

Newsletter



CANCER
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MANCHESTER
INSTITUTE

Winter 2016

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The University of Manchester

Director's Introduction



This summer we said goodbye to two of our Group Leaders. John Brognard has returned to the US to set up a lab at the National Cancer Institute in Maryland while Valerie Kouskoff is continuing her research at the Division of Musculoskeletal and Dermatological Sciences at The University of Manchester. I would like to thank both them, and their research teams, for their hard work and contributions to the Institute over the last few years and wish them all every success in the future.

In July, I chaired the biannual meeting of the European Association for Cancer Research in Manchester. It was a pleasure to welcome the world's cancer research community to our city and I hope that those of you that participated found the meeting enjoyable. Another opportunity to bring the cancer research community together is provided by the National Cancer Research Institute (NCRI) meeting in Liverpool in November, which was chaired, this year, by Caroline Dive. I would like to congratulate Caroline and her colleagues for putting together a fantastic programme that resulted in a stimulating and exciting meeting. It was pleasing that there was so much involvement from our researchers, in particular with an excellent plenary presentation from Iain Hagan and a *Women in Science* workshop that was organised and chaired by Caroline.

Keeping with this theme, Caroline is also chairing our Athena Swan self-assessment team together with Caroline Wilkinson. I'd like to thank everyone on the team for their efforts in this important process and would urge you all to take part in the upcoming survey that the team is preparing. It is important that we capture everyone's views about working at the Institute and we want to hear your thoughts on our culture and policies. We look forward to using the Athena Swan process to reflect on our practices and to make changes and develop initiatives where possible. We have a strong record on gender equality across the Institute so we shall use this process to ensure that we continue to create an environment that not only supports women in science, but which is also welcoming and nurturing for all.

It is always exciting and immensely rewarding to follow the development of our young scientists and to witness the progress that they are making. Two former post-doctoral fellows at the

Institute are now beginning their independent scientific careers. Romina Girotti has moved back to Argentina while Amaya Viros is remaining at CRUK MI but with a Wellcome Trust-funded Intermediate Clinical Fellowship to establish her own group. Anna Marusiak, a former post-doc has her own fellowship back in Poland while Elvan Boke, a former PhD student, is starting her own group in Barcelona after a successful post-doc fellowship at Harvard University.

At this time of the year, our new PhD students arrive and get established and this year we are pleased to welcome 14 students representing six different countries. The international nature of our Institute is a key factor in our success and creates a diverse and enjoyable working environment. It is important that we create a welcoming atmosphere for new students and staff and a vital component in this regard is our STAy group that provides a forum for students, post-doctoral fellows and scientific officers. The group is going from strength to strength in organising a wide range of imaginative social and scientific events and I would like to congratulate and thank the organising committee for their efforts in co-ordinating and driving this activity.

Another initiative that is providing valuable support to young scientists is the Institute's Grants Committee, chaired by Iain Hagan. This has helped our post-doctoral fellows with their fellowship and career development award applications and interview preparations. The committee is also helping more established scientists to develop the strongest possible funding proposals and so I would like to thank everyone involved in this process.

Richard Marais
Director

Dates for your diary

 **Research café series**
Keep a look out for these regular, informal talks in the MCRC Building café aimed at a general audience. Upcoming dates are, 15th December, 26th January, 16th March and 27th April

 **4th February 2017**
World Cancer Day
Help us celebrate our international #DayToUnite against cancer

Cover Image: Caroline Dive, opening the NCRI 2016 meeting in Liverpool in her capacity as chair of the scientific committee



Fundraising and Engagement activities

By Sive Finlay

Communicating our research

We've had a packed couple of months of public engagement events, bringing our research to new audiences and thanking our fundraisers for their fantastic support. Here are some of the highlights.

In May, we celebrated International Clinical Trials Week with our *Platform for Investigation* day at the Museum of Science and Industry. This was our first solo event at the museum, taking over the ground floor with a range of hands on activities that attracted just over 800 visitors. Highlights included our new animal research engagement activities led by the Biological Resources Unit, clinical trials activities with the Christie NHS Foundation Trust research nurses

and a hands on guide to the steps involved in radiotherapy treatment led by Professor Marcel Van Herk. Putting this event together required a real team effort - huge thanks to all of our brilliant volunteers!



Pi at MoSI: Some of our researchers showing off our circulating tumour cells activity at Platform for Investigation.

Fabric of Research Exhibition

Our main event for the European City of Science Festival was the week-long Fabric of Research Exhibition at Manchester Craft and Design Centre.

The exhibition brought our work to life like never before as textile designers from The University of Manchester and Manchester Metropolitan University worked with researchers and patients to create unique artworks that showcase our latest research and

tell the personal stories of people affected by cancer. Particular thanks go to Steve Bagley, Head of Imaging and Cytometry, for providing a wealth of images and expertise and to everyone who helped bring this project to life.

Images left to right: Designer Jayne Mechan used quotes from patients to inspire her work; Sonja Andrew's scarf designs inspired by research images and techniques; A signature scarf from our researchers representing our united efforts to beat cancer





Images left to right: Lucky prize winners in the tumbola; Playing "Your Choice" at Manchester Science Festival to learn about cancer research; Some of our drug discovery researchers standing up to cancer

Stand Up to Cancer

In October, our Stand Up to Cancer fundraising fete at the MCRC Building offered plenty of tasty treats and unusual prizes, linking in with the national campaign that raised a record amount of over £16 million to fund translational research.

We rounded off the month with our Manchester Science Festival events including Your Choice (an interactive board game about the challenges of research) and our "Cell Explorers" stand at The University of Manchester's Science Spectacular.



Our inaugural pumpkin carving competition in aid of Stand Up to Cancer

European City of Science Festival

The European City of Science Festival in July celebrated Manchester's year as Europe's science capital, the first time the title has been awarded to a UK city.

We had a busy week of activities which included a *Science Lates* evening at Manchester Museum, Anne Largeot leading a team of researchers taking part in activities for the European Commission's "Science is a revolution" fair at the Museum of Science and Industry and Marina Parry and Alba Maiques-Diaz taking to their soapboxes in Piccadilly Gardens to speak about their research.



Images left to right: Alba Maiques-Diaz takes to the soapbox in Piccadilly Gardens; Our activity stand at Manchester Museum Lates

Staff fundraising



Well done to Clare Staplehurst (BRU) who led an intrepid team of climbers who conquered Snowdonia on a wet July Sunday, raising £1,325 for CRUK.

Congratulations to the Drug Discovery team who took on the Bear Grylls survival race at Tatton Park to raise a fantastic £1,780 for Stand Up to Cancer.



Well done to our Relay for Life Stockport team for braving a wet July weekend in support of CRUK. Led by Steve Lyons, Julia Draper and Ben Hodgson, the team held fundraising events throughout the year, including the ever popular plant sale, and even brought our virtual reality lab tour along to the event to give supporters an insiders' view of our research. Stockport Relay had one of its most successful years yet, the Institute team raised a fantastic £2,757.86 to contribute to the impressive event total of £84,617, all of which will go directly to funding work at CRUK MI.



Images top to bottom: Clare Staplehurst and her intrepid team of Snowdonia climbers; Our Drug Discovery team proudly displaying their Bear Grylls survival race medals; Steve Lyons and Ben Hodgson using their green fingers to raise money for Stockport Relay

European Research Night

In September, we took part in lightning talks and science speed dating sessions at Manchester Museum's European Research Night showcase, a fun evening filled with hands on activities where our virtual reality lab tour proved to be a hit.



A visitor enjoying our virtual reality lab tour at European Research Night

Open Day

Our Open Day in June marked both 10 years of the Manchester Cancer Research Centre (MCRC) partnership and one year since the MCRC Building was officially opened.

We had talks and tours for invited CRUK supporters and members of the public, many of whom were local residents who had watched the building being constructed but this was their first chance to see inside the labs. It was a busy day with over 120 people joining us for fundraising and research talks, lab tours and hands on activities. Thanks to Café Vivo for opening especially to keep everyone fed and watered and a big thank you to everyone who volunteered to help out on the day.

Images left to right: Our "genetic taste test" volunteers at Open Day; One of our Open Day displays explaining how clinical trials operate and how we use mice in our pre-clinical research.



Featured Publications

Wonder material graphene could aid blood cell growth

Institute scientists have shown that a form of graphene can be used to boost the growth of blood cells in the lab.

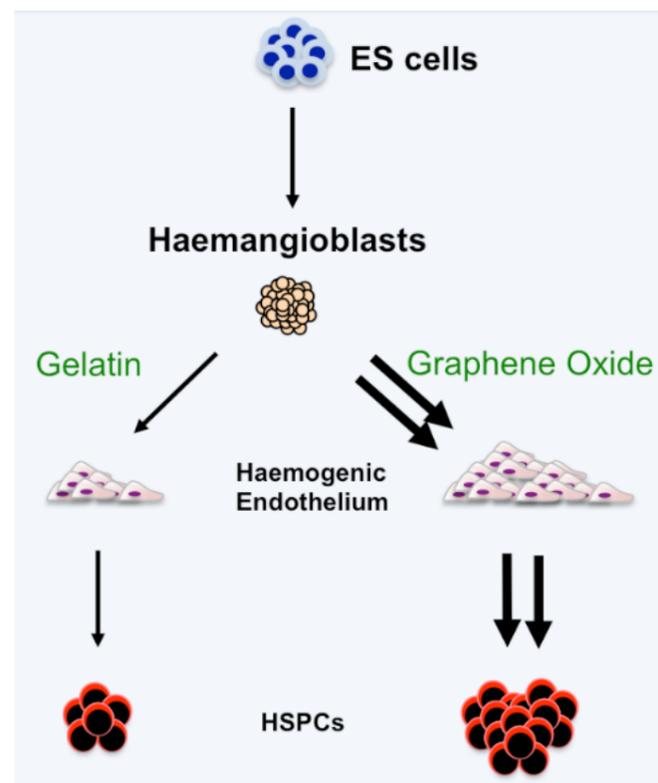
The team used graphene oxide (GO), a variant of graphene laced with oxygen, to enhance the creation of haematopoietic progenitor cells – the precursors of all other blood cells – offering a potentially improved source for transfusions to treat patients with cancer.

Graphene is a single two-dimensional layer of carbon atoms and is one of the strongest, lightest materials in the world. First isolated in Manchester in 2004, there is now great interest in using its properties in a vast range of products, processes and industries.

In this latest study, researchers from the Stem Cell Biology group have collaborated with the National Graphene Institute to investigate whether graphene oxide can increase production of early blood cells.

The group compared graphene oxide with gelatin as a base for conversion of cells known as haemangioblasts into blood cell precursors. They found that the graphene oxide promoted greater differentiation of the cells, leading to production of more haematopoietic cells.

Garcia-Alegria E, Iluit M, Stefanska M, Silva C, Heeg S, Kimber SJ, Kouskoff V, Lacaud G, Vijayaraghavan A, Batta K. (2016) Graphene Oxide promotes embryonic stem cell differentiation to haematopoietic lineage. *Nature Scientific Reports* 20;6:25917.



Graphene induces the transition of haemangioblast to haemogenic endothelium thereby promoting the generation of haematopoietic stem cells (HSPCs).

Exploring how a lack of oxygen gives cancer the evolutionary advantage

The RNA Biology group has shown how hypoxia – a lack of oxygen – in cancer cells can shift protein-coding genes into becoming non-coding ‘dark matter’. Their findings could explain how the DNA damage response is regulated, allowing cancer to gain an advantage.

Much of our DNA does not code for proteins – the large biomolecules that control many of our body’s basic functions at a cellular level. Even within protein-coding sections of the genome, scientists have revealed through analysis of the patterns encoded in the DNA sequence that a large amount appears to not be protein-coding.

Our scientists looked at colorectal cancer cells over time as they grew in a reduced oxygen environment. They combined this with a fresh analysis of existing sample databases.

The team found that under hypoxia, many genes across the genome switched from a coding to a non-coding form. A significant number of these genes play a role in the DNA damage response pathway.

Such changes could be responsible for allowing elevated rates of genetic mutation – giving cancer cells the ability to evolve and gain an advantage.

Memon D, Dawson K, Smowton CSF, Xing W, Dive C, Miller CJ. (2016) Hypoxia-driven splicing into noncoding isoforms regulates the DNA damage response. *npj Genomic Medicine* 1, Article number: 16020

Cutting-edge model reveals potential of two-pronged attack for lung cancer

Researchers from the Clinical and Experimental Pharmacology group have shown that a new drug combination can halt the growth of lung tumours in the lab. They hope that this two-pronged approach can in future improve survival for patients with lung cancer.

Currently, less than 5% of patients diagnosed with small cell lung cancer (SCLC) survive for more than five years. The best treatment option is still chemotherapy, but the majority see their disease relapse and progress within 18 months.

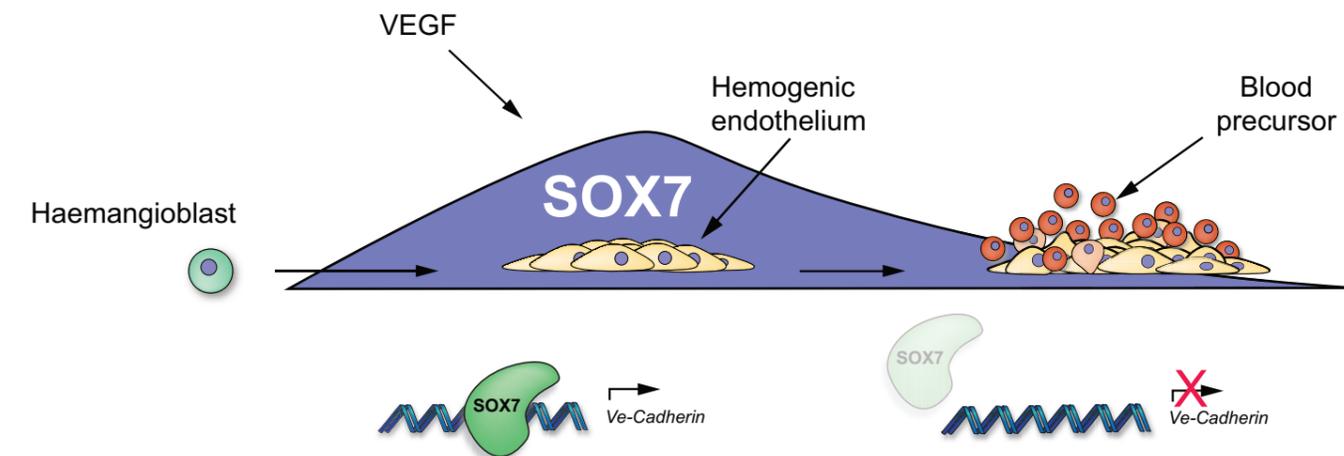
By themselves, modern drugs that target specific genetic mutations have proven ineffective at changing the outcome

SOX7 gene keeps leukaemia going

Institute scientists, working with others at The University of Manchester, have explored the role of the SOX7 gene in a subtype of acute lymphoblastic leukaemia.

B cell precursor acute lymphoblastic leukaemia (BCP-ALL) is the most frequent type of cancer in children. The disease also affects adults and is much harder to treat in older patients - the intensive chemotherapy can lead to serious complications.

The SOX family of genes plays a variety of roles in human development. SOX7 in particular is involved in the growth of blood cells, and is also suppressed in various cancer types.



A model for the action of Sox7 during haematopoietic development.

for lung cancer patients. Now a new lab technique has allowed researchers to test potential treatment combinations in a clinically relevant model.

The group used their previously developed circulating tumour cell derived explants (CDX) mouse models to test two potential therapies in combination. In this study, the CDX model was created using a sample from a SCLC patient whose disease had progressed following treatment.

One of the pair of drugs tested was designed to target BCL-2, which controls cell death, while the other blocked the activity of PI3K/mTOR – a cell survival signalling pathway. The team found that together the two drugs were well tolerated by the mice.

More importantly, the treatment combination blocked tumour growth much more effectively than either drug by itself.

Potter DS, Galvin M, Brown S, Lallo A, Hodgkinson CL, Blackhall F, Morrow CJ, Dive C. (2016) Inhibition of PI3K/BMX Cell Survival Pathway Sensitizes to BH3 Mimetics in SCLC. *Mol Cancer Ther* 15(6):1248-60.

In this latest research, the team from Manchester has found that SOX7 is frequently expressed in BCP-ALL, but not in other types of blood cancer or in healthy blood cells. They also show that reducing the amount of SOX7 in leukaemic cells led to lower levels of growth and a delay in the onset of leukaemia.

SOX7 and its pathway could therefore offer new targets for the treatment of this type of leukaemia.

Cuvertino S, Filiciotto G, Masurekar A, Saha V, Lacaud G, Kouskoff V. (2016) *Oncotarget*. SOX7 promotes the maintenance and proliferation of B cell precursor acute lymphoblastic cells. doi: 10.18632/oncotarget.10472.

Pseudo-blood vessels linked to poor survival in lung cancer

The Clinical and Experimental Pharmacology group has worked with scientists in the US to explore vasculogenic mimicry (VM) – where tumour cells form themselves into blood vessels – in small cell lung cancer (SCLC).

They looked at circulating tumour cells (CTCs) taken from patient blood samples and assessed them for VE-Cadherin, a molecule responsible for maintaining newly-formed blood vessels.

VM is associated with more aggressive disease, and poor outcome, in several different tumour types – possibly because it aids the spread of cancer cells around the body. The researchers aimed to see if VM behaviour could be detected in CTCs, and how VM affects response to chemotherapy.

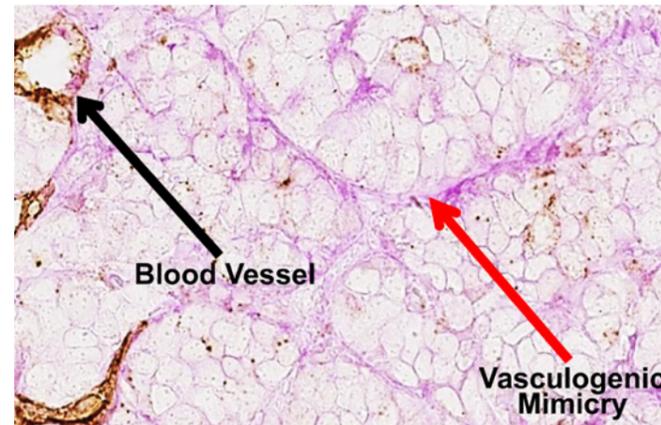
The team found that a subset of CTCs were positive for VE-Cadherin. When they then explored SCLC patient tumour samples, they found that high levels of VM linked with poor survival.

Interestingly, when the group compared tumours with lots of or little VM, they saw that delivery of chemotherapy drugs was improved with greater VM, but that the subsequent response to

treatment was reduced. Future research could develop ways of targeting VM to improve the effectiveness of chemotherapy.

Liquid biopsies and the analysis of circulating tumour cells offer a non-invasive way to assess VM in individual cancer patients – allowing doctors to better predict outcome.

Williamson, SC, Metcalf RL, Trapani F, Mohan S, Antonello J, Abbott B, Leong HS, Chester CP, Simms N, Polanski R, Nonaka D, Priest L, Fusi A, Carlsson F, Carlsson A, Hendrix MJ, Seftor RE, Seftor EA, Rothwell DG, Hughes A, Hicks J, Miller C, Kuhn P, Brady G, Simpson KL, Blackhall FH, Dive C. (2016) Vasculogenic mimicry in small cell lung cancer. *Nat Commun.* Nov 9;7:13322. doi: 10.1038/ncomms13322.



Vasculogenic mimicry in SCLC CTC-derived explant tumours. The black arrow indicates an endothelial channel versus the VM network indicated by a red arrow.

Liquid biopsy reveals 'Jekyll and Hyde' nature of rare melanoma

Using blood analysis to probe the genetics of a case of mucosal melanoma, the Molecular Oncology group has shown that it has a split identity.

The study demonstrates how doctors could in future monitor tumour evolution without needing to take invasive biopsy samples.

Mucosal melanoma is a rare form of the disease, accounting for around 1% of cases. As with all cases of melanoma, it occurs when melanocytes – the body's pigment producing cells – turn cancerous, but involves only those within mucosal surfaces such as those that line the sinuses, nasal passages and oral cavity.

The genetics of this type of melanoma are typically different to other forms of melanoma. As a result, the treatment options are also different for these patients. Approximately 40% of mucosal melanoma cases harbour changes in the KIT gene, and drugs exist which target KIT mutations.

The group followed the response of a KIT-mutant patient to a series of different treatments: imatinib 'smart drug' therapy that specifically targets KIT mutations, immunotherapy and two types of chemotherapy. To explore the underlying genetic identity of the remaining cancer, they looked at blood samples, and measured levels of tumour DNA containing the mutation in KIT.

Meanwhile, doctors tracked the size of the patient's various secondary tumours in the liver and lymph nodes. Their scan results showed that there was a mixed response to the various therapies.

When the research team probed the blood analysis, they found that there were in fact two separate genetic identities – one lacking a KIT mutation. By tracking the two identities, they saw that they both responded to chemotherapy but had a mixed response to both targeted therapy and immunotherapy. As one subclone relapsed, the group were able to spot this before it showed up on a scan.

Gremel G, Lee RJ, Girotti MR, Mandal AK, Valpione S, Garner G, Ayub M, Wood S, Rothwell DG, Fusi A, Wallace A, Brady G, Dive C, Dhomen N, Lorigan P, Marais R. (2016) Distinct subclonal tumour responses to therapy revealed by circulating cell-free DNA. *Annals of Oncology.* 27(10):1959-65.

Welcome to the Skin Cancer and Ageing group



The Skin Cancer and Ageing group: Amaya Virós, Matthew Winder and Katharina Röck

The CRUK Manchester Institute welcomed a new research team in September, the Skin Cancer and Ageing group, led by Amaya Virós.

Amaya was awarded the prestigious Wellcome Trust Intermediate Clinical Fellowship, which has allowed her to establish her own group to research why older patients are less likely to survive following a melanoma diagnosis. She also won the Wellcome-Beit Prize, which consists of a monetary reward of £25,000 given by the Wellcome Trust to their best intermediate fellows, to use in their ongoing research.

More than 80% of melanoma deaths occur in patients who are older than 50 years of age, and mortality is specifically increasing in the elderly. Older patients are more likely to

suffer from multiple melanocytic and non-melanocytic skin cancers.

Melanomas, in the elderly, more frequently present as aggressive primary lesions, thick primary tumours that predominantly comprise the high-risk primary melanoma stages (Stage IIB-IIC). The overall survival for Stage IIB-IIC patients of all ages at 5 years is 60% and 45%, respectively, despite being localised to the skin and non-metastatic at diagnosis. There is a gradual decline in 5-year survival with increasing decades of life, with an almost 20% decrease from ages 60 to 69, to ages greater than 80 years. Additional characteristics of poor prognosis, such as ulceration and elevated mitotic rate, are also more common in the elderly. However, even after taking the main prognostic factors into account, there is a survival discrepancy between elderly and young patients, and age is the strongest independent adverse prognostic factor together with tumour thickness.

Understanding the mechanisms that drive poor outcome in the elderly represents a critical current problem in melanoma care. The Skin Cancer and Ageing group focuses their research on understanding the changes in aged skin that promote melanoma and the biology of aggressive disease affecting the elderly, in order to identify new strategies of adjuvant therapy.

The group includes Matthew Winder, who is in his first year as a PhD student (read more about him in Education News) and Katharina Röck, a postdoctoral scientist who joined the laboratory in November. Previously, Katharina was working as a junior group leader at the University of Düsseldorf, in the department of Pharmacology and Clinical Pharmacology, and as a visiting postdoctoral fellow at the University of Hamburg, in the department of Tumor Biology.

LEO Pharma Research Foundation Award



Amaya and Thomas Wiesner with their awards in Munich.

Further success for Amaya Virós has come via an award for making exceptional advances within dermatology research presented by the LEO Pharma Research Foundation.

Each year, the foundation presents two awards to promising and talented scientists and this year

the Danish Krone 1 million Gold Award goes to Dr Virós for her important contributions to the area of skin research by describing mechanisms behind the development of squamous cell carcinoma and melanoma. The Silver Award was presented to another talented dermatologist, Dr Thomas Wiesner of the Medical University of Graz, Austria.

"We are proud to present two talented scientists with this year's LEO Pharma Research Foundation Awards. Both scientists have advanced our understanding of skin diseases and made valuable contributions to the scientific community. Their outstanding research has the potential to pave the way for new and improved treatment for the millions of people worldwide suffering from skin cancer," says Thorsten Thormann, Chairman of the LEO Pharma Research Foundation Award Committee. The award ceremony took place in Munich at the European Society for Dermatological Research's annual meeting.

Education News

Meet the new students



Sophie Adlard

Hi, I'm Sophie and I'm originally from Hull. I completed my undergraduate degree at The University of Manchester, where I studied Biochemistry.

As part of my degree, I had the opportunity to complete a placement year within the Oncology group at AstraZeneca. My project there involved knocking-down components in well characterised oncogenic pathways, and comparing the effects of this knock-down in 2D and 3D cell culture. Through this, I became interested in how dysregulation of signalling pathways can result in cancer, and so I was really excited to be offered a PhD in the Cell Signalling group. My PhD project covers both my interests in signalling pathways and in cancer; I will be looking at the role of Tiam homologues and Rac GEFs, in invasion and migration of small cell lung cancer cells. I really enjoyed living in Manchester for my undergrad as it is a vibrant city and is also close to the Peak District, where I enjoy hiking. I am looking forward to spending my next four years here, and I'm lucky that I can carry out my work at a Lung Cancer Centre of Excellence in a city that I love!



Tristan Henser-Brownhill

Hi, I'm Tristan and I am starting my PhD in the Prostate Oncobiology group. My project will focus on the identification and characterisation of cancer cell subpopulations that show an increased capacity to resist conventional treatments such as chemotherapy and hormone-deprivation.

Through genome-wide comparative epigenomic and transcriptomic approaches we hope to identify new therapeutic targets and clinically relevant biomarkers. I received my undergraduate and master's training from the University of York, where I developed a fascination with epigenomics and advanced imaging technology. During my Master's year I undertook a research placement in the Cancer Epigenetics lab at the CRUK London Research Institute (LRI), now part of the Francis Crick Institute. There, I utilised multiparametric imaging flow cytometry (IFC) to study the role of rare linker-histone variant H1.0 in tumour maintenance and excitingly the findings were included in a recent publication in *Science*. I returned to the Cancer Epigenetics lab as a Scientific Officer, where I designed, constructed, and

validated a focused, arrayed lentiviral CRISPR library targeting epigenetic regulators that can now be used for both selection and high-content screens, and will provide a lasting source of pre-made constructs for targeted knock-out experiments. I am looking forward to applying the knowledge that I have gained and advanced research techniques that I have mastered to discover new ways to combat resistant lethal prostate cancer.



Vicky Foy

I'm Vicky and I've recently taken up the role of clinical research fellow in the Clinical and Experimental Pharmacology group.

Prior to this I was a Medical Oncology Registrar at The Christie, a role I will return to on completion of my four year project. My undergraduate studies were in medicine and pharmacology and it was during this time I developed an interest in targeted cancer therapies and personalised medicine, a theme I have repeatedly returned to during my six years as a doctor. My PhD will explore the expanding clinical utility of circulating tumour cells in small cell lung cancer and I will specifically be researching RNA profiling from single cells. Ten years ago I moved to Manchester from Liverpool and have enjoyed the great shopping and restaurants in the city. I've had a great welcome to the Institute and I'm excited about the opportunity to work with world leading researchers.



Pablo Garcia-Martinez

My name is Pablo and I am from Barcelona in Spain. I studied medicine at the University of Barcelona, after which I undertook my specialty training in dermatology at the Hospital del Mar, again in Barcelona.

During my residency I became particularly interested in skin cancer, pathology and translational research. I truly wanted to dedicate some part of my career to research so I am really happy to have this opportunity and to start my PhD at the CRUK Manchester Institute. I will be working in the Molecular Oncology group where I will focus on circulating tumour cells in melanoma. This is my first time living overseas as well as working full time in a lab, so it is quite a big change for me. I find Manchester is really active, vibrant, and there is always something going on. In my free time I enjoy playing sport, mainly football. Overall, I hope to make the most out of this experience, both personally and professionally.



Eimear Flanagan

Hello! My name is Eimear Flanagan and I am from Co. Mayo in the west of Ireland. I have just completed my undergraduate degree in Biomedical Science at University College Dublin (UCD).

During one of my summers at UCD I had the opportunity to complete a research project on the genetic variants of rheumatoid arthritis. In addition, I completed my final year undergraduate research project on exosome signalling in triple negative breast cancer. Combining my interests in immunology and cancer, I am delighted to be starting my PhD in Cancer Inflammation and Immunity under the supervision of Santiago Zelenay. My project will be focused on identifying and characterising the mediators of tumour promoting or inhibitory inflammation with the hope of identifying some of the underlying mechanisms that allow evasion of immune control and enable progressive tumour growth. I am very excited to be starting my PhD at the Institute and as I am new to Manchester I look forward to exploring what the city has to offer!



Manuela La Montagna

Hi, my name is Manuela and I come from Italy. The desire to understand life on a deeper, unseen level inspired me to pursue a career in science.

I completed my undergraduate degree in General and Applied Biology at the University Federico II of Napoli and I went on to achieve an MSc in Molecular Biology. As part of my studies, I spent a year at the VU University Medical Center of Amsterdam, where I had the opportunity to work on cervical cancer. I am very excited to be starting my PhD in the Transcriptional Networks in Lung Cancer group, under the supervision of Michela Garofalo. The aim of my project is to investigate the AMPK signalling pathway in the development of Non-Small Cell Lung Cancer, using in vitro studies and mouse models. It is a great pleasure to be part of such a stimulating and collaborative environment as the CRUK MI Institute where I hope to acquire new knowledge and skills. Besides research, I love travelling and as I am new to Manchester I look forward to exploring the city and the surrounding areas.



Maximilian Schenk

Hi, I'm Max Schenk, and I am originally from Heidelberg in Germany. I graduated from the University of Heidelberg with a master's degree in Cancer Biology.

During the last year of my Master's studies, I had the great opportunity to perform a research internship in David

Sabatini's lab at the Whitehead Institute, where I had the chance to work on a CRISPR screen. Back then, I got very excited about this new technology, since it enables you to explore so many areas of biology. Therefore, I was happy to set up a CRISPR screen throughout my Master's thesis project, in which I investigated potential candidate genes that drive metastasis in squamous cell carcinoma. Due to my strong interest in using this technology, I am very excited to start my PhD project in Caroline Dive's group, where I will investigate resistance mechanisms in small cell lung cancer performing a genome wide CRISPR screen on our CDX models. Throughout my free time, I really enjoy running and I am excited about running in next year's Manchester marathon. If there are any runners currently in the Institute please get in touch.



Sarah Pearsall

Hi, my name is Sarah and I'm from Derbyshire. I have recently graduated from the University of Leeds with an undergraduate Master's degree in Medical Biochemistry, and now I am starting a PhD at CRUK MI.

During my undergraduate degree, I undertook a summer studentship working in a research lab focusing on engineering specificity into viral hexameric helicases to bind and translocate RNA molecules. Then, in my final year research project for my Master's, I worked in an enzymology lab, engineering a terpene synthase enzyme to create novel natural products. Now I am excited to change fields and start my PhD in lung cancer, with the wonderful opportunity to work in the Clinical and Experimental Pharmacology group with the pre-clinical team. My project is focused on vasculogenic mimicry, aiming to characterise small cell lung cancer undergoing this phenomenon at the genomic, transcriptomic and protein expression levels, hoping to identify novel drug targets. Spending just two months in Manchester has shown me how wonderful this city is, and I am excited to explore and make this place my home.



Matthew Winder

My name is Matthew and I have just started my PhD in the Skin Cancer & Ageing group led by Amaya Viros.

My project will attempt to decipher the reasons for such a disproportionately poor prognosis in elderly patients diagnosed with skin cancer when compared to their younger counterparts. Having completed my degree in Biology at The University of Manchester last summer, encompassing a year of applied research in York, I returned to my home town of Leeds. Here I worked as a research assistant studying genetic variants associated with a familial predisposition to enhanced melanoma susceptibility. During

this time, I actively re-engaged my thankless support of Leeds United FC. As well as following professional football, I am a keen centre-half and my career highlight (to date) was captaining my team in a County Cup final at Elland Road. I possess an ardent interest in real ale which has spilled over into home brewing of beer and wine, something which I conduct in my loft here in Manchester. I couple my enthusiasm for live music and travel by journeying to music festivals, attending over 25 across Europe in the last five years. Despite my proud Yorkshire heritage, I am unafraid to admit that the music, history and culture make Manchester an ideal city for me.



John Chadwick

Hello, my name is John and I'm from Aberdeen, Scotland. My undergraduate Medical degree was at Newcastle University and since then I've worked in Kent, New Zealand and for the last two years, Manchester.

My introduction to research was during an intercalated Master's during which I was lucky enough to complete my research project in the Stanford Cancer Center. After a few years of clinical work, and on my return from NZ, I turned my view again to research and met Tim Somerville on the ward at The Christie. With his honest and insightful advice I was able to secure an NIHR academic clinical fellow post which gave me the opportunity to spend time in the group for a few months last year. I've now taken the plunge and am starting my PhD as an MCRC clinical fellow, looking at the role of mis-expressed transcription factors in acute myeloid leukaemia. I am all too aware of just how devastating the diagnosis of leukaemia can be for patients and hope that my research will be able to contribute to our understanding of this awful disease. Outside of work I can be found climbing, cycling, and generally being outdoors. I also love my food and Manchester has an ever-changing collection of restaurants to explore.



Jakub Chudziak

Hi, my name is Jakub and I'm originally from Leek in Staffordshire (but I've lived in a fair few places since).

I completed my undergraduate MSci in Biochemistry and Biological Chemistry and MSc in Oncology at the University of Nottingham. I moved to Manchester in 2012 to work as a Scientific Officer in the Clinical and Experimental Pharmacology group, working on the development of a novel methodology of isolating circulating tumour cells from patient blood. Four years down the line I'm starting my PhD project (still with Clinical and Experimental Pharmacology), working towards creating new ways of modelling early events in the development of small cell lung cancer, looking specifically at the innate immune

system of the airway. The ultimate goal is finding biomarkers of early disease that could be deployed in a clinical screening setting. Manchester has been home for the last four years and it's been pretty great; hopefully the next four years will be equally enjoyable. I divide my free time between archery, snowboarding (in the winter), sailing (in the summer) and sleep (whenever, wherever).



Ronnie Rodrigues Pereira

Hi, I'm Ron and I hail from the sunny beaches of the south of Brazil. Academically, I hold a MSc in Computational and Systems Biology,

while personally my interests lie in travelling, cooking and classical music.

I was trained as a Chemical Engineer in Brazil. However, I have always been fascinated with the intersection of maths and biology. As such, I spent six months modelling the life cycle of a bacteriophage at the Colorado State University in the US. The project involved the prediction of protein levels targeted at the treatment of tuberculosis. This experience opened the doors to an entirely new world to me. The next leg of my journey consisted of an Erasmus Mundus Master's program to strengthen my understanding of biology as well as computer skills geared towards bioinformatics and machine learning. Consequently, I studied at KTH – Royal Institute of Technology (Sweden) and Aalto University (Finland) as well as completing an internship at the California Institute of Technology (USA). I am now very excited to begin my PhD studies in collaboration with the RNA Biology and the Prostate Oncobiology groups. The work involves identifying long non-coding RNA that potentially regulate chromatin state and are indicative of disease progression and treatment sensitivity.



Zaki Fadlullah

Hi, my name is Zaki and I'm a new PhD student in the Stem Cell Biology group. I grew up in Malaysia until my senior high school years then pursued my undergraduate studies at the University of Queensland, Australia.

In my final year I studied in the laboratory of Sean Grimmond to decipher the whole genome architecture of pancreatic cancer patients. I then returned to Malaysia to work as a Bioinformatician at Cancer Research Malaysia where I worked to characterise the transcriptional profile of oral cancer cell lines. Now as a PhD student supervised by Georges Lacaud and Magnus Rattray, I aim to use single cell sequencing to decipher the development of hematopoietic stem cells. Thank you CRUK MI for this opportunity!



Emma Williams with her Prize.

Emma Williams Wins IPSCC Prize

We are delighted to announce that Emma Williams was awarded the prize for the best talk at the 10th International PhD Student Cancer Conference (IPSCC). This is an annual event organised by students, for students and this year it was held in Cambridge in June.

Emma, a PhD student in the Leukaemia Biology group led by Dr Tim Somerville, presented her work describing how "Pharmacologic inhibition of LSD1 selectively targets pathologic megakaryocyte expansion in myeloproliferative neoplasms" and delegates voted it their favourite talk. The talk prize was sponsored by the European Association for Cancer Research.

The conference was attended by over 90 students from CRUK Institutes and Cancer Research Institutes from the UK, Germany, Netherlands and Italy, with 24 student talks packed in over the three days. The students also enjoyed keynote talks from the eminent Professor Sirs Mike Stratton and Tim Hunt.

Last year the IPSCC was hosted here in Manchester. Emma was co-chair of the organising committee and the event was a great success.

Where are they now?

We catch up with our former PhD student Elvan Boke



Elvan Boke

I carried out my PhD studies with Professor Iain Hagan in the Cell Division group at CRUK MI. My PhD research elucidated a novel mechanism of mitotic control via a phosphatase relay in fission yeast.

This proved to be a major discovery not only because it helps us understand mitotic progression better but also introduces a new, less kinase-

centric view of mitosis and resulted in a *Nature* publication (Grallert et al., *Nature* 517, 94-98 2015).

For my post-doctoral studies, I joined the laboratory of Professor Tim Mitchison in the Department of Systems Biology at Harvard Medical School. I decided to move away from enzymatic control of the cell cycle, and work on the organisation of cytoplasm. Cytoplasm was until recently assumed to be a colloidal liquid, with specialised reaction centres bordered by membranes; like the nucleus, mitochondria etc. My research yielded the first example of a membrane-less compartment, a giant body, formed by amyloid-like assembly of a conserved protein. A Balbiani body is a non-membrane bound compartment packed with organelles, present only in dormant oocytes. My postdoctoral research has led to the discovery that the Balbiani body is held together by a protein glue that is made of a reversible amyloid. This novel organisational principle also offers a means to explain the link between the Balbiani bodies and oocyte dormancy. This

finding led to a first-author paper in *Cell* (Boke et al., *Cell* 166, 637-650, 2016).

I will soon establish my own lab in the Centre for Genomic Regulation (CRG) in Barcelona and continue my studies on oocytes, cells that become eggs. My lab will try to answer a fundamental question for life: **how does an oocyte maintain a young cytoplasm with its complement of organelles, while the somatic cells age and die?** Oocytes can stay dormant in a female body for many years. For example, dormant oocytes in humans can live up to 50 years, from birth to menopause. My lab will study the mechanisms that protect oocyte organelles from ageing and the function of the Balbiani body in this process. I am passionate about this line of research, as it will provide important clues on the age-related decline of oocytes, and its concomitant effect on fertility.

If I look back at my career so far, I can say that choosing a post-doc lab is the most important decision in your academic life, as your post-doctoral research will be crucial for your chances in the academic job market. In my case, I was lucky to find a mentor who has given me great freedom to pursue my own interests, and to work on an understudied field. When choosing, it is really important to check how the alumni of the lab performed. You should also resist the temptation of doing the standard thing in your field, because it is much harder to get jobs on subjects that tens of other labs are already working on. You would be much better off looking for a novel idea.

I would like to finish with some advice I was given: *Science must be fun. If it is not, then there is something wrong.*

Awards and Events

Double Success for Institute at University's Distinguished Achievement Awards

The success of two members of the Institute was celebrated at a ceremony at The University of Manchester in June. This was part of the University's annual Distinguished Achievement Awards.

Institute Director Richard Marais received one of the four *Researcher of the Year* awards that were presented by the University's President, Dame Nancy Rothwell. Criteria for award winners stipulated that their research should have either "successfully challenged dogma, created a new field of research, elucidated a new paradigm, made a fundamental change in thinking or impacted significantly on society." Richard's award citation mentioned his recent work providing experimental proof that UV causes melanoma and that sunscreen only provides partial protection, along with his work towards delivering personalised medicine for melanoma to the clinic.

Tim Somerville was one of four students to be awarded *Postgraduate Research Student of the Year 2016*. He returned from the USA, where he is currently a post-doctoral research fellow at Cold Spring Harbor Laboratories, to attend the ceremony with his parents at the Whitworth Hall. During his doctoral studies at CRUK MI, Tim discovered a completely novel tumour forming mechanism which is active in one in five of all patients with acute myeloid leukaemia, a life threatening form of blood cancer. In addition to delivering profound mechanistic insights, his discoveries hold the prospect of improved risk stratification of patients and consequently enhanced personalisation of therapy for better outcomes. His ground breaking discovery was published in the prestigious journal *Cancer Cell*, with Tim as the sole first author.



Tim Somerville receiving his award from Dame Nancy Rothwell



Richard Marais receiving his award from Dame Nancy Rothwell

Awards for Richard Marais

Institute Director Richard Marais has been awarded The Colin Thomson Memorial Medal from Worldwide Cancer Research for his outstanding contribution to cancer research.

The medal is named after Dr Colin Thomson, a lecturer in theoretical chemistry who established Worldwide Cancer Research in 1984. The award ceremony took place at The Beatson International Cancer conference in Glasgow in July.

Later on in the summer, Richard received another award, the Fritz Anders medal from the European Society for Pigment Cell Research which aims to promote interdisciplinary knowledge and research in the pigmentary system. The award was presented by the society's President Professor Ian Jackson at their conference in Milan.



Richard Marais receiving the Fritz Anders medal from Ian Jackson

Caroline Dive wins AstraZeneca Prize for Women in Pharmacology



Professor Caroline Dive

Professor Caroline Dive was recently awarded a prestigious British Pharmaceutical Society prize.

Nominated by Professor Dame Nancy Rothwell, President and Vice-Chancellor of The University of Manchester and a fellow British Pharmacological Society (BPS) member, Caroline has received the BPS AstraZeneca Prize for Women in Pharmacology.

Although there are more women than ever studying science in general – and pharmacology in particular at university – those who reach the pinnacle of the profession remain few and far between. To address this important issue, BPS runs a number of innovative initiatives including this prize which acknowledges women whose career achievements have contributed significantly to our understanding of pharmacology through excellence in research.

Caroline has an international reputation for the validation and implementation of pharmacodynamic, prognostic and predictive biomarkers, particularly in the field of circulating biomarkers. She heads the outstanding Clinical and Experimental Pharmacology group at the Institute, one of the largest multidisciplinary translational oncology research groups in the CRUK network. The great success of the group is facilitated by her extraordinary aptitude for coordinating the activities of some 70 plus scientists, bioinformaticians and clinicians.

The quality and impact of Caroline's research in the field of pharmacology, coupled with her tireless commitment to nurturing the next generation of clinical researchers, and her pivotal role in establishing powerful alliances between academia, industry and the NHS, have all led to the advancement of biomedical science and patient benefit.

Upon receiving the award, Caroline said, "I am both honoured and delighted to receive the British Pharmacological Society AstraZeneca Prize for Women in Pharmacology. This prize serves to highlight such an important and exciting scientific discipline and encourages female scientists to engage in it."

The prize will be officially awarded as part of the Society's flagship meeting Pharmacology 2016, where Caroline will give a keynote lecture.

Aishwarya Payapilly poster prize

We are pleased to announce that Dr Aishwarya Payapilly, a postdoc in the Cell Signalling group, won best poster prize in the Euro PDX workshop in Switzerland.

Her poster highlighted her project on the role of TIAM1 in small cell lung cancer and she was delighted to win the award. For Aishwarya, the best aspect about the workshop was learning about the use of patient-derived xenograft (PDX) models in real time to determine the best line of treatment for patients. She also found the meeting overall to be informative and useful in terms of appreciating the technological advances of the PDX field.



Anne Largeot

Anne Largeot Poster Prize

Congratulations to Dr Anne Largeot on winning the Best Poster Award at the XXI

Wildede "Modern Trends in Human Leukemia and Cancer" meeting, held in June this year.

This specialised conference takes place in Germany and scientists present the most recent and exciting developments in the field of leukaemia and cancer biology – from basic science to new clinical concepts. Talks were given by leading specialists in the fields of stem cell and cancer biology.

Anne is a postdoctoral fellow based in the Stem Cell Biology group led by Dr Georges Lacaud. She was awarded Best Poster for her work on the "Requirement and function of MOZ in normal haematopoiesis and leukaemia". She also holds a prestigious Marie-Curie-Sklodowska Action Individual Fellowship, which part funded this work, alongside support from Cancer Research UK.

On receiving this prize, Anne observed that it is highly motivating that her work is recognised by the peers in her field.

The first recipient of the Christopher J. Marshall Award



Romina Girotti has been chosen as the first recipient of the Christopher J. Marshall Award for Studies on Signal Transduction and Melanoma, awarded by the Society for Melanoma Research (SMR), in conjunction with the Melanoma Research Foundation.

Romina Girotti

The award consists of an unrestricted honorarium of \$5,000, a commemorative plaque and support for her to attend the SMR 2016 Annual Congress in Boston.

Romina was nominated by her mentor, Richard Marais, who was himself mentored by Chris Marshall. Even though this did not play a part in Romina's recognition, it added some extra meaning to the award, since she can be considered a "scientific grandchild" of Chris.

"I feel very honoured to be the first recipient of this award and for being nominated by an amazing mentor like Richard. I had the pleasure to have known Chris at the Institute of Cancer Research where he inspired many young scientists like me, so this is a very special award", concluded Romina.

Research Engagement Award



Allan with his award

Dr Allan Jordan, Head of Chemistry in the Drug Discovery Unit, is the well-deserving recipient of a Research Engagement Award, from Cancer Research UK.

Allan received the award at a ceremony in London hosted by CRUK's Chairman, Michael Pragnell and was praised for his dedication in raising awareness of his research to approximately 830,000 supporters over the past six years.

Allan speaks at various events including charity galas, science festivals, lab tours and Institute open days as well as publicising the work of CRUK through interviews on social media, radio and TV. Allan also fundraises for the charity and has been known to go the extra mile – literally – through various fun runs across the region.

On receiving his award, Allan commented: "It's fantastic to have the opportunity to share our work with our fabulous supporters, explaining the work we do in an accessible way so they can not only understand it, but feel empowered to share those messages too. I'm absolutely delighted to receive this award, which I believe also recognises the hard work of all the Cancer Research UK scientists – it is, after all, their work I'm lucky enough to be able to talk about."

Pezcoller Symposium Prize

Dr Esther Baena, who leads the Prostate Oncobiology group, recently received one of the three Begnudelli-Pezcoller awards for her poster that she presented at this year's Pezcoller Symposium.

This is the 28th Symposium which takes place every year in Italy and this year focused on "Initial Steps on the Route to Tumorigenesis."

Esther presented her group's work uncovering the prostate luminal lineage heterogeneity and identification of LY6D as a novel tumour-initiating cell marker of castration-resistant prostate cancer.



Esther (3rd from the left) with her fellow prize winners at the Pezcoller Symposium and the Pezcoller Foundation President. From left to right: Prof Davide Bassi (Pezcoller Foundation President), Fulvio Chiacchiera, (European Institute of Oncology, Milano, Italy), Esther Baena, Elisa Donato (Italian Institute of Technology, Genova, Italy).

Latest Grants and Funding News



The Drug Discovery Unit

September Successes for Drug Discovery

By Ian Waddell

September gave particular cause for celebration in the Drug Discovery Unit (DDU). Firstly and most importantly the RET project declared its first pre-clinical candidate drug. This is a first for the team as a whole and represents an outstanding achievement.

The RET project, which is targeted against lung adenocarcinoma patients displaying an activating RET fusion, is partially funded by the venture capital company 6th Element Capital (6EC). This decision has triggered the availability of extra funds from 6EC for both the additional work required to take the candidate drug into the clinic and also to accelerate the development of a back-up series which will be done here at the CRUK Manchester Institute.

A second project, in this case our ongoing epigenetics collaboration with GlaxoSmithKline target focused on haematological disease, also announced a piece of good news in September. The DDU have now transferred the lead series which was designed, synthesised, tested and developed here in Manchester to the Pharma partner, which resulted in a success payment being made to the DDU via Cancer Research Technology. Again, this direct appreciation of the value created in a Manchester-based project represents a first for the DDU. This collaborative project remains active with GSK, who are driving the lead series towards the clinic in no less than three disease areas from their site in Upper Providence, Philadelphia, whilst the DDU here in Manchester are now focusing upon the delivery of a back-up compound series.

Despite the focus on these two major projects, the rest of the DDU's portfolio continues to make good progress. Our PARG project is the subject of late stage partnering discussions. Alongside this, our SMARCA2 project moved into the lead

identification phase. There will be significant capability build over the coming months as the group undertakes full scale phenotypic cell based screening for the first time. However the next six months will see the group increase the emphasis on target identification and validation as it refills its portfolio of projects. As always the DDU wants to hear from anyone in the Institute with an interesting drug discovery target idea.

Grants Committee update

In the last edition of our Newsletter we reported on the inception of the Institute's Grants Committee, whose role is to strengthen funding applications submitted by our researchers.

The Committee, chaired by Professor Iain Hagan, is composed of several Group Leaders who generously give their time to review grant proposals on behalf of their colleagues. They have already helped one member of the Institute to secure funding – Eduardo Bonavita – and have reviewed a number of pending applications that we hope will also be successful. This process is now firmly embedded in the grant application pipeline and is helping both our young and experienced researchers in the art of grant writing. Learning to articulate novel ideas is crucial to selling the project to potential funders. Drawing on the wealth of expertise of the Committee members will give our researchers a more competitive edge in an increasingly tough environment. We would like to thank the members of the Committee for their hard work which helps our scientists to increase the breadth of the work they undertake by obtaining additional funding.



EMBO Fellow

Dr Eduardo Bonavita, a postdoc in the Cancer Inflammation

Eduardo Bonavita

and Immunity group, was awarded a highly competitive European Molecular Biology Organization (EMBO) Long-Term Fellowship.

These prestigious fellowships support research throughout Europe and the world, with international exchange a key feature – Eduardo comes to us from Italy. With strong interests in cancer-related inflammation, he was keen to work at the Institute due to the exciting research being undertaken by Dr Santiago Zelenay, who leads the group he has joined.

Immunotherapy has recently emerged as one of the most promising areas of cancer research. Trials in melanoma are yielding notable and durable responses, highlighting the great potential of immune-based approaches in this particularly intractable cancer. Eduardo will study the molecular mechanisms by which melanoma cells evade immunity, looking at the cellular and molecular factors that regulate the balance between tumour protective and tumour-promoting inflammation.

Besides funding the research, another great benefit of this programme is the connection with the EMBO community, which will be important for sharing experiences and establishing new collaborations and contacts.

Eduardo is a highly accomplished young researcher and the combination of an exciting project and an outstanding host institute helped him secure the fellowship. His success was also facilitated by our recently formed Grants Committee who carefully reviewed the application and provided constructive input.

Manchester partnership with the US Cancer Moonshot

Professor Caroline Dive and her team in CEP focus their research on biomarkers, an important strategy in the fight against cancer. So it's with great excitement that we report their collaboration with a US group to develop advanced cancer cell detection technology, in one of the first international collaborations inspired and funded by US Vice-President Joe Biden's Cancer Moonshot.

Joining expertise, the two groups will develop and refine approaches that will revolutionise how researchers capture and analyse cancer cells circulating in patients' blood. Using a platform known as the high-definition single cell assay (HD-SCA), developed by Professor Peter Kuhn at the University of Southern California, Caroline Dive and colleagues based in the newly formed Manchester Centre for Cancer Biomarker Sciences will analyse blood samples from lung and colorectal cancer patients with early-stage disease to identify those who still have traces of cancer after surgery and so will be more likely to relapse.

Professor Dive says: "The prospect of using blood samples to detect and track cancer – so-called liquid biopsies – is set to transform cancer care over the next few years. We are exhilarated by the prospect of this new partnership, and at bringing this exciting new technology to the UK."



Claus Jorgensen

Further Rosetrees Trust funding

Dr Claus Jorgensen, who leads the Systems Oncology group focusing on pancreatic cancer, has recently been awarded further funding from the Rosetrees Trust.

Following on from the success of ground breaking work partially funded by the Rosetrees Trust, where he shed light on how cancer cells and normal cells communicate with each other, Claus will now use this additional money to differentiate between the good and bad impact that the microenvironment has on tumour cell behaviour.

Pancreatic ductal adenocarcinoma (PDA), a notoriously lethal disease with a dismal prognosis, poses an unsolved problem in cancer medicine due largely to late presentation, aggressive disease progression and limited treatment options. Claus will focus on understanding the specific composition of particular cells in the microenvironment – extracellular matrix (ECM) components of the PDA stroma – and how they change during tumour progression in order to further characterise the disease. Specifically, he will quantify the abundance and determine the relationship of ECM components in patients with good or bad outcome. Ultimately, this study will provide important leads for the development of prognostic biomarkers and evaluation of therapeutic strategies.

Manchester – Cambridge Collaboration

Earlier this year, to stimulate collaboration between the CRUK Cambridge and Manchester Cancer Centres, Cancer Research UK created a new award with the aim of initiating joint projects. The plan is that they will facilitate a wide range of joint activities that will maximise and exploit the expertise at both sites to improve patient outcomes.

Recent Events

NCRI 2016



Participants in discussion at the Women in Science Workshop at the NCRI 2016 meeting.

In November, scientists from the CRUK Manchester Institute attended the 12th annual National Cancer Research Institute (NCRI) Cancer Conference in Liverpool. The NCRI was set up in 2001 with a mission to bring together all the key organisations involved in cancer research in the UK to work together to direct research where it is most needed.

It comprises over 20 Partner organisations and as part of their activities, the NCRI organises an annual meeting to provide an opportunity for the partners to come together and exchange ideas and develop collaborations.

Professor Caroline Dive, Deputy Director and Senior Group Leader at the CRUK Manchester Institute, was the Chair of the Scientific Committee which was responsible for the development of the scientific programme for this year's meeting. There was plenty of involvement from our scientists including an excellent plenary presentation by Iain Hagan explaining the pivotal contributions made by yeast cell cycle research to our understanding of the biology underpinning the cell division defects that cause cancer. Crispin Miller presented an entertaining and highly informative workshop explaining the critical role of bioinformatics in cancer research. Other highlights included a talk from Mark

CRUK MI's Professor Caroline Dive and Dr Natalie Cook from the Christie NHS Foundation Trust received one of two "CRUK Cambridge and Manchester Cancer Centres Collaboration Awards" given to work with Drs Simon Buczacki and Doug Winton from Cambridge. Their project aims to generate three-dimensional cell clusters – organoids – from tumour cells to improve personalised treatments for patients with colorectal cancer. They hope to assess the utility of these patient-derived organoids for real-time drug testing to assist an individual patient's treatment selection.

Krasnow from the Stanford University School of Medicine who presented his group's elegant developmental biology studies identifying the potential cells of origin and signalling defects that contribute to lung cancer. David Currow from Flinders University in Australia described the need to improve the evidence base for various symptom control measures currently in use for patients with advanced cancer and in particular, the need for more clinical trials in this area. Caroline Dive hosted a well-received "Women in Science" workshop which included talks and discussions covering topics such as leadership skills, mentorship, clinical scientist careers, and starting your own lab.

Launch of Manchester Centre for Cancer Biomarker Sciences

Building on the existing strengths in biomarker research, the Clinical and Experimental Pharmacology (CEP) group at the Cancer Research UK Manchester Institute, led by Professor Caroline Dive, have further reinforced their strong links with Professor Andrew Hughes' Experimental Cancer Medicine team at The Christie NHS Foundation Trust to establish the Manchester Centre for Cancer Biomarker Sciences.

The expanding CEP group are relocating to laboratories and offices that are co-located within a single corridor, to enable closer working and seamless workflows.

The new Centre will drive forward the development and clinical implementation of biomarker sciences, with a focus on liquid biopsies, exploring circulating tumour cells and DNA within blood samples to guide treatments that are 'made to measure' for individual patients.

Institute scientists centre stage as Manchester hosts EACR meeting

By Katy Holliday

During the summer Manchester was centre of the European science stage in 2016 - acting as 'European City of Science' as part of its role in hosting the EuroScience Open Forum meeting.



Ged Brady

In addition, in early July, cancer experts from across Europe and further afield converged on Manchester as it hosted the biennial Congress of the European Association for Cancer Research (EACR).

The meeting was chaired by President of the EACR, Professor Richard Marais, Director of the Institute. It was a fantastic opportunity for our world-leading scientists to share expertise and to show that Manchester is a global centre of excellence for cancer research.

Professor Marais opened the scientific programme by welcoming delegates to the city. He then introduced Sir Harpal Kumar, chief executive of Cancer Research UK, to give the Opening Address.

Over 80 of our researchers attended the Congress, with around a third presenting work during the four-day meeting. Also present were operations staff members from the Manchester Cancer Research Centre, on hand in the Exhibition Hall to promote training and career opportunities and to raise the Centre's international profile. Manchester's research strength was emphasised by the heavy presence of our scientists speaking in symposia. A high number of poster presentations demonstrated the sheer quality and breadth of activity from our groups.

Highlights included a cancer immunotherapy symposium featuring Dr Santiago Zelenay, leader of the Cancer Inflammation and Immunity group. Santiago spoke on his

work exploring the mechanistic basis of tumour immunity, with an emphasis on the processes that regulate the balance between tumour-protective and tumour-promoting inflammation.

Sunday also saw Professor Caroline Dive chairing a session on liquid biopsies, where she gave a presentation on the utility of circulating tumour cells (CTCs) in lung cancer. Her Clinical and Experimental Pharmacology group is world leading in circulating biomarkers and had a number of posters covering various aspects of biomarker research, including CTCs and circulating tumour DNA in both small cell lung cancer and non-small cell lung cancer, as well as in pancreatic cancer. These minimally-invasive measures appear to hold great promise in selecting and monitoring treatment, and detecting relapse.

On Monday Dr Tim Somerville took part in a symposium on novel targeted therapies, explaining his research into epigenetic approaches in acute myeloid leukaemia. The Leukaemia Biology and Drug Discovery teams at the CRUK MI collaborated on a hugely successful project to better understand the role of LSD1 in Acute Myeloid Leukaemia (AML) and to develop drugs to target this protein. Tim is now leading a clinical trial at The Christie NHS Foundation Trust for patients with AML, in partnership with a Spanish biotechnology company.

There was great representation of the Institute's research and a demonstration of our strong collaborations: researchers from the Cancer Research UK Lung Cancer Centre of Excellence and the Prostate Cancer UK/Movember Belfast-Manchester Centre of Excellence were among those presenting during the conference. In many cases, doctors are working together with those in the laboratory to better understand the biology of cancer and to identify new lines of attack.

Overall the work on show revealed that the Institute is home to great cancer research – from fundamental studies investigating the genetic basis of cancer right through to trials revealing how to maximise patient benefit for new and existing therapies.



Sir Harpal Kumar presenting the opening address. Photo credit:EACR

Colloquium 2016



Institute Director Richard Marais (left hand side) with the Poster Prize winners (2nd left to right) Stuart Williamson, Gauri Deb and Emma Williams.

The Institute Colloquium took place at Lancaster University in September. This is an annual event that offers the chance for our staff and PhD students to present and discuss their work and to develop new collaborations. There were oral and poster presentations covering all aspects of cancer research taking place within the Institute and also from our colleagues in The University's Division of Molecular and Clinical Cancer Sciences.

The event offered us a chance to say farewell to Group Leader John Brognard who gave a presentation on the work of his Signalling Networks in Cancer group. John has recently moved back to the US after six years at the Institute during which time he and his group have been active and enthusiastic participants at the colloquium.

Another highlight was the talk given by Professor Stephen Taylor from the Division of Molecular and Clinical Cancer Sciences who spoke about an exciting collaboration with the Institute's Drug Discovery Unit on ovarian cancer.

Each year, we feature the work of the core facilities and in keeping with this theme, Natalia Moncaut spoke about the newly established Transgenic Production Facility and the potential of CRISPR-Cas. Richard Oakley from Cancer Research UK joined us to provide an insight into the charity's various fellowship schemes and to give valuable advice when preparing grant applications.

There were two vibrant and busy poster sessions with the best posters chosen to receive one of two prizes. The prize for best poster by a Post-doctoral Researcher or Scientific Officer was shared by Stuart Williamson and Gauri Deb. Stuart, from the Clinical and Experimental Pharmacology group, has investigated the ability of small cell lung cancer cells to form vascular structures in a process known as vasculogenic mimicry. Gauri works in the Leukaemia Biology group and has identified factors which could be potential targets for therapy, in combination with Lsd1 inhibitors, for the treatment of acute myeloid leukaemia.

The Lizzy Hitchman prize for best poster by a PhD student was awarded to Emma Williams, also from the Leukaemia Biology group. Emma's project has established that Lsd1 inhibitors have the potential for treating other haematological disorders such as essential thrombocythemia.

Latest from the Athena Swan Team

By Caroline Wilkinson

The Institute's Athena Swan team are making good progress towards submitting an application for an Athena Swan award.

The Equality Challenge Unit's Athena SWAN Charter encourages and recognises commitment to advancing the careers of women in the scientific areas of technology, engineering, maths and medicine (STEMM) in higher education and research. More recently, the charter has been expanded to recognise work that addresses gender equality more broadly, and not just barriers to progression that affect women.

Here at the Institute, we are in the process of preparing an application to be submitted in 2017. The Institute has an Athena Swan Self-Assessment Team (SAT) who have been meeting every month since March to analyse relevant data, policies and practices. This has culminated in the team producing a bespoke staff survey based on the Athena Swan agenda that we shall be asking all staff and students to complete in the coming weeks.



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

Opinion will be canvassed on various topics including information and support provided to new starters, training opportunities, flexible working, awareness of promotions, the timing of Institute seminars and social events as well as a range of other issues. In addition, we shall be capturing the views of those leaving the Institute through a leavers' survey that has been produced by a sub-group of the SAT, Marina Parry and Colin Hutton.

As part of our application for an award, we shall draw up an action plan based on the survey responses and other analysis carried out by the team. We hope that you will take this opportunity to help shape your Institute!

Welcome to the iDECIDE team

By Donal Landers



The iDECIDE team, who are based on the ground floor of the Paterson Building: Back row, left to right: Donal Landers, Andrew Hughes and Jason Swift. Front row, left to right: Jenny Royle, Lisa Kennedy and Carla Siswick

A new team has recently been established at the Institute to harness clinical bioinformatics to deliver personalised healthcare for cancer patients. The iDECIDE project is a five-year collaboration between the CRUK Manchester Institute, The University of Manchester, The Christie NHS Foundation Trust and AstraZeneca with the team being based at CRUK MI.

iDECIDE is a clinical informatics Research and Development framework to support early decisions in Phase 1 studies. It leverages real-time patient information during an ongoing clinical study with the specific dual purpose of enabling early decision making, in order to keep patients safe, and support effective adaptation of the clinical trial design, if required, for their benefit.

The application of clinical trial informatics will better identify the right cancer treatment for the right patient at the right time. AstraZeneca have provided £11.5 million to support clinical informatics research within the recently established Centre for Cancer Biomarker Sciences led by Caroline Dive, and will be carried out in the partnership with the state-of-the-art clinical trials unit of The Christie NHS Foundation Trust, which is at the forefront of experimental cancer medicine in the UK.

Projects will include the development of a new clinical informatics system to capture and integrate clinical trial safety, efficacy, biomarkers and drug distribution data in real time, presenting the information in the form of graphs that can be easily interpreted by clinicians to help tailor the treatment for patients. The collaboration will also support new training programmes in clinical research and pharmacokinetic and pharmacodynamics modelling for investigators to understand the distribution and clinical effects of medicines within the body.

iDECIDE consists of 4 key components at present: REACT (Real Time Analytics for Clinical Trials); PROACT (Patient Reported Outcomes about Clinical Tolerability); WATCHER (Artificial

Intelligence) clinical reasoning over REACT data; and FORSEE (disease landscape and competitive intelligence).

The goal of the iDECIDE programme is to further enhance these systems and, additionally, to develop further new and innovative solutions within the context of the oncology clinical trial. The programme is ambitious, but over the next five years, through close collaboration between the iDECIDE partners, these systems will be fully implemented delivering real benefit to our patients.

The iDECIDE project brings a number of benefits to the clinical trial process. It enables real-time capture of clinical trial data in Phase 1 studies allowing an earlier understanding of the patient risk-benefit trajectory. It will improve the quality and completeness of the data through early source data verification and allows adaptive trial design such as the adding or removing of arms, the changing of doses and/or regimens, and the modification of Go/No-Go criteria while the study is ongoing. In addition, iDECIDE enables important benefit-risk actions to be taken regarding the trial design based on the receipt of real-time data on how patients feel. It will enable data visualisation and reasoning, making it easier to see/decipher thousands of data points quickly and easily, which allows the early identification of safety and efficacy signals.

The project is designed around the ergonomics of the patient, allowing patients to communicate to the clinical team and indirectly to AstraZeneca regarding important issues relating to their clinical trial such as tolerability, formulations, and dose frequency. Finally, iDECIDE enables deeper insights into the patient's experience of the 'new' drug, creating a more collaborative model of clinical trial care.

Wedding bells

Ruth Cox née Perkins, EA to the CRUK MI Director, got married this September to Callum Cox. The wedding took place in the beautiful Lake District and the happy couple enjoyed a great weekend with family and friends before setting off to a fantastic honeymoon in Iceland and New York. Congratulations!



Callum and Ruth Cox

Staff News

New Arrivals



Elia (left) and Andrés (right)

Congratulations to Alba Maiques-Diaz, from our Leukaemia Biology group, who gave birth to Elia and Andrés, her beautiful baby twins, in August.



Freya Rosie Jones

Laura Jones, HR Adviser, gave birth to a lovely baby girl. Freya Rosie Jones was born in July, weighing 9lb 8oz. Congratulations!

Social Events



A warm welcome to all the newcomers

Once more CRUK MI welcomed the new members of the Institute with the annual Newcomers Party, which took place in October. It was a great opportunity for our staff to step away from work for a while and meet the people who had recently joined our team, or even put names to faces we are used to seeing.

The party was a great success and it inspired the new PhD students to get to know each other better by going out together afterwards.

Walks, races and a big jump

Fabiola Fernandez-Gutierrez, from the Clinical and Experimental Pharmacology group, walked all over cancer this September. She joined the challenge to walk over 10,000 steps every single day of the month and she rocked it fundraising over £100 for CRUK. Thank you!

Congratulations to **João Barros-Silva**, from the Prostate Oncobiology group, who joined the Great Manchester Run 2016 and raised £203.14 for CRUK. He ran a great race and managed to finish the 10K in less than an hour.

Scientists from our Stem Cell Biology group, together with colleagues from The University of Manchester, left the sterile labs behind and went all dirty to fundraise money for Breast Cancer Now.

Georges Lacaud, Rob Clarke, Bruno Simões, Gray Kueberuwa, Vanessa Clay, Aida Sarmiento, Alice Greenhalgh, Aoife Kilgallon and Fen Tang completed the Tough Mudder challenge and raised over £300 for breast cancer research.

When it comes to fundraising, not even the sky is the limit for CRUK MI staff. **Rachel Walker**, scientific officer at the BRU, jumped from 11,000ft and fundraised over £1,000 for her chosen charities.

Rachel decided to split the money between Prostate Cancer and Leukaemia Research, areas of cancer that are close to her family and friends, and the children's department at



Rachel Walker sky-diving from 10,000ft.

Manchester Royal Eye Hospital, where she has been a patient since she was four, when she was diagnosed with glaucoma.

"I'm not sure why I would choose to jump out of a perfectly good plane but if it helps raise some money to support these great charities, then it will give me the 'push' I need when

I am 15,000ft above the ground!", said Rachel before her adventure with Black Knights Skydiving. But as soon as she completed the challenge all her fears disappeared: "It was brilliant, I loved every minute of it, free falling at 130mph is a feeling I just can't describe."

In the spotlight with John Weightman



John is a Scientific Officer in the Molecular Biology Core Facility (MBCF) where he is responsible for running the Next Generation Sequencing service as part of the NGS team. He joined the Institute in 2012 after completing a degree in Cell and Molecular Biology at Manchester Metropolitan University. In addition to his main role, John is also a member of the organising committee for the STAy group providing a forum for Post-docs, PhD students and Scientific Officers and also plays a key part in the Institute's research engagement efforts, in particular through demonstrations of the work of MBCF to CRUK's supporters.

1. What is your favourite part of the UK?

Newcastle! I love living in Manchester but once a Geordie, always a Geordie.

2. What was your best ever holiday and why?

I spent a month in Costa Rica doing voluntary work on a turtle conservation project, helping build a village clinic and jungle trekking, as well as getting to experience some Costa Rican life along the way. It's the furthest I've travelled to date, and getting to experience the brilliant nature and lifestyle of somewhere so different made it my best trip so far.

3. Which website do you always check, and why?

Spotify. Some of my personalised song suggestions are getting eerily accurate.

4. What is your favourite film?

For a laugh, Shaun of the Dead or Hot Fuzz. Otherwise there's no beating the Bourne trilogy. Is five cheating?

5. What is your favourite band/singer?

Devin Townsend (and his various projects)

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

I'd quite like to go at stage lighting for music concerts and clubs

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

Happiness is not a destination, but a way of life.

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

A solar-powered MP3 player, a well-stocked portable espresso machine (Google says it does exist!) and a lifetime supply of factor 50.

9. What is your greatest fear?

Discovering just too late that the previous question actually meant survival essentials.

10. How would you like to be remembered?

As someone who cares, has time for, and has a laugh with others – and enjoys life!

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

My lottery numbers?

12. What is your signature dish to cook?

I prefer to keep trying new dishes, but I like to think I make a pretty good chilli or Thai curry.

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

Idealistically my first ticket of many to travel the world. In reality probably a celebratory drink!

14. What is your idea of perfect happiness?

Goat's cheese lasagne day at The Christie canteen.

15. What keeps you awake at night?

The ability to check on our sequencing runs online surely doesn't help!

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The University of Manchester
Royal Charter Number: RC000797