograms of mRNA.

Garry Ashton

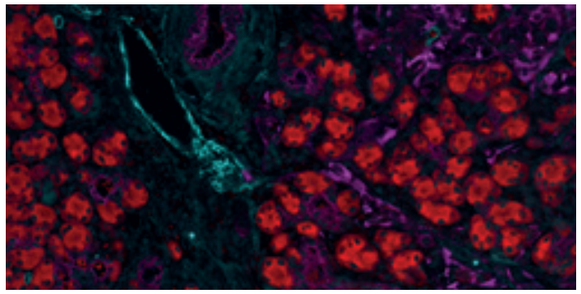
The Histology Facility -Development and Expansion

By Garry Ashton

The Histology core facility allows researchers to apply cutting-edge techniques to tissue-based experimental approaches, which are vital for both basic cancer biology as well as translational studies. As more groups are using our ever-growing repertoire of services, the unit is expanding in order to be able to provide new techniques, technologies and throughput. There are now four staff dedicated to providing these services with a further two staff who collect and process samples for the MCRC Biobank. The recruitment of another scientific officer is currently underway to provide greater throughput of samples.

The conversion of a dark room into lab space will allow the facility to house two additional immunohistochemistry (IHC) platforms. These new IHC platforms will ensure the unit is able to cope with current and future demand whilst also offering flexibility for developmental work. In addition, a new tissue processor, cryostat and a further cutting station will soon arrive.

Until recently, our ability to study protein-protein relationships in histological specimens and relate this to tissue heterogeneity has been limited. However, now with the availability of multispectral imaging and analysis capabilities (PerkinElmer Vectra) in the Imaging and Cytometry facility, we are currently developing complex multiplex immunohistochemistry. This will allow us to study the levels of expression of multiple proteins within the same tumour tissue and the interactions between proteins to aid our understanding of tumour heterogeneity.



A composite image of triplex immunofluorescent staining of orthotopic pancreatic cancer as a direct comparison to triplex colorimetric (front cover) showing acinar cells in red, alphaSMA positive myofibroblasts in green and cytokeratin positive epithelial cells in purple

The unit is currently evaluating in situ hybridisation assays (chromogenic and fluorescent) that enable visualisation and quantification of multiplex mRNA expression at the single-transcript/single-cell level, which will ultimately allow for quantitative gene expression to be determined within the context of the cells' morphology. There is also a greater demand on more downstream analysis on smaller clinical samples; consequently, we are continually looking at developing methods that require smaller but more homogeneous amounts of starting material.

Tissue microarray (TMA) construction as a service was introduced in anticipation of the expansion of tissue biomarker research on site. As this research has gathered pace, the number and complexity of TMAs constructed has increased. The service is now well established and embedded within the facility with TMAs from disease groups, including breast, melanoma, prostate (cores and chips), bladder, lymphoid, small cell and non-small cell lung cancer, having all been constructed. Working with the Imaging and Cytometry Facility, routines are being developed to put numbers to these cores to allow statistical analysis.

I look forward to the further development of the Histology Facility as we continue to play a part in the world class cancer research taking place at the Manchester Institute.

The Histology Team: Garry Ashton, Michelle Greenhalgh, Deepti Wilks, Caron Abbey, David Millard and Joanna Molenda.

Recent Awards and Events

Lung Cancer Centre of Excellence

Professor Richard Marais and Professor Chris Boshoff of the University College London (UCL) recently secured £5 million of funding to establish a joint CRUK Lung Cancer Centre of Excellence between the University of Manchester and UCL. This exciting partnership will play a key role in strengthening and coordinating lung cancer research across the UK. This new status represents a significant achievement for Manchester that will provide the infrastructure for new groups to accelerate vital work on this disease.

The Manchester-UCL Lung Cancer Centre of Excellence will combine the unique and complementary strengths of both sites in discovery, translational and clinical research to enable basic research into lung cancer to flourish and to develop state-of-the-art technology. Improved understanding of the biology, genetics and adaptation of lung tumours is essential to the development of therapeutic intervention. A key research strategy is reverse translation, relaying valuable clinical trial data and unexpected patient responses back into the laboratory to stimulate new hypotheses that may help refine the next clinical experiment. The ultimate objective is to detect lung cancer earlier and better define the risk of recurrence post-surgery. It is anticipated that patients will be monitored with minimally invasive biomarkers and re-emergent disease will be controlled through personalised therapy.

Movember Centre of Excellence

On 13 February 2014, we launched the Movember Centre of Excellence in partnership with Prostate Cancer UK, a pioneering joint enterprise between CRUK MI and Queen's University Belfast (the Belfast-Manchester Centre of Excellence), working alongside the other Centre of Excellence in London.

Professor Richard Marais and Professor David Waugh of Queen's University Belfast are the joint Scientific Directors of the Belfast-Manchester Centre of Excellence, supported by the Clinical Lead, Professor Noel Clarke of the Christie NHS Foundation Trust, together with several world-renowned co-applicants and collaborators. Prostate Cancer UK awarded £5 million to the Belfast-Manchester Centre of Excellence over a period of five years, which will be used to develop a personalised medicine platform to optimise DNA-damaging therapies for localised and metastatic prostate cancer. The program aims to identify patients with high-risk early disease to prevent recurrence, improve the delivery of radiotherapy to the prostate, and target chemotherapy to those patients most likely to benefit. The collaboration of leading prostate cancer scientists and clinicians will combine a broad range of expertise that will benefit the lives of men with prostate cancer.

Griem Award for Richard Marais

Institute Director Richard Marais has been awarded the Griem Lectureship in Molecular and Cellular Oncology from the University of Chicago Medicine Comprehensive Cancer Center. Richard was invited to Chicago recently to receive the award from the family of two Chicago physicians, Dr. Melvin L. and Dr. Sylvia F. Griem, after whom the award is named. He spent the day at the University of Chicago campus meeting students and faculty members as well as giving a presentation on his research into the molecular mechanisms underpinning melanoma.

Richard Marais receiving the Griem Award from Michelle M. Le Beau, Arthur and Marian Edelstein Professor of Medicine and Director of the University of Chicago Medicine Comprehensive Cancer Center.

Post-Doc Committee

Amit Mandal, Franziska Baenke and Andrew Porter.

Hello! We have recently formed a new Post-Doc committee, with the aims of increasing networking opportunities, helping new starters feel welcomed and become quickly settled, and for providing opportunities for training and career development.

Over the last few years, James Lynch, who many of you know, has largely been responsible for coordinating social events for post-docs, but as we knew he was planning to leave we saw a gap developing. We've therefore formed a committee around five post-docs, to be a working committee for this first year. Our other objective is to establish the role and activities of the committee over the coming year, find out what it can and can't do, make it more visible, and then open up positions again for new applications in the new year, hopefully with more awareness of the opportunities it presents.

The committee for this year is:
Chair - Andrew Porter (Cell Signalling)
Welcome - Jila Ajeian (Cancer Biology)
Social - Franziska Baenke (Molecular Oncology)
Liaison - Amit Mandal (Molecular Oncology)
Training - Zoi Diamantopoulou (Cell Signalling)

We see real potential in getting to know each other better – for sharing ideas and initiating collaborations across different labs and all the different sets of experience people have in the building; for future planning – people have come here from all around the world, so there's a wealth of knowledge of labs, institutes and cities to be tapped into; and for building friendships and a support network, especially for those who are far away from friends and family. I'm sure many of us feel we'd like to know each other better, so a lot of this is just about providing a space to do that without feeling awkward about how many times you've seen someone at talks, but never spoken to them!

We will continue to help run the P3 meetings, along with the student representatives, and hopefully as the year goes on will be organising more social and training events, so keep an eye out for these. We have lots of plans, but this is very much a work in progress, so we'd certainly appreciate any ideas, feedback or suggestions, as well as patience if we get things wrong. We look forward to hearing from you on our shiny new email address - postdocscommittee@cruk.manchester.ac.uk.

2013 Dexter Award Winner

Eva receiving her award from Richard Marais.

We are delighted to announce that PhD student Eva Barkauskaite, formerly of the DNA Damage Response group, has been selected as the winner of the Cancer Research UK Manchester Institute Dexter Award for Young Scientists for 2013.This honour is in recognition of her outstanding contribution to research and her dedication to public engagement with science. She has achieved academic success for her structural and mechanistic work on poly(ADP-ribose) glycohydrolase, which has culminated in an impressive set of publications in just over three years. In addition, Eva has received a number of prizes and scholarships from external bodies, including an award for the best presentation at the International Student Cancer Conference in 2013.The Dexter Award is a well-deserved honour for Eva and we wish her all the best in her career, which she is commencing as a post-doctoral fellow at the University of Oxford.

Award for Kate Hogan

Kate Hogan, a PhD student in Molecular Oncology, has been awarded a 'Gold Level Sponsorship' by Primerdesign Ltd. Kate is one of 20 research students from across the UK to receive the sponsorship under which she will receive over £3000 worth of qPCR kits and training.

It is an award from which the Institute will benefit as a whole, as Primerdesign will present an expert seminar on Real-time PCR to help further the level of real-time PCR expertise within the Institute.

Kate's project was chosen because of the elegant, ground breaking questions that she hopes to answer through her research which focuses on investigating the molecular mechanisms that drive melanomagenesis.

Richard Marais, Institute Director and Head of the Molecular Oncology Group said "I am delighted that Kate has been selected for this sponsorship. Her project will investigate gene-gene and gene-environment factors in the induction of melanoma. This is an exciting project and this sponsorship will go a long way to enabling her to reach her aims. We are grateful to Primerdesign for awarding this sponsorship to Kate."

Staff News

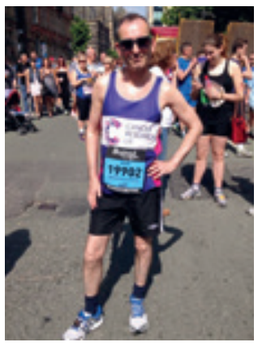
Fond Farewells

David Broadbent (centre) with Jolyon Hendry and Catharine West who both worked with David during his time at the Institute.

In January we said goodbye to David Broadbent, a stalwart of our Institute for forty years, renowned for many years of service in several labs and facilities around the Institute. At his retirement party, Institute staff came to wish him well and David was thrilled to receive some vintage port and LNER pocket watch and whistle set. We wish him all the best on his retirement.

The Institute also bid a fond farewell to Fran Hockin, an integral member of the Laboratory Services team who retired in March after 27 years at the Institute. Fran celebrated her retirement with members of Lab Services and the Institute, and received a bottle of champagne to toast her many dedicated years. We wish her a wonderful retirement.

Also retiring after eight years as Head of the Logistics team is Maurice Cowell. Maurice did a fantastic job of helping to keep the Institute running smoothly and we wish him all the best as he looks forward to spending more time with his grandchildren and improving his golf handicap.



Manchester 10K with David Jenkins

For the 4th year running, David Jenkins, CRUK Manchester Institute's Purchasing Officer, has taken part in the Great Manchester Run to raise vital funds for Cancer Research UK.

The annual 10k run brings thousands of people to the streets on Manchester City Centre. This year more than 30,000 people ran and many more volunteered and came to cheer on the runners. It is a day of fun and enjoyment for all with music and lots of activities to keep everyone entertained.

This year the sun turned up too and as temperatures reached 22 degrees the organisers set up run-through showers to cool people down. The heat made it a tough challenge but David completed this year's run in 1 hour, 6 minutes and 40 seconds, a time David is very proud of.

David has already raised a tremendous £705 for CRUK but he is holding one more raffle before the summer with lots more prizes. David says "I'm not super fit and I don't do it for the love of running - truth be told I hate running! I do it for the fundraising, which I really enjoy and for the actual day, which is great fun! The running is just an extra bonus which forces me to keep fit".

Well done to David and all of the Institute's runners.

Race For Life

Danielle Potter and Melanie Galvin from the Clinical and Experimental Pharmacology group are running CRUK's Race for Life in Stockport this summer. They held a cake sale and raffle at the Institute to support their fundraising efforts and raised a very impressive £304.

Welcome to the World

Moses

Adam Freestone and his wife started 2014 by celebrating the birth of their baby boy. 'Moses Jon David Freestone' was born at on January 12th and weighed 9lb.

Sofia and parents on a boat trip across Windermere Lake

Bruno Simoes and his wife Asun, received the "best Christmas gift ever last December" when Sofia was born on the 7th of December.

Countdown to completion for the Manchester Cancer Research Centre building

Approaching the final phase of construction, work is continuing on the new Manchester Cancer Research Centre (MCRC) building, which will mark a new phase for cancer research in Manchester.

The MCRC brings together world-class research into cancer biology, drug discovery and clinical trials on one site and is one of Europe's biggest comprehensive cancer research centres. The new MCRC building will be home to 250 staff, including 150 University scientists whose research will focus on understanding how cancer starts, develops and progresses. "Developing new tests and treatments for cancer patients that ultimately improve patient survival requires a detailed understanding of the multitude of factors that drive cancer development. Studies in the new MCRC building will be focussed on gaining key insights into the essential processes and molecules that represent potential targets for new anticancer therapies," said Professor Nic Jones, MCRC Director. With scientists and doctors working together on one site, the MCRC will speed up the translation of lab discoveries into new strategies and interventions for cancer patients.

MCRC researchers will be working alongside around 100 of The Christie's clinical academics and Research and Development staff, who will be located on the top floor of the building. Overall the new building provides over 6,000m^2 for the expansion of research activity, which has been designed to promote interaction between the different research groups with sharing of common resources and equipment.

Following planning approval in March 2012, enabling works began on site in May 2012. In November 2012, the start of construction was marked with a special breaking the ground event. By March 2013, foundations had been excavated, reinforcement steel and concrete placed in the building foundations and work on structural walls had begun. During summer 2013, structural steelwork was being installed and in November 2013 a Topping Out ceremony was held to mark the completion of the highest point of the building. The building was made weather-tight in January 2014, enabling internal works to progress.

As the development enters its final phase, the focus continues on completing the specialist installations within the new state-of-the-art facility. Currently, the internal fit out - electrical cables, pipework, ceilings, doors and flooring - is in progress and work on the external landscaping will begin soon.

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
Winter 2014	Building completed and ready for use

In the spotlight with Emma Newsham

Emma is the recently appointed Scientific Officer in Claus Jorgensen's new Systems Oncology group at CRUK MI. She has enjoyed an interesting and diverse career path before her arrival here, mostly by way of (in her own words) "the farmyard"! Emma's background is in bioveterinary science, where she researched a variety of projects from feline viruses, horse tapeworms, to vaccination effects in broiler chickens. A short stint in an animal health company allowed her to investigate forage analysis of ruminants and to develop toothpaste for our beloved cats and dogs. Emma is now looking forward to returning to systems biology and adding two legged (non-scaly) animals to her research portfolio.

1. **What is your favourite part of the UK?**
   As a Cumbrian I feel obliged to say the Lake District but in all honesty it is probably the highlands of Scotland. Stunning scenery, best enjoyed with a single malt in hand.

2. **What was your best ever holiday and why?**
   I'm hoping this is still to come – me and my other half are planning for our honeymoon to coincide with the England test tour of the West Indies. I am also hoping that this will coincide with an upturn in performance!

3. **Which website do you always check, and why?**
   BBC sport to check out the football gossip. One day Everton will be linked with Messi, I'm sure of it!

4. **What is your favourite film?**
   Star wars

5. **What is your favourite band/singer?**
   Foo fighters - I love Dave Grohl.

6. **If you had to change careers tomorrow, what would you do?**
   Dog trainer. I haven't got time for a dog at the moment so this would let me play with other people's dogs and get paid for it!

7. **What is the most important lesson that you have learnt from life?**
   Trust your gut instinct

8. **Name three things you would take with you to a desert island?**
   Kindle, ipod and a good supply of ice-cold cider!

9. **What is your greatest fear?**
   Spiders, always spiders!

10. **How would you like to be remembered?**
    As a happy, easy-going person who always tried to make time for everyone.

11. **If you could change one thing in your past what would it be?**
    I would like to be fluent in another language and if I could go back I would keep up with Spanish lessons once I left school.

12. **What is your signature dish to cook?**
    Spanish rice. It is essentially chicken and chorizo paella but our version is a bit anglicised so we always call it Spanish rice!

13. **You've just won the lottery and have £5 million pounds to spend. What do you buy first?**
    A dog.....then a house with a garden big enough to keep the dog in!

14. **What is your idea of perfect happiness?**
    Spending plenty of time in the company of those I care about most.

15. **What keeps you awake at night?**
    Nothing – I love sleeping!

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