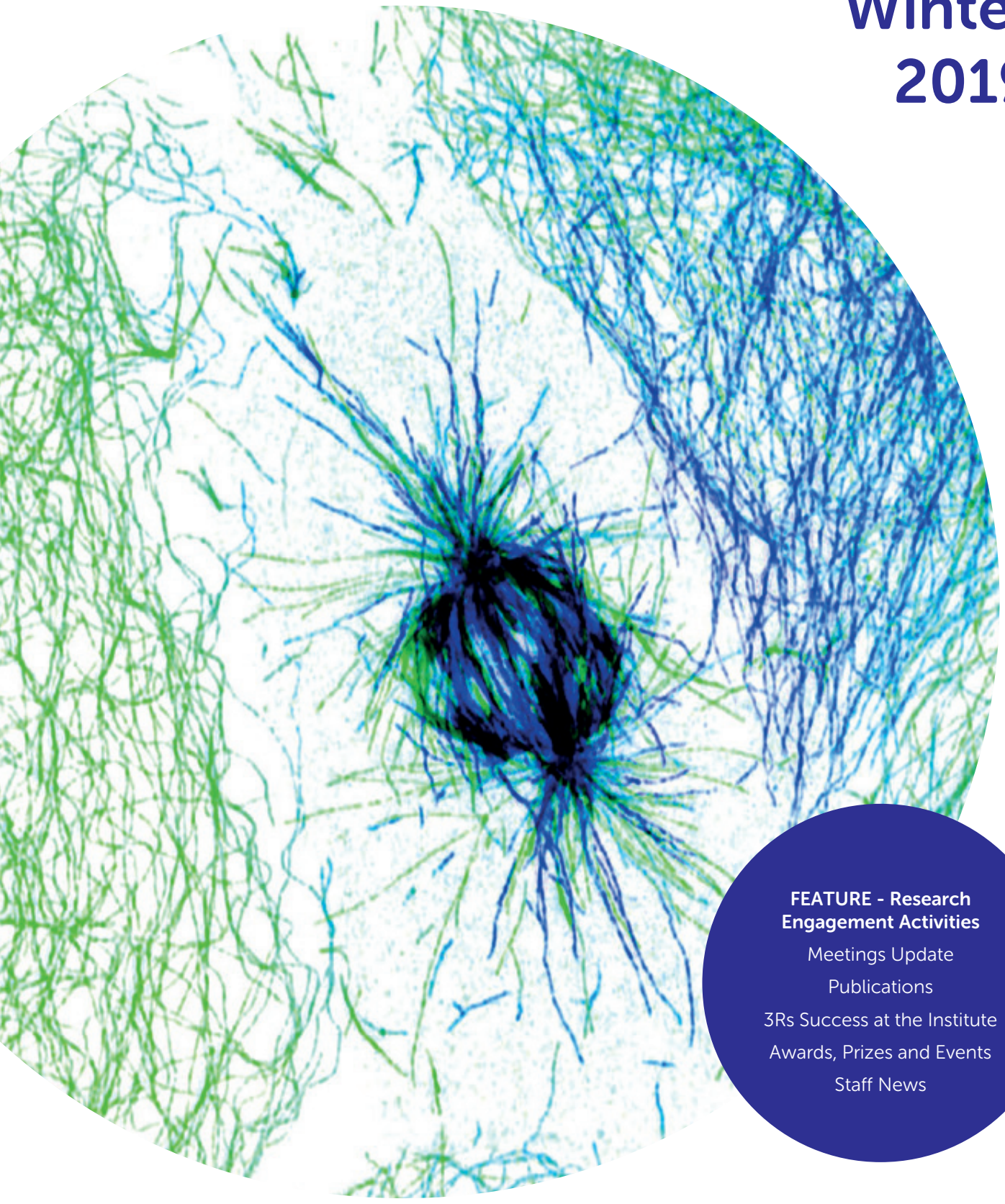
Newsletter

CANCER RESEARCH UK | MANCHESTER INSTITUTE

Winter 2019



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MANCHESTER 1824
The University of Manchester

Director's Introduction

The last six months have seen the Institute settle into life at Alderley Park, developing new relationships and exploring opportunities here whilst enjoying the beautiful surroundings and excellent facilities. We have worked hard to optimise operations at our interim home and it is encouraging to see how much progress has been made despite the extensive disruption that everyone has experienced.

The plans for the redevelopment of the Paterson Building site are well underway and offer an exciting future for cancer research in Manchester. We are grateful for the level of engagement from staff and students across the Institute in submitting ideas for the project and I would like to thank everyone who is working hard to ensure that the redevelopment will be a success.

In September two of our Senior Group Leaders, Iain Hagan and his Cell Division group and Tim Somervaille and his Leukaemia Biology group, underwent successful quinquennial reviews of their research programmes. I would like to extend my congratulations to them for achieving excellent ratings for their past work and future plans from the international panel of experts.

Institute Deputy Director Caroline Dive and her Clinical and Experimental Pharmacology group are working hard to prepare for their quinquennial review in April. They have enjoyed considerable recent success including the completion of the first phase of TARGET, which is a circulating tumour DNA (ctDNA)-driven phase I clinical trial conducted together with colleagues at The Christie NHS Foundation Trust and The University of Manchester. This work was presented at the Experimental Cancer Medicine Centre (ECMC) showcase held recently at the Oglesby Cancer Research Building. The Manchester ECMC is co-led by Caroline to drive the discovery, development and testing of new treatments for patients and is jointly funded by Cancer Research UK and the National Institute for Health Research.

Joint ventures such as these are essential for us to deliver on our precision medicine ambition and it is exciting to see how our range of collaborations is evolving across an array of disciplines from basic science through to clinical trials and into new areas including immunology and nanomaterials. Caroline Dive and her CEP team are establishing colorectal circulating tumour cell organoids to support a joint precision medicine approach with scientists in Cambridge and clinicians at the Christie Phase I Unit. They are also working alongside Claus Jørgensen and his Systems Oncology group on the UK wide PrecisionPanc project, the aim of which is to personalise treatments for pancreatic cancer patients, and which recently recruited its 100th patient. My own Molecular Oncology group is part of a recently announced CRUK Grand Challenge international consortium seeking to understand why specific oncogenes are associated with particular cancers but not in others.

In October 2018, I was extremely proud to help bring the Society for Melanoma Research Congress to Manchester. It was a pleasure to host this prestigious event in my city, and it offered us the opportunity to showcase our fantastic cancer research ambitions to the worldwide melanoma community. Becki Lee, one of the Clinical Research Fellows in my group presented her data at the congress, followed a few weeks later by a successful defence of her PhD thesis. Her research demonstrates that circulating tumour DNA predicts relapse and survival in high-risk resected melanoma patients and could aid in their stratification for adjuvant therapy. This important work resulted in Becki receiving the Dexter Award, the Institute's prize for the best young scientist of 2018. I would like to congratulate Becki and wish her all the best as she enters the next phase of her career in clinical research.

Developing our early career researchers is an essential part of our research strategy, and as a new initiative this year, we have allocated several slots in our external seminar series for our young scientists to invite speakers of their choice. They will host the visits and have the opportunity for one-to-one meetings with leading cancer researchers who are also encouraged to include a section in their presentation about their career. This is a valuable experience that is being co-ordinated through our STAy group of PhD students, postdoctoral fellows and scientific officers. STAy have also organised several other events during the year including some aimed at understanding the experience of cancer patients. I would also like to highlight the work of those who have organised the peer-to-peer mentoring circles. I very much hope that our new cohort of students, who joined in the autumn, will get involved with these valuable initiatives which contribute to a vibrant and stimulating environment for our early career researchers. You can find out more about the new students and all of these initiatives and other achievements made by our young scientists in this issue.

Professor Richard Marais
Director, Cancer Research UK Manchester Institute

Cover Image: Zeiss AiryScan image showing dramatic rearrangement of the microtubule cytoskeleton of a mitotic epithelial cell, with ultra-fine astral microtubules radiating from the mitotic spindle to the cell cortex, compared with the dense, overlapping microtubules in the surrounding cells. The colouring from blue to green represents the height of the microtubules as captured in the original three-dimensional image. *Image supplied by Andrew Porter (Cell Signalling)*

Research Engagement Activities

Researchers Engage at Manchester's Science and Industry Museum

Over 40 researchers, scientists and research nurses from across the Manchester Institute and CRUK Manchester Centre took part in the Science and Industry Museum's *Platform for Investigation – Powered by Siemens* in May.

Co-organised by Tim Hudson, CRUK's Research Engagement Manager, and the NIHR Manchester Biomedical Research Centre, the team took over the museum's main entrance hall on Saturday 19 May, interacting with over 400 visitors throughout the day.

Activities included demonstrations on advanced radiotherapy, DNA building, flow cytometry and animal research. Marking International Clinical Trials Day, CRUK Senior Research Nurse Clare Dickinson and a team of Research Nurses demonstrated patient stratification and personalised therapies through a clinical trials demo.

Tim said: "This was a great opportunity for us to showcase the research taking place in Manchester and the impact this is having on patients all over the world."

Images top and bottom: DNA building at the Museum, and Platform for Investigation takes over Science and Industry Museum

Pint of Science – Of Mice and Men

As part of Manchester's 2018 Pint of Science Festival, Institute and other University scientists delivered a series of talks on the use of mice in cancer research to science curious pub-goers at Didsbury's The Albert Club.

The Institute's Caroline Wilkinson, Filipa Pereira Lopes and Melanie Galvin were joined by Denis Alferez-Castro from James O'Connor's Oncology Imaging group, within The University of Manchester's Division of Cancer Sciences, to discuss how mice help us to understand cancer and how the principles of replacement, reduction and refinement are embedded in our work with animals in research.

The event, organised by University of Manchester-based PhD student Charlotte Criscuolo, who was part of the Manchester Pint of Science team, allowed the speakers to illustrate how progress in cancer research is being made using animal models and how that work is underpinned by the 3Rs. This included descriptions of those projects aiming to discover better and more efficient ways of utilising animal models or removing the need for them entirely.

Pint of Science is a non-profit organisation that brings some of the most brilliant scientists to your local pub to discuss their latest research and findings. The festival runs over a few days in May every year, but occasional events are run during other months.

Images left to right: Melanie talks about the principles of the 3Rs, and Pint of Science beer mat.

Cancer Team Science at the Manchester Science Festival

Families went hands-on with a range of cancer research science-based activities, from prevention to proton therapy, when they met Institute and other University scientists together with Christie NHS Foundation Trust researchers at the Manchester Science Festival 2018.

The University of Manchester's Science Spectacular event, part of the Festival each year, attracts over 1500 members of the public, young and old, who get the opportunity to engage with science research taking place across the university community.

Over 25 researchers, scientists and research nurses teamed together at the event in October to tell the story of the wealth of cancer research taking place in the city; how we can better prevent the disease occurring, basic biology, liquid biopsies, clinical trials and the cutting-edge high-energy proton beam therapy recently installed at The Christie.

Cancer detectives at the Science Festival

Scientists Sign-Up to Bee-at Cancer

Institute scientists and staff featured on one of 80 giant bee sculptures which went on display in Manchester city centre last summer, celebrating the city's pioneering spirit.

The Bee in the City sculpture trial – which ran for 8 weeks from July until September – was inspired by Manchester's celebrated worker bee emblem, which has been part of the city's heraldry for over 150 years and is synonymous with Manchester's pioneering and creatively industrious spirit – pollinating progress and renewal.

Scientists and researchers from the MI together with others from The University of Manchester were invited to add their signatures to artist Kelly Stanford's STEM Bee (Science Technology Engineering and Mathematics). The 12 cancer research autographs joined signatures from over 80 physicists, biologists, chemists, mathematicians and engineers in the city.

Sir Richard Leese, Leader of Manchester City Council, said: "The bee symbolises the industrious, creative and energetic spirit of Manchester and its people. Bee in the City will build on Manchester's reputation for innovation and the role that culture plays at the heart of city life."

After the trail ended the bees were auctioned to raise funds for The Lord Mayor of Manchester's charity – We Love MCR Charity – to improve the lives and life chances of Manchester people, with Kelly's STEM Bee selling for an incredible £20,000.

Images below, left to right: Bee-ting cancer sooner, and Our cancer researchers with the STEM Bee.

Ten years of Fundraising for Movember

By David Jenkins

David raffles off book signed by astronaut Tim Peake

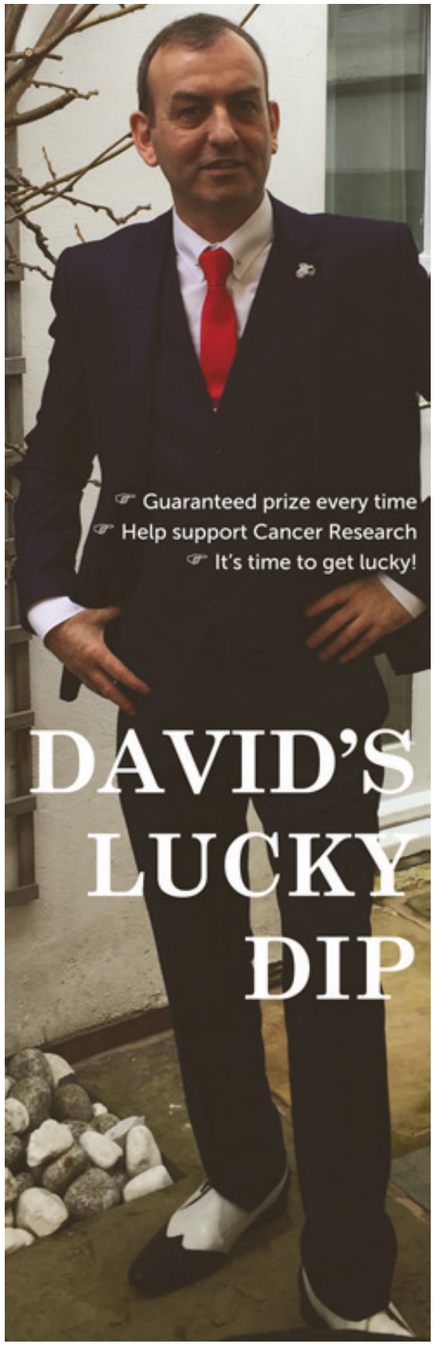
In November 2018, I celebrated 10 years of fundraising for the Movember Foundation. I started back in 2008 as part of a team of scientists at the Institute. On this first occasion, we managed to raise around £1,300, a fantastic sum.

As I had wholeheartedly embraced the fundraising – at the time there was very little fundraising opportunities for men with cancer – I ended up raising the majority of the funding myself. This inspired me to keep going and I knew I could do it alone.

It is not easy fundraising year on year, as colleagues, friends and family can soon tire of all the requests, unless you can manage to keep it fun and creative. As purchasing officer I am in a good position to reach out to our suppliers and ask them for any promotional items or branded merchandise, which I use in my very popular "David's Lucky Dip". Also, my bake sales known as "David's Great British Bake Off" are always a hit – home baked products taste so much better than shop bought and are greatly appreciated by staff! I always start the Movember fundraising with a tasty Halloween special and at the end of November a festive themed bake sale. In October British astronaut Tim Peake was signing his book at Waterstones in Manchester, so I went a long and purchased a book and asked him to sign it "In Support of Movember", which he kindly did. This fantastic prize went towards my Movember raffle, which proved to be very popular and helped sell lots of raffle tickets.

Cupcakes for Movember

During a Movember Fundraising Day at Alderley Park, I ran a stall called "Jenkins Jams & Preserves", which included my homemade piccalilli, pickled red cabbage, 'Festive Jam' and lemon curd. Altogether, from these events I managed to raise £1,025 for Movember last year. I also received many kind donations online.



David raises money for Movember with his Lucky Dip

The Newsletter editorial team note that this is a remarkable achievement and highlights David's dedication to supporting men with cancer. We congratulate David on his success and look forward to the next tasty bakes.

Featured Publications

Protein Linked to Nuclear Orientation

A recent study has provided new insight into the regularity mechanisms behind the perinuclear actin cap, a key regulator of the shape of a cell's nucleus.

Led by Angeliki Malliri, findings of the study have recently been published in *Nature Communications*.

Migration of cells is important for many normal physiological processes – such as wound healing – but it is also required for cancers to spread. When cancer cells invade, they often have to squeeze through tight spaces between tissues, which requires correct orientation of the cell nucleus, the largest structure within the cell.

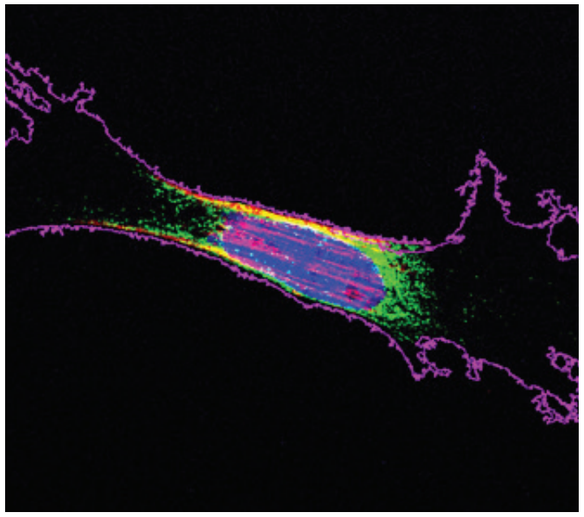
By using individual cell tracking, scientists from the Cell Signalling group have shown that loss of STEF reduces cell migration, and that STEF – also known as Tiam2 – localises to the outer membrane of the nucleus.

In cells plated onto micropatterns, which force them to take on a migrating shape, the long axis of the nucleus tends to align with the front of the cell. STEF depleted cells show a disruption of this nuclear orientation. Adding STEF back to the cells restores normal orientation, but not when using a version of STEF which is unable to activate Rac1.

The researchers were able to restore the actin cap in cells lacking STEF by specifically targeting an activated form of Rac1 – which no longer requires STEF – to the outer nuclear membrane.

Using Atomic Forces Microscopy, the scientists showed that a lack of actin cables in STEF depleted cells led to reduced nuclear stiffness, which in turn increased nuclear height. The researchers showed that this also affected signalling within the cell, including through the HIPPO pathway, which is often deregulated in cancer.

Woroniuk A, Porter A, White G, ...Malliri A. STEF/TIAM2-mediated Rac1 activity at the nuclear envelope regulates the perinuclear actin cap. *Nature Communications* 2018; 9(1):2124.



STEF-depleted cell showing nucleus (blue) with active Rac1 (green) targeted to the nuclear membrane where it has restored the cables of the actin cap (red). Outline of the cell shown in magenta.

Pattern Revealed in Lung Cancer Relapse

Researchers based in the RNA Biology group have explored the genetics of lung adenocarcinoma and identified a pattern of mutations that predicts survival.

The team, led by Crispin Miller, looked at mutation patterns in 660 samples of lung adenocarcinoma.

By creating network models based on the genetic profiles of normal tissue samples, they could map the mutation patterns and understand the relevance of the changes. This allowed them to identify a set of genes associated with key cancer behaviours such as tumour dissemination and metastasis, and a pattern that could predict disease-specific survival.

Their findings suggest that the accumulation of multiple mutations, each with a weak effect, is what ultimately alters cell behaviour and patient outcome. They highlight the importance of considering the whole genome, and all changes within, rather than focusing on individual genes.

Bennett L,.. Miller CJ. Mutation pattern analysis reveals polygenic mini-drivers associated with relapse after surgery in lung adenocarcinoma. *Sci Rep.* 2018; 8(1):14830.

Institute Scientists Explore Cells within Cells

A team involving researchers from the Tumour Suppressors group has shown that a mutant gene is linked to the formation of cell-in-cell structures.

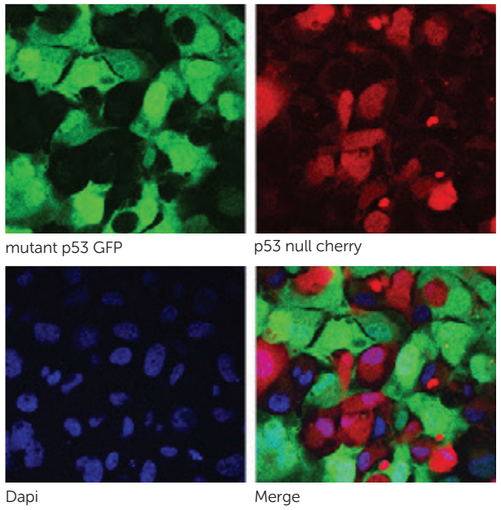
They investigated the role played by the p53 gene in a process known as entotic engulfment, where one viable cell exists within the membrane of another, in a type of lung cancer.

Such cell-in-cell (CIC) structures have been observed in several different cancers, including breast, lung, endometrial, pancreatic, skin and oral cancer. It is thought that they could have a role in tumour growth.

Now a group, led by Patricia Muller from the Institute and involving scientists from Leicester, London, Glasgow and Manchester, has looked at CIC formation in lung adenocarcinoma, and in particular the effect of mutations in p53. They found that there was a strong association between the frequency of CIC and the expression of mutant forms of p53.

In their laboratory experiments, they showed that mutant p53 encourages the cellular engulfment process. Crucially they also observed that these mutant p53 cells survive and are able to overcome failures in cell division, resulting in cells with more than one nucleus and the production of extra daughter cells.

Mackay HL,.. Muller PAJ. Genomic instability in mutant p53 cancer cells upon entotic engulfment. *Nature Communications* 2018; 9(1):3070.



mutant p53 GFP | p53 null cherry

Dapi | Merge

Green fluorescent mutant p53 H1299 cells engulfing red fluorescent p53 null H1299 cells with Dapi in blue

Probing Mechanism of Anti-Leukaemia Drug

The Leukaemia Biology group has explored how targeting LSD1 leads to cell differentiation in a particular type of acute leukaemia.

LSD1 is a gene that is highly expressed in cases of prostate, lung, brain and breast cancer with poor prognosis, and knockdown of LSD1 has shown promise as a therapeutic target in acute myeloid leukaemia (AML). Drugs that target LSD1 are now being investigated in clinical trials for AML and other diseases.

The Institute scientists looked at the mechanism behind one such potential drug – known as OG86 – in AML cells. They found that OG86 disrupted the interaction between LSD1 and GF11, a transcription repressor that is known to associate with LSD1.

This further suggests that GF11 is also a potential target for treating some types of leukaemia.

Maiques-Diaz A, Lynch JT, Spencer GJ, Somervaille TCP. LSD1 inhibitors disrupt the GFI1 transcription repressor complex. *Mol Cell Oncol* 2018; 5(4):e1481813.

Review of Clinical Trials in Salivary Gland Cancer

Robert Metcalf, who works alongside the Clinical and Experimental Pharmacology group, has carried out a systematic review into the potential of tumour profiling for stratifying patients with salivary gland cancer.

In conjunction with colleagues from The University of Manchester and The Christie NHS Foundation Trust, he identified only 20 relevant clinical trials for patients with this disease. The team found that the majority included no molecular stratification – that is allocating participants to one of multiple targeted drugs based upon the genetics of their tumour.

They discussed how trials that covered a range of molecular sub-types made it harder to implement findings into the clinic. Their conclusion was that collaboration across institutions and international borders was essential for any future studies.

Rack S, Rahman R, Carter L, McKay C, Metcalf R. Impact of tumour profiling on clinical trials in salivary gland cancer. *Clin Otolaryngol.* 2019; 44(1):1-6.

Discovery of common markers of tumour hypoxia across 19 cancer types

Published in *Nature Genetics*, researchers have discovered molecular hallmarks of hypoxia in the first-ever pan-cancer analysis of low oxygen in human tumours, with a special focus on prostate cancer.

Unlike healthy tissues, tumours thrive in low-oxygen environments, often acquiring the ability to resist treatment and spread to other sites in the body. Despite being a well-known cause of therapy resistance and metastasis, the impact of low oxygen, known as hypoxia, on tumour cells is poorly understood.

The study, led by MCRC Director and Institute Group Leader Rob Bristow and colleagues in Canada, investigated more than 8,000 human tumours across 19 different cancer types, including prostate tumours from the Canadian Prostate Cancer Genome Network (CPC-GENE). The authors discovered common markers of hypoxia that could help predict cancer aggressiveness and inform treatment decisions.

These findings, which include several genes more commonly mutated in hypoxic cancers and new information about hypoxia-related patterns of tumour evolution, make up the largest resource available for hypoxia research.

The markers observed in this study also open new opportunities for researchers to develop therapies that target hypoxia-related treatment resistance and metastasis across many types of cancer, including prostate cancer.

Bhandari V, Hoey C,... Boutros PC & Bristow RG. Molecular landmarks of tumor hypoxia across cancer types. *Nature Genetics* [epub 14 January 2019]

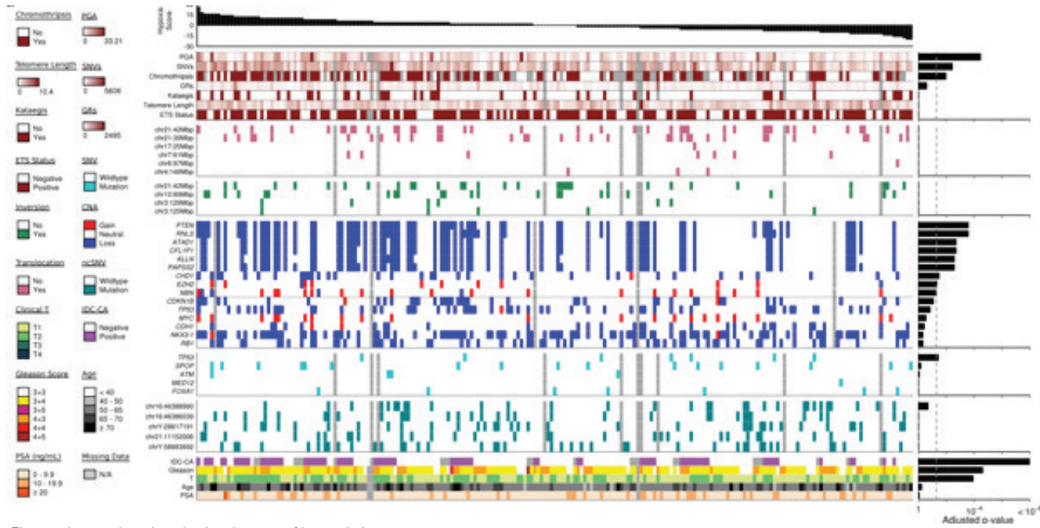


Figure above, showing the landscape of hypoxia in prostate cancer.

Two-Pronged Attack Against Lung Cancer

Institute scientists have used patient derived models to investigate the potential of using two targeted drugs together to treat small cell lung cancer.

Our Clinical and Experimental Pharmacology group harnessed their recently developed CDX (circulating tumour cell derived xenograft) platform – based on circulating tumour cells taken from individual patients and implanted into mice. The resulting tumour models mirror the biology of the donor, and their response to chemotherapy closely follows too.

The researchers looked at the combination of two types of targeted agents – PARP inhibitors and Wee1 inhibitors. They found that individually the two drugs had varying effectiveness in halting tumour growth. However as a combination, there was a better response, and one that was more durable than the response to established chemotherapy agents.

Exploration of the genetics of each tumour model suggested that those patients with defects in the DNA damage response pathway may be more sensitive to this new combination.

Lallo A,.. Dive C. The combination of the PARP inhibitor Olaparib and the WEE1 inhibitor AZD1775 as a new therapeutic option for small cell lung cancer. *Clinical Cancer Research* 2018; 24(20):5153-5164.

The Paterson Building Redevelopment Project

Project branding on the hoardings around the Paterson Building site

Following the devastating fire at the Paterson Building in April 2017, plans to redevelop the site at The Christie have been discussed in earnest.

So the announcement by Manchester Cancer Research Centre partners (The Christie NHS Foundation Trust, The University of Manchester and Cancer Research UK) of those innovative plans was met with great excitement.

The ambition for the Paterson Redevelopment Project is to transform the disaster of the fire into a bold and exciting future by creating one of the world's top five cancer research centres. In addition to housing the Cancer Research UK Manchester Institute, it will integrate other University of Manchester researchers and clinicians in a state-of-the-art building, who together will develop new ways to conduct team science approaches to accelerate the translation and adoption of research into the clinic to improve outcomes for patients around the globe. The multi-million pound development will be led by The Christie on behalf of the MCRC partners.

What has happened so far?

Over the summer, staff displaced by the fire were invited to participate in 'Synergy Group' workshops to offer their views about the potential for the new building. It was a great opportunity for staff to get together and discuss how we can make it a future-ready, collaborative environment to reflect our world-leading ambitions, and to ensure it's an effective and healthy space for everyone.

According to development pipeline requirements, a Principal Supply Chain Partner (PSCP) for the project was appointed and a project team formed. They have carried out initial design and technical work to inform the redevelopment of the building. The outline Business Case has been prepared and approved by the project partners.

Early works undertaken so far include specialist site surveys. New project branding has now been added to the hoardings, communicating the exciting new future for the site.

What is happening now?

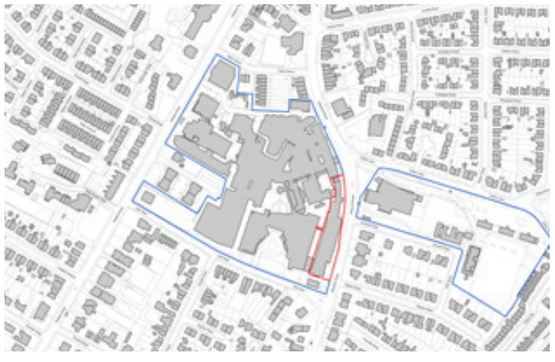
Following a review of the damage caused by the fire, The Christie has concluded that it is not feasible to leave the Paterson Building in its current state. Demolition of the building and its replacement with a modern facility represents the most appropriate way forward.

The Christie has submitted planning applications to Manchester City Council relating to the proposed demolition. The demolition planning application has now been approved and demolition will begin in February. The initial demolition works include erecting fencing and scaffolding, and removing some parts of the building.

Despite the devastating circumstances behind this redevelopment, we are excited about the unprecedented opportunities created by the fire. We are now able to be part of a truly unique research centre that will be integrated within the hospital with our scientists, researchers and consultants all working together in one place, developing and shaping treatment and research from basic scientific discoveries through to patient care. This is an incredible opportunity for us to make Manchester world leading for cancer research and treatment.

We are looking forward to moving back to Withington and to a new future.

Aerial view of the Paterson Building demolition site in red



Plan showing Christie site in blue and Paterson Building demolition site in red

3Rs Success at the Institute

By Janet Watson

Animal Welfare and Ethical Review Body

Our Institute's Animal Welfare and Ethical Review Body (AWERB) is responsible for overseeing the welfare of our laboratory mice, reviewing the ethics of our research projects involving animals and promoting all efforts to replace, reduce and refine (the 3Rs) our use of animals.

The 'body' comprises representatives of all staff involved with animal research and includes a veterinarian, a biostatistician and lay members. AWERB exists to support all staff in the Institute, whether or not they conduct animal research, and it advises Caroline Wilkinson who is the holder of our establishment's licence under the UK's Animal (Scientific Procedures) Act 1986.

3Rs Network

A focus on replacing, reducing and refining our use of animals (the 3Rs) is an important responsibility and the CRUK MI 3Rs Network was established several years ago to facilitate this approach.

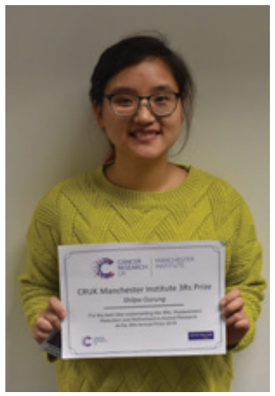
The network receives input from all research groups to share ideas and information, and arranges a stimulating programme of seminars and hosts impactful 3Rs' poster events each year to celebrate the innovations and improvements made by our scientists. We are in the process of re-establishing this group following the temporary relocation to Alderley Park and aim to resume the speaker programme later this year. Sharing our 3Rs' ideas and improvements with the wider research community is critical to implementing change in the approach to animal research to benefit animal welfare and promote ethical science. Two recent events highlight our progress on the 3Rs.

Events promoting the 3Rs

In September, a new collaboration was announced between Cancer Research UK and the UK's National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) to offer joint funding to support the sharing of 3Rs skills, tools and technologies within cancer research.

We were invited to contribute to the opening workshop, where Joanne Roberts of the Biological Research Unit at the Institute gave a well-received presentation on practical examples of how to develop and refine techniques in mouse models of bladder cancer, ocular melanoma and breast cancer.

Engaging scientists at the 3Rs poster event



3Rs poster prize winner Shilpa Gurung and Joanne Roberts speaking at NC3Rs workshop

In October, our 3Rs poster event at Alderley Park was joined by others at the site from AstraZeneca and Agenda Life Sciences. A total of 31 posters were on display championing improvements in animal housing, welfare, refined experimental techniques and methods replacing the use of animals. Prizes were awarded for the best poster from each company and an overall winner who demonstrated the use of mathematical modelling approach using 40% fewer mice. Helen Prior of NC3Rs awarded best poster prize to Shilpa Gurung and colleagues from the Skin Cancer and Ageing group for their novel work on 2D and 3D invasion assays in understanding the invasion properties of melanoma cells in vitro, reducing the number of mice used. Yannick von Grabowiecki and Callum Hall from the Tumour Suppressors group were also highly commended by Helen for integrating the 3Rs in their experimental approaches while investigating p53 mutant tumour cell growth in mice.

Funding

Institute researchers set to receive over £2 million funding from Cancer Research UK

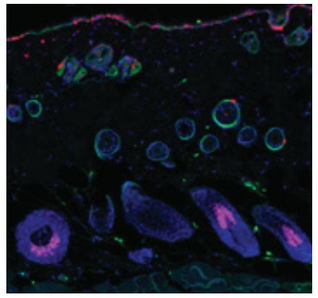
We are thrilled to announce that scientists from our Institute will benefit from one of the biggest funding grants ever awarded by Cancer Research UK.

Researchers from the Molecular Oncology group are set to receive over £2 million as part of a £19 million investment by the charity in a five-year global research project to investigate why some cancers are specific to certain tissues and not others. The funding for the ground-breaking research will come from Cancer Research UK's Grand Challenge awards – set up to revolutionise the prevention, diagnosis and treatment of cancer.

Institute Director Richard Marais and his group are part of a team of experts from Glasgow, the US and the Netherlands who beat stiff international competition to secure the funding. They will bring their world-leading expertise in skin cancer to the pioneering project which was selected by an international panel of experts from a shortlist of ten exceptional, multi-disciplinary collaborations from universities, institutes and industry across the globe.

Richard Marais said: "We are delighted to be part of Cancer Research UK's Grand Challenge. This award endorses Manchester's position in the global fight against cancer. It will allow us to answer fundamental questions about cancer biology, how it is caused in different tissues and why particular cancers kill some people but not others. This is not something we could do by ourselves, so being part of this international team is important to our success."

Richard Marais leads one of the UK teams in the Grand Challenge Consortium



An Image of healthy skin identifying the different types of cells that develop into melanoma (pink) or squamous cell carcinoma (green and red)

Cancer Research UK's Grand Challenge was established to help scientists attack some of the hardest, unanswered questions in cancer research. The international project team is looking to understand why genetic faults only affect certain tissues. If someone carries a potentially cancer-causing gene mutation, this fault can exist in every cell of the body, but only causes specific cancers, such as breast or skin. The team is studying why this is the case and will use this information to find ways to prevent or treat cancer in these organs.

Richard continued: "My team will be looking at DNA damage in skin cancer. We want to understand why a particular type of DNA damage causes the most-deadly type of skin cancer, melanoma, but not squamous cell carcinoma, a more common form of skin cancer.

"Sharing the knowledge gained by different researchers in the consortium will give us an insight as to why particular-types of DNA damage drive different cancers in different parts of the body."

This Grand Challenge funding will provide a fantastic opportunity for our researchers to address complex questions and cross new frontiers in our understanding of cancer, to transform the lives of patients.

EMBO Advanced Fellowship

We have previously reported that Postdoctoral Fellow Eduardo Bonavita was awarded a prestigious EMBO Long-Term Fellowship in 2016. So it is with great pleasure that we can now tell you he has been awarded an exclusive EMBO Advanced Fellowship.

The Advanced Fellowship offers an additional two years of funding for EMBO Long-Term Fellows who have demonstrated exceptional progress during their current postdoctoral work. Eduardo is based in Santiago Zelenay's Cancer Inflammation and Immunity group, where his work on tumour cell-intrinsic cyclooxygenase (COX)-2 and its associated inflammatory signature has demonstrated its potential as a useful biomarker of patient survival and potentially of response to immunotherapy. His contributions to the field have been recognised by his publication in high impact journal *Cell*.

This fellowship will enable Eduardo to complete his postdoctoral research at the Institute and work towards establishing his own line of research.

In addition, EMBO Advanced Fellows are entitled to attend a Laboratory Management Course for Postdocs, free of charge, which is a great opportunity for those taking the next step towards independence.

We wish to congratulate Eduardo on his continued success.

Meetings Update

Society for Melanoma Research annual conference comes to Manchester

Amaya Viros and Piyush Mundra speaking at SMR

In October 2018, Manchester hosted the 15th Society for Melanoma Research Congress. This was the first time the prestigious annual meeting has been held in the UK.

The SMR works to find the mechanisms responsible for melanoma and new therapies for the cancer, whilst bringing together scientists and clinicians from across the globe.

Institute Director and Molecular Oncology Group Leader Richard Marais, together with Medical Oncologist Paul Lorigan, who leads the Melanoma Team at The Christie NHS Foundation Trust, led the organisation of this important event in the melanoma research calendar.

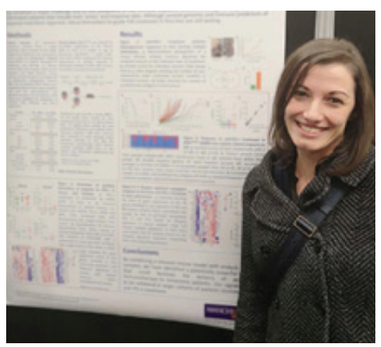
The opportunity to host this international meeting was a great triumph for Manchester – it recognises the important work the Christie does in the field of melanoma research and the global significance of Manchester's wider scientific community. The congress brought to our city world-leading scientists in melanoma research who presented the latest developments in the field, ranging from basic science to translational and clinical research.

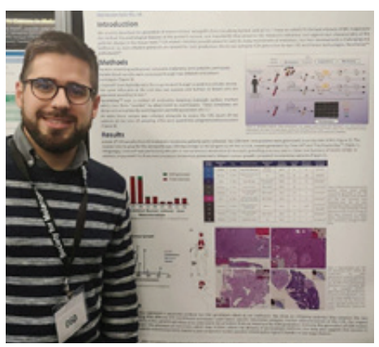
Clinical highlights of the conference focused on the new advances in immunotherapy (anti-CTLA4 and anti-PD1), which have revolutionised the treatment of melanoma patients. Of particular interest were talks about on-going clinical trials – we heard about the promising results for the use of immunotherapy in the adjuvant and neo-adjuvant setting of the disease, as well as new possible combination therapies and targets to enhance the efficacy of immunotherapy.

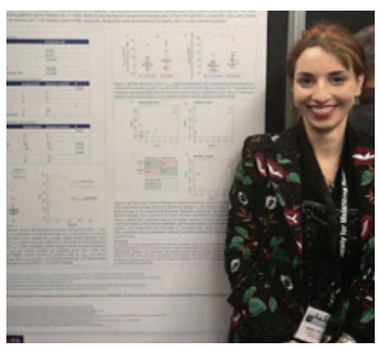
From the viewpoint of fundamental science, some of the key highlights came from the growing fields of tumour microenvironment and metabolic programming in melanoma.

It was pleasing to see that the research of CRUK Manchester Institute was widely represented at this meeting. We heard fascinating talks from Amaya Virós, who leads the Skin Cancer and Ageing group, presenting her work on how ageing affects melanoma; and from Piyushkumar Mundra based in the Molecular Oncology group dissecting the role of UVR exposure patterns in melanoma development and progression. Posters from postdoctoral scientists Elena Galvani, Sara Valpione and Pablo Garcia-Martinez from Molecular Oncology and Victoria Pelly from Cancer Inflammation and Immunity were also displayed. Additionally, Amaya Virós and Richard Marais chaired two different sessions.

Overall the meeting was a great success, encouraging interdisciplinary collaboration and helping drive forward progress in melanoma research. Critically, it gave Manchester the opportunity to showcase its impressive research and progress in melanoma in a global setting.







Elena Galvani, Pablo Garcia-Martinez and Sara Valpione present their posters

Richard speaking on melanoma and personalised medicine

NCRI 2018 Highlights

Last year the annual National Cancer Research Institute conference was hosted in Glasgow and the importance of Scotland hosting the meeting for the first time was highlighted through its opening by the First Minister of Scotland Nicola Sturgeon.

It was particularly pleasing to hear her acknowledge PrecisionPanc – an important initiative aiming to improve treatment options for pancreatic cancer patients that as an Institute we are part of – both Claus Jørgensen and Caroline Dive contribute.

The first day saw Institute Director Richard Marais giving a talk on precision medicine in melanoma. Claus Jørgensen gave a fascinating interpretation for tumour-environment interaction, talking about his work on tumour-stromal interactions in pancreatic ductal adenocarcinoma, in the 'best of translational science' session. Rebecca Lee, who was recently awarded her PhD, gave a presentation as part of the ACP McElwain prize she received earlier this year for her work on using circulating DNA in predicting melanoma relapse.

And last but not least, Allan Jordan from our Drug Discovery Unit talked about the development of DNMT1 inhibitors.

Claus Jørgensen

Rebecca Lee

Allan Jordan

International PhD Student Cancer Conference

The 12th International PhD Student Cancer Conference (IPSCC), an annual event organised by students for students, was held at The Francis Crick Institute, London in June 2018.

We are delighted to announce that Joe Maltas in the Cell Signalling group led by Professor Angeliki Malliri was awarded joint first poster prize (session 2), showcasing his work on "The nuclear roles of the Rac activator tiam1 in NSCLC". Posters were scored and ranked by the student delegates during the two poster sessions, with the top 3 posters from both sessions receiving prizes.

The conference was attended by over 90 students from CRUK and cancer research participating institutes from the UK, Italy, Germany and The Netherlands, with 18 talks and 74 posters scheduled over the two and a half days. The students enjoyed a welcome talk from Professor Sir Paul Nurse, and keynote lectures from Dr Patrick Vallance, Professor Fiona Watt, Professor Ester Hammond and Professor Steve Jackson. The CRUK Manchester Institute was represented by 12 second and third year students and provided a unique opportunity for them to present their work and network with some of Europe's best cancer research institutes - the event was a great success.

Colloquium 2018

In September, the annual Institute Colloquium took place at Lancaster University.

The three-day event offers the chance for our staff and PhD students to present and discuss their work and to develop collaborations with each other. It's also a great opportunity for our incoming students to meet their new colleagues and learn more about what we do.

Opening the first session, Institute Director Richard Marais gave an enthralling presentation on exciting new data generated by postdoc Haoran Tang in his group. In the subsequent sessions over the science-packed two days, there were a variety of interesting talks on both fundamental and translational research. Caroline Springer gave her first Colloquium talk, introducing her ambitions for DDU and emphasising its collaborative spirit. Regional Translation Lead for CRUK Commercial Partnerships Martin Bottomley provided a useful update on how he supports translating research in Manchester. New to the programme, winners of the inaugural CRUK MI Innovation Award also presented their 'dragon den' style pitches.

Each evening, a poster session took place. We had a record number of fantastic posters this year, making it especially challenging to select the best to receive one of two prizes. The Lizzy Hitchman student prize went to Colin Hutton from Systems Oncology for his PhD work describing a novel approach in identifying two fibroblast populations in pancreatic tumours. However, judging the best poster by a postdoctoral researcher or scientific officer was so difficult that two were awarded.

The joint winners were Victoria Pelly from Cancer Inflammation and Immunity for her work on the role of COX-2 inhibition and the efficacy of immunotherapy in cancer patients, and Anthony Tighe from the Division of Cancer Sciences based group Mitosis and Cancer Pharmacology, for his studies into the potential of PARG inhibitors in the treatment of ovarian cancer.

Colin and Victoria with their poster prizes

Anthony and his poster prize

ESMO 2018

Caroline Dive CBE is named "Rock Star of Science and Medicine"

In October, Allan Jordan from the Drug Discovery Unit was invited to chair two sessions and speak at ESMO, Europe's major clinical cancer conference, attracting over 28,000 attendees.

Allan notes "The ESMO meeting is very much focused upon forefront clinical practice and it's very rare for a chemist to be invited to participate – I was delighted that the reputation of the Drug Discovery Unit was recognised by ESMO and were invited to join the Organising Committee. This gave us the opportunity to share some of our thinking on the latest innovations on cancer drug design". At the meeting, Allan was invited to discuss three new Phase 1 clinical trials and contextualise how the advances presented might impact future drug discovery and development activities.

Also recognised at the conference was our Deputy Director Professor Caroline Dive CBE, who was named amongst the "Women Rock Stars of Science and Medicine" for stellar contributions in the field that have paved the way for advances in cancer research and biomedical science. Caroline also sat on the steering committee for the conference and was Joint Chair for ESMO 2018 Translational Research Track.

Allan discusses how Phase 1 clinical trials impact drug discovery

IPSCC Poster Prize Winner

By Joe Maltas

Joe with his travel mug prize

I was awarded joint first poster prize for my poster highlighting what I have achieved so far after three years of my PhD.

The poster was focused on nuclear localised Tiam1 and a novel interactor that I have found. I discussed the BioID mass spectrometry technique I used to find this interesting interactor. Furthermore I showed how this complex is regulating the migration of these cells and what this could mean in the context of a tumour in vivo.

It was rewarding to win the student poster prize as it was great that my work over the past three years was acknowledged. With one year left to go of my PhD it was nice to have a motivational boost to conclude the story behind my hypothesis of how nuclear Tiam1 is regulating non-small cell lung cancer invasion.

I also received a £20 amazon voucher and a travel mug – essential for keeping much needed coffee warm on the go.

Educational News

Meet the new students

Jack Ashton

Hi, my name is Jack and I'm from Harpenden in Hertfordshire. I originally studied Biomedical Science at The University of Manchester with an integrated year in industry at Novartis in Switzerland, working on cellular senescence and muscle sarcopenia. After graduating, I joined AstraZeneca as part of their innovative medicines graduate programme and began to form a strong interest in translational oncology research and the DNA damage response pathway. I completed three 8-month job rotations, two of which were oncology based in the Molecular Pathology and Early Clinical Trials groups respectively. I am therefore delighted to be joining Rob Bristow and the Translational Oncogenomics team here at CRUK Manchester Institute. I will be working on the role of tumour hypoxia in BRCA2 associated prostate cancer progression and look forward to utilising the close collaborations we have with the Christie Hospital and wider research community in Manchester. Outside of work I love playing sport and play hockey for Didsbury Hockey Club. The Peak District is also the perfect place to head out for a motorbike ride on a sunny day.

Alessia Catozzi

Hi, I am Alessia. I am Italian, from Ferrara, a small town near Bologna –between Venice and Florence and also between Rome and Milan – a beautiful little city overall. I completed my undergraduate in Biotechnology in Bologna and decided to undertake my MSc in the Netherlands, at Wageningen University. Wageningen is in central Netherlands, and although quite isolated was great fun. I performed my research thesis on cancer metabolism and decided to learn more about it during my internship at Harvard Medical School in Boston, where I spent half a year. The winter in Boston can be brutal, especially while you freeze waiting for the bus. However, during my time there I realised that cancer metabolism was not what I wanted to study for my PhD and that I preferred my research to be more translational. I decided to join Caroline Dive's group and I am going to work on the role of neurogenic transcription factors in small cell lung cancer. Small cell lung cancer is a very heterogeneous tumour and the final aim of my project will be to try and classify it based on its molecular profile and expression patterns of neurogenic transcription factors. When I am not in the lab, I enjoy playing volleyball, cooking and going to as many concerts I can – fortunately Manchester offers many opportunities, which I hope to seize soon.

Felix Heider

Hi, my name is Felix and I have started my PhD in the Systems Oncology group led by Claus Jørgensen. My project will focus on the heterogeneity of cancer-associated fibroblasts and I will try to delineate regulators of fibroblast activation in pancreatic cancer. I grew up in Germany in a small village called "Moitzfeld", which is close to Cologne. For my undergraduate studies I went to the University of Cologne, with the exception of my master thesis, which was carried out in collaboration with the company Miltenyi Biotec and focused on genome editing of haematopoietic stem cells for gene therapeutic approaches. Following on, I continued to work at Miltenyi for a year before hearing about the great studentship opportunities at CRUK MI. I am looking forward to spending the next four years in Manchester, a city that has so much to offer. Outside of academia, I used to enjoy competitive swimming. Although I have since quit swimming after moving to Manchester I still play sports on a daily basis and have traded the pool for the gym. I also enjoy cooking and reading in my free time as well as enjoying the landscape that UK's National Parks have to offer.

Ryan Guilbert

Hello, my name is Ryan and I come from Guernsey in the Channel Islands. I recently completed my undergraduate degree in Biochemistry at the University of Surrey, where for my final year project I investigated the transcriptional effects of a number drugs commonly used to treat bipolar disorder. During my undergraduate degree I undertook a placement year with AstraZeneca in Cambridge where I investigated the use of ADP biosensors for profiling kinase kinetics. I have joined the Cell Signalling group with Angeliki Malliri and I am delighted to be part of this research institute. Here I will be investigating the function of a number of GEFs in small cell lung cancer. I am looking forward to this exciting project and all the opportunities available to me at the Manchester Institute and the wider university. Outside of academia I am a judo and windsurfing enthusiast.

Shilpa Gurung

Hi, my name is Shilpa Gurung. I am undertaking my PhD in the Skin Cancer and Ageing group led by Amaya Virós. I will be studying the role of adipocyte biology on melanoma progression. I am particularly interested in studying how ageing of the skin affects adipocyte biology and how these microenvironment changes affect melanoma progression. I am originally from a small country in Asia called Nepal. I completed my high school in Nepal and moved to Hong Kong where I completed my undergraduate studies majoring in Applied Biology with Biotechnology. With the aim to study cancer biology, I enrolled for an MPhil under Dr Terence Lee studying the influence of the tumour microenvironment on the enhancement of cancer stemness properties. The project introduced me to the field of cancer biology but also to the major role tumour microenvironment plays on providing a favourable environment for cancer development and progression by protecting tumour cells from chemotherapeutic drugs and in development of stemness properties. This experience motivated me to apply for a PhD project studying the communication between cancer and its microenvironment. I am very much delighted to be part of a team comprising of clinicians and scientists to better understand cancer biology from both perspectives. Outside of work, I enjoy hiking in the countryside. I find Manchester to be the perfect blend of city life and nature and I am very much looking forward to making the most of my time here.

Amelia Jones

My name is Amelia and I grew up in a small village in Cornwall. Before joining CRUK Manchester Institute I studied biochemistry at Cardiff University. During my undergraduate degree, I undertook a placement year at GSK where I worked in the Cell Sciences department, optimising protocols for monoclonal antibody production. On returning to Cardiff for my final year, I worked on a project to develop early diagnostic tools for lysosomal storage diseases. I enjoyed all my research throughout my undergraduate degree, but I knew that I wanted to move more into basic science/cell biology, so I was thrilled to be accepted for a PhD in Iain Hagan's Cell Division group. Our group uses fission yeast and human cells to investigate how cell division is regulated, and my project will explore the specific function of a subunit of protein phosphatase 2A in cell cycle control. Outside of work I love to read – I love classics especially but am open to anything. I also play saxophone (but only when my housemate isn't in). When I was 17 my family moved north and now live just an hour outside of Manchester, so I know the area quite well and I am looking forward to spending the next 4 years exploring it properly.

Katherine Moran

Hi my name is Katherine. I'm originally from a small village in the Yorkshire Dales, but have spent the last four years studying at St Catharine's College in Cambridge. I completed my undergraduate degree in Biological Natural Sciences and then continued for a further year carrying out a research masters investigating the regulation of morphogenetic events during Drosophila oogenesis. I really enjoyed working in a research environment and decided that this was definitely the career path I wanted to follow. I am now pleased to be back up north having joined the Cell Plasticity and Epigenetics group, led by Maxi Portal. I will be working on the molecular mechanisms underlying reversible drug tolerance with a specific focus on the role of non-coding RNA molecules. Away from the lab, I enjoy dance classes, photography and walking in the Lake District and Yorkshire Dales.

James Stratford

Hi, I'm James and I have just started a PhD project at CRUK MI in the Drug Discovery Unit led by Caroline Springer. I grew up just a short drive away in south Cheshire and spent the last 4 years of my life living in Newcastle whilst studying for a MChem in Chemistry with Medicinal Chemistry at Newcastle University. During my time in Newcastle I undertook a project in the Northern Institute for Cancer Research, where I designed and synthesised novel small molecule inhibitors of the thrombopoietin receptor for the treatment of essential thrombocythemia (platelet cancer). Alongside this, I also developed an interest in chemical fluorescence and I am very excited to have been given the opportunity to combine both of these passions here in Manchester, as I am now working on developing near infrared molecular imaging probes with applications in the early detection of cancer metastasis. Aside from the cutting edge research, Manchester also provides me with the opportunity to pursue my love for sport; with Old Trafford cricket ground just around the corner, some fantastic football teams in the region and Manchester United!

Alexandru Suvac

Hello, I'm Alexandru and I originally hail from Moldova. Having emigrated to Ireland when I was ten, it went so well that I decided to do it again and move to Manchester! All jokes aside, I came here in the pursuit of my passion: research. My first real research experience was in the Genome Stability lab of Noel Lowndes at National University of Ireland Galway, where I realised that research is what I wanted to pursue after university. Having just completed my undergraduate degree in Genetics at Trinity College Dublin, I joined Rob Bristow's Translational Oncogenomics group at CRUK MI. I am interested in elucidating the molecular link between tumour hypoxia and selection for PTEN loss in prostate cancer, and then to test whether this drives a more severe prostate tumour. To be honest, I can't wait for the next four years and what I will discover. On top of this, living in the UK is quite similar to Ireland, which is great – people have the same friendly attitude and there are lots of options to meet with friends and keep entertained.

Zena Salih

Hi, my name is Zena and I'm from Scotland. I completed my undergraduate medical degree at The University of Glasgow in 2009 and chose to move to Manchester in 2011 to complete my postgraduate medical training. Following this, I was successfully appointed to The Christie in 2014 to undertake my specialist training in Medical Oncology, gaining my core completion of training as a Medical Oncologist in August 2018. As a clinician, I have witnessed first-hand the dramatic improvement in patient outcomes with the use of targeted and immunotherapies in melanoma. However, the identification of the mechanisms, underlying response and resistance to immunotherapy, forms a crucial topic of modern oncology that has yet to be fully explored. In September 2018, I had the privilege to join Richard Marais' group as a Clinical Fellow. My PhD will focus on the hypothesis that a multi-component fully human ex vivo organoid system can facilitate personalised immuno-oncology approaches in melanoma. This model will be used to study mechanisms of response and immune evasion to immunotherapy, with the potential to predict treatment response and test new drugs. I relish the opportunity to work alongside world leading experts, in the field of molecular oncology, to advance understanding in this area with the hope of having a clinically meaningful impact on patient outcomes and translational research. Away from work, I am a bit of a gym junkie, but I also love socialising and I'm a big foodie, so love trying out the latest Mancunian eateries.

Awards Prizes and Events

Distinguished Achievement Award Winners

We are delighted to announce that Stuart Pepper, Caroline Wilkinson and Kenny Nolan were together Team Winners in The University of Manchester Distinguished Achievement Awards 2018.

The exceptional trio were nominated by Institute Director Richard Marais for the Small Team Award. Judges of these annual awards were looking for outstanding performance and how the teams have significantly and tangibly contributed to maintaining a positive, open and respectful working environment. In addition, they had to demonstrate that they have a shared ethos which has led to a significant one-off achievement.

It was the tragic fire in the Paterson Building in April 2017 that brought together the Institute's Chief Operating Officer Caroline Wilkinson and Chief Laboratory Officer Stuart Pepper, together with Kenny Nolan, Deputy Director of Estates and Facilities at The University of Manchester, as a team.

This incredible team was nominated for their expert and consistent support throughout the road to recovery since the fire. Without their commitment, diligence and level-headed approach we would not be where we are now.

Working together, from the outset they provided much needed support, ensuring the salvage of critical samples and helping staff who had lost personal items with emergency accommodation or a way of getting home. As the scale of the disaster became apparent, the team managed the enormous logistical challenges of relocating staff, emptying the building, providing temporary storage for salvaged items and moving and servicing crucial scientific instruments. They chaired regular and deeply complex meetings with the University, the Christie and CRUK as well as solicitors, loss adjusters and insurers. Within four months they had helped to relocate 80 staff.

Later, the team focused on managing the move to Alderley Park. This involved identifying space and instigating complex negotiations, as well as justifying necessary modifications to the various labs.

Throughout this whole process what was notable was their visibility and compassion as they communicated regularly with staff and beyond about the progress, particularly valuable in such distressing times.

Thrown together in unusual and testing circumstances, this exceptional team tackled the challenges with great positivity, humour and respect and ably delivered the immediate and mid-term solutions for the Institute.

The nomination was supported by Caroline Dive, Tim Illidge, Peter Reid and Core Facility members Garry Ashton, Lisa Doar and Wolfgang Breitwieser. On behalf of the team, Stuart Pepper received the prize from Nancy Rothwell, President and Vice-Chancellor.

Stuart Pepper commented: "We are thrilled to receive this award. The relocation of staff from the Paterson Building after the fire was a complicated project that required a huge amount of effort. This award not only reflects the work of the team but the fantastic support from our colleagues within the CRUK MI and the wider University."

Stuart receiving the award from Nancy Rothwell

STAy up to date news

By Ester Fagnano of the STAy committee

STAy (short for Science Take-Away) is run by junior scientists and brings together CRUK Manchester Institute and the University's Division of Cancer Sciences early-career students, postdocs and scientific officers. We get together to network, share ideas and discuss topics of scientific relevance in a social setting.

Our monthly events aim to:

- Provide a forum for discussions and training related to our research
- Help us communicate our work well and engage with the wider world of science
- Develop social opportunities and networking for early career scientists

In October, STAy organised a week long Treasure Hunt that challenged the Institute's new starters and old veterans to answer questions and find out facts about the people, research groups and facilities, in the Oglesby Cancer Research Building and Alderley Park. Prizes were awarded to the best-performing teams, and the event was greatly enjoyed by all who took part, with many people making new connections.

November saw the first of two patient-focused engagement events; "STAy Patient With Us" explored the challenges that scientists can face when speaking to patients and members of the public about their work in cancer-related research. With expert the help of Clare Dickinson, a CRUK Senior Research Nurse based at the Christie NHS Foundation Trust, Tim Hudson, our CRUK Research Engagement Manager, and public engagement maestro from DDU Allan Jordan, we aimed to provide researchers who want to engage in patient- and public-focused events with an opportunity to address common concerns and ultimately increase their confidence when communicating their work to the wider community. Particularly useful were role plays where participants alternated between patient and researcher perspectives.

Our next eagerly awaited gathering will be "Behind the Labels", an event allowing researchers to directly engage with patients and clinicians. The event, to be held in February 2019, will consist of an evening of informal chats where researchers, patients and clinicians can interact, share experiences and address each other's questions, with the aim of getting to know the people sometimes hidden 'behind the labels' in cancer-related research and healthcare.

Future events will cover topics such as career development and grant writing, in addition to social events such as "Speed Networking" and our annual Science Showdown, showcasing the fantastic science performed around the whole of The University of Manchester, and promoting interactions within different scientific faculties.

Tips for patient engagement

Treasure hunt

We welcome ideas and input from everyone. So if you would like to suggest topics or join the committee please come speak to us, or follow us on Twitter @ScienceTakeAway.

Institute Clinical Fellow wins McElwain Prize

We are delighted to announce that Rebecca Lee from the Molecular Oncology group won the Association of Cancer Physicians McElwain translational research prize for "Circulating tumour DNA as a tool to guide clinical decision making in melanoma".

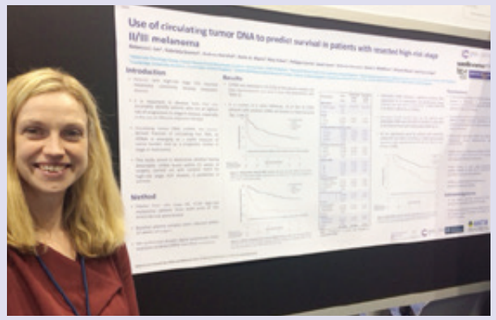
These annual awards were established by the friends and colleagues of Professor Tim McElwain to commemorate his extraordinary contribution to the development of Medical Oncology in the UK.

Rebecca has been a Clinical Fellow for the past our years and recently passed her PhD viva – congratulations! She is now back at the Christie NHS Foundation Trust and was recently awarded an NIHR funded clinical lecturer post.

Upon receiving the McElwain Prize, she says, "I'm really honoured to receive this prize and I want to thank everyone in the Institute for their support, especially Molecular Oncology, Molecular Biology Core Facility, Clinical and Experimental Pharmacology and the Biobank, who all helped me greatly with these projects".

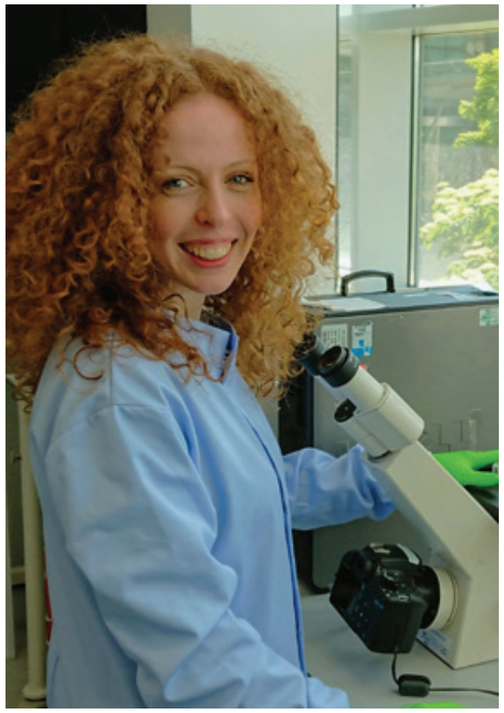
As part of the prize, Rebecca gave a thought-provoking and well-received presentation at the National Cancer Research Institute Conference at Glasgow in November this year.

We are all incredibly proud of her achievements and wish her all the best in the next stage of her career.



Rebecca with her winning poster

Winner of the 2018 BACR Chris Marshall Prize for Cell Signalling



Zoi Diamantopoulou

Until recently, Zoi Diamantopoulou was a Postdoctoral Fellow in Angeliki Malliri's group where she was based for several years, and it was while she was still there that she was awarded the prestigious BACR Chris Marshall Prize for Cell Signalling. This award recognises and rewards the achievements of a young scientist in the field of cell signalling.

Chris Marshall was a world renowned cell biologist best known for his contributions to cell signalling via Rho family of GTPases, especially to our understanding of how the Ras-Raf-Mek-Erk pathway enables cancer cells to disseminate in the body.

Since Zoi has been at the Institute, she has made a number of important contributions in science and most notably uncovered dual mechanisms of inhibiting YAP/TAZ by TIAM1, a specific GEF for Rac1, that oppose invasiveness of colorectal cancer cells, leading to a first author publication in Cancer Cell. Critically she demonstrated that TIAM1 interacts with TAZ in the cytoplasm to promote TAZ degradation by the destruction complex, whereas it antagonises binding of TAZ/YAP to TEAD in the nucleus. This study is of great significant interest in the field as it provides new insights into the Rac1 and YAP/TAZ signalling pathways.

Upon receiving the prize, Zoi said, "I am truly honoured that BACR recognised my scientific contribution of how different signalling pathways regulate cell migration and I deeply appreciate that I was nominated by Professor Caroline Dive, an accomplished and renowned woman in science."

Zoi received a prize of £1,000 and an invitation to present her research at the British Association for Cancer Research Student Conference. Held at the Francis Crick Institute in November, Zoi was pleased have the opportunity to discuss her research with experts in the cancer cell biology field.

We warmly congratulate Zoi on her success and wish her all the best in pursuing an independent research position.

Professorships announced

The Institute was proud to host the inaugural lectures of recently promoted Professor Georges Lacaud and Professor Angeliki Malliri in October last year.

Professor Paul Coulthard chaired the event in his capacity as Faculty Vice Dean and Head of the School of Medical Sciences. The formal event was supported by MCRC Director Rob Bristow, Head of Division of Cancer Sciences Tim Illidge, as well as our own Caroline Dive and Caroline Springer.

Introductions were given by Institute Director Richard Marais, who first outlined Georges Lacaud's career in the field of haematopoietic development and blood cancer, and highlighted his key achievements over the last ten years. Georges was then invited to deliver his Professorial Inaugural Lecture: "From Gene Therapy to Stem Cell Biology". Georges, who leads the Stem Cell Biology group at the Institute, gave an interesting overview on his research career to date, highlighting the beginning in his home country of France at University Louis Pasteur in Strasbourg and his all-important move as CRUK Group Leader at Manchester.

Next up to deliver her Professorial Inaugural Lecture was Angeliki Malliri. Richard gave an overview of Angeliki's research focus on the RHO GTPases and her most notable discoveries. Angeliki, who leads the Cell Signalling group, presented: "My TIAM investigating how cells move". She entertained the audience, which included her husband and two children, with anecdotes of her research journey and the choices she made. Angeliki started her career in her home nation of Greece before arriving in Manchester via a PhD in Glasgow and a stint as a postdoctoral research fellow at NKI in the Netherlands.

We warmly congratulate both Georges and Angeliki on their well-deserved promotion to Professorship.

Image right: Inaugural Professors Georges and Angeliki with hosting entourage

Eduardo Bonavita

Acteria Prize winner

Eduardo Bonavita, a Postdoctoral Fellow in the Cancer Inflammation and Immunity group led by Santiago Zelenay, won the Acteria Prize for the best PhD thesis in Immunology in Europe.

Acteria Prizes are awarded by the European Federation of Immunological Societies, with the aim of singling out Europe's young talents in immunology. Eduardo, who completed his PhD in Italy, was nominated by the Italian Society of Immunology, Clinical Immunology and Allergology (SIICA) for his outstanding work.

Eduardo joined the Institute in 2016 from the renowned laboratory of Professor Alberto Mantovani where he carried out his ground breaking doctoral research. His findings that the deficiency of long pentraxin 3 (PTX3) was associated with higher tumour burden, increased proinflammatory cytokine production, increased complement deposition and higher gene instability, as well as being epigenetically regulated in selected mesenchymal and epithelial cancers, critically demonstrated that PTX3, a regulatory molecule of the humoral arm of innate immunity, acts as an extrinsic oncosuppressor gene in mouse and humans and led to a key first-author publication in Cell. Further work characterising a new molecular mechanism regulating NK cell biology in cancer resulted in another high impact publication in Nature.

Soon after Eduardo arrived at the Institute, he was awarded a highly competitive European Molecular Biology Organization (EMBO) Long-Term Fellowship and continues to make important discoveries and author publications.

The prize includes an honorarium and 150,000 euros for his lab. Eduardo was invited to give a specially organised Plenary Lecture at the European Congress of Immunology in September last year. He was presented with the prize at the congress in Amsterdam, where he also gave two talks.

Commenting on the meeting, Eduardo said "in the same meeting where I received the prize I was also selected to give a short talk and I presented the data I obtained during the last two to three years in Santiago Zelenay's lab. In this presentation I described the fundamental role of Natural killer cells in orchestrating tumour inhibitory inflammation and driving the anti-tumour response in patients treated with immunotherapy".

Early Career Researchers mentoring circle

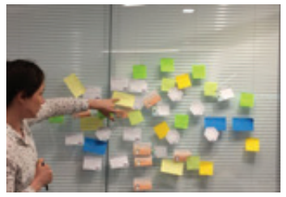
Effective mentoring is critical for professional success at every career level in scientific research. It can help further career prospects by increasing competitiveness in a chosen field and provide support for periods of transition and change.

"If I have seen further it is by standing on the shoulders of giants."

— Isaac Newton

Traditional mentoring consists of pairing a junior trainee (i.e. a postdoctoral researcher) with an experienced senior investigator in the same academic discipline. Nowadays a career in science is extremely versatile, making it difficult for a single mentor to fulfil all the expectations of the mentee. Peer-to-peer mentoring groups are formed of researchers at similar stages in their careers who become both mentees and mentors through sharing their own experiences and working towards common goals, resulting in a dynamic and approachable method of mentoring to complement more traditional mentoring. Inspired by previous successful initiatives, we launched the Early Career Researchers mentoring circle (ECRmc) within the Institute, together with colleagues from The University of Manchester's Division of Cancer Sciences, that focused around strategic professional development and guided self-assessment, with the overarching aim of identifying future career opportunities and enhancing our chances of success in obtaining them.

A small group of researchers in postdoctoral or scientific officer positions based at the CRUK MI, OCRB and The Christie NHS



ECR mentoring circle holds interactive sessions and elevator pitch

Foundation Trust joined the Early Career Researchers mentoring circle pilot programme in May 2018. Each session, organised on a monthly basis, was led by one or two members of the group and covered topics that were chosen by all participants to reflect a range of interests. Through the use of presentations, interactive exercises and discussions, we have worked on career self-assessment, effective networking and communication (through an elevator pitch) and shared resources and guides for funding opportunities and grant writing. We have discussed ways to improve management of people and time and the role public outreach and engagement can play in our career. Most importantly, we have built a friendly and confidential network of peers who will no doubt support each other outside the sessions.

We are currently evaluating this initiative and will likely launch a new call in February 2019. Let us know if you are interested in joining.

Committee:

Alba Maiques-Diaz
Isabel Peset Martin
Victoria Pelly
Franziska Baenke

ECR mentoring circle

Dexter Prize 2018

We are delighted to announce that Rebecca Lee was awarded the Dexter Prize for Young Scientists for 2018. The prize recognises the most impressive scientific achievement of the year and is named after former Director of the Institute, Mike Dexter.

At the time, Rebecca was a Clinical Fellow and during her PhD in the Molecular Oncology group she demonstrated remarkable ambition and determination in translating her studies to the clinic. She published an Annals of Oncology paper in the beginning of 2018, demonstrating the utility of ctDNA analysis of stage II/III melanoma patients in predicting both disease-free and long-term survival. She has followed up this retrospective study with a prospective study, in collaboration with a team in Australia, and this study has been submitted to Annals of Oncology. Using these studies as a spring board, Rebecca has written and successfully sought ethics and funding for a clinical trial, CACTUS: A parallel arm, biomarker driven, phase II trial to determine the role of circulating tumour DNA in guiding a switch between targeted therapy and immune therapy in patients with advanced cutaneous melanoma, which is due to open at the Christie in April. In addition, she has written, and is actively seeking funding for a second trial, DETECTION, in which circulating tumour DNA will be used to guide therapy for stage IIB/C surgically resected melanoma. Rebecca is also the recipient of last year's ACP McElwain Prize, which was presented at the NCRI meeting in Glasgow in November. She also successfully defended her thesis in November. Rebecca has recently secured an NIHR Clinical Lectureship position, which will enable her to finish her specialty training at the Christie NHS Foundation Trust and continue her academic training at The University of Manchester.

We wish to congratulate her on this impressive achievement and wish her all the best in future career.

Lung cancer researcher goes to USA on a Fulbright Award

By Stuart Williamson

Stuart enjoying the sunshine outside Stanford University

With the support of a CRUK-Fulbright Scholar award, since September 2018 I have been fortunate to have the opportunity to continue my research for six months in the United States – I am normally found in the labs of the Clinical and Experimental Pharmacology group working on lung cancer.

The Fulbright Award scheme was established post World War II by the U.S. Government as a global academic exchange programme, with the belief that providing an opportunity to immerse oneself in another culture, nations would no longer find a reason for war. Since then, the Fulbright Programme has grown to support every discipline, with exchange programmes between the United States and partner nations supporting awards for artists, scientists and business professionals. Notable alumni have gone on to be politicians, Pulitzer Prize winners and Nobel Laureates (so no pressure!).

Last year the US-UK Fulbright Commission celebrated their 70th anniversary, although, this is the first year that CRUK have partnered with Fulbright to support a cancer research specific award.

I am using my Fulbright Scholar award to work with Professor Julien Sage at Stanford University, which is situated about 35 miles southeast of San Francisco, in the heart of Silicon Valley. Professor Sage is an expert in Genetically Engineered Mouse Models of Lung Cancer and has developed a number of models that allow lung cancer to be studied from its initiation within the lung, through to extensive metastasis in the presence of a functioning immune system. These models complement my previous work using patient derived material, which often come from cancer cells which have already metastasised out of the lung, and are grown with the absence of an immune system, making studies of initial metastasis and the early stages of cancer challenging.

In Stanford, I am continuing my work on Vasculogenic Mimicry, a process where tumour cells can generate their own blood vessels, independently to the body's normal process. We have previously shown that Vasculogenic Mimicry is present in more aggressive tumours, and that it has an important role in tumour growth, chemotherapy drug delivery and drug response. By exploring Vasculogenic Mimicry in Professor Sage's mouse models, I am learning more about when this process begins and how it contributes to the events leading to metastasis. Also, as it is an academic exchange, I have been able to share my experience looking at circulating tumour cells in mouse models with the lab here at Stanford. Excitingly, my work so far has shown the biology driving Vasculogenic Mimicry in patients' tumours is the same as the process in the mouse models, leaving me with plenty of work to do in my time left!

In addition to lab work, my award is allowing me to experience life as a postdoc at Stanford. The University is famed for its multidisciplinary team work, utilising cutting edge technology and collaborating with industry partners in Silicon Valley. This cross discipline collaboration is supported by philanthropic programmes such as the "Chan-Zuckerberg Biohub", but also an ethos of working together to solve problems. It has been exciting as well as intimidating to learn that many of the cutting edge technologies being used were developed in the labs around me (RNAscope, CyTOF, ATAC-seq and even Flow Cytometry, to name just a few!).

With success however comes a price as the Bay Area has one of the highest costs of living on the planet, driven by the close proximity of Stanford, and Berkeley UCSF along with the headquarters of Facebook, Google and Apple to name just a few. I hope to return to the UK later this year with many newly developed skills and experiences.

Stuart (top right) is part of a multidisciplinary cohort of UK Fulbright scholars travelling to the US

Accelerating research

Our Deputy Director Professor Caroline Dive CBE is part of the winning team who have recently received funding from Cancer Research UK in partnership with two European charities, the Italian Association for Cancer Research (AIRC) and the Spanish Association Against Cancer Scientific Foundation (FC AECC), for ACRCelerate: Colorectal Cancer Stratified Medicine Network.

CRUK's Accelerator Award enables translational research by funding cross-institutional teams to produce tools, platforms and resources that will transform the research landscape. ACRCelerate: Colorectal Cancer Stratified Medicine Network is led by Professor Owen Sansom at the Cancer Research UK Beatson Institute in Glasgow and will deliver on an ambitious project with up to £5 million funding to find new routes for personalised bowel cancer treatment.

The European-wide team will be looking to identify new targets so that patients can be stratified into different treatment groups, which may lower the risks for patients in clinical trials.

Caroline and her team in Clinical and Experimental Pharmacology will contribute to the development of novel preclinical models, which will also help to reduce the level of animal research required.

Staff News

A graduation and a wedding

It's been a great year for Saba Ferdous, computational biologist within the TARGET team in the Clinical and Experimental Pharmacology group.

Last summer she graduated from UCL and she also got married. Big congratulations are in order!

Saba and her husband, Asad Ashfaq, had two celebrations: a Pakistani wedding in April and an English one in August

Suppliers a Go-Go

On 16 November, we had a great event where scientists had the opportunity to meet with different suppliers and to discuss new technologies and appliances.

David Jenkins, from our Finance Department, was instrumental in organising this exhibition that attracted over 15 suppliers and included workshops and fundraising for Movember.

A big thank you to all the suppliers who took part.

David sharing a laugh with one of the suppliers

Our own Best British Home Cook!

Pippa (middle) with the judges Mary Berry, Chris Bavin and Dan Doherty and the host Claudia Winkleman

We were so excited to see one of our own being crowned as the "BBC Best British Home Cook" last Summer.

Pippa Middlehurst, who was a Biobank technician based within the Molecular Oncology group, amazed the judges with her cooking skills and was the winner of the first edition of the TV show.

"It was a great experience and I learnt so much about cooking and what I'm capable of. I am now going to follow my passion in cooking and see where that takes me", said Pippa.

Pippa is now doing workshops, supper clubs and keeps delighting us with her recipes with an Asian twist on her blog Pippyeats.com.

Getting fit with Jo

Joanna Grabarek, from our Drug Discovery Unit, is teaching Zumba and fitness classes at Withington Baths and Leisure in her spare time.

With 13 years of experience as a Fitness Instructor, Jo can help you get fit while sharing a laugh in her classes. If you are interested in Zumba Fitness, Zumba Toning (zumba with weights) or PiYo (low impact strength workout inspired by pilates and yoga), don't hesitate to get in touch with her! Find more: http://www.lovewithingtonbaths.com/

New Born!

Eadie, Bess and Tim

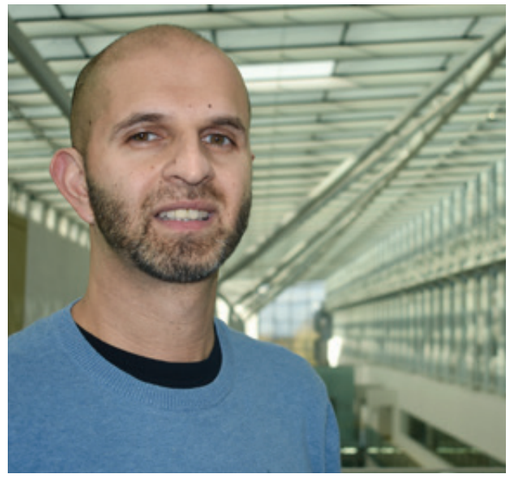
Tim Hudson, Research Engagement Manager, welcomed his new baby girl in November!

Bess Sparling Hudson was born at home on 12th November, weighting 7lb 8oz. Her dad tells us she is doing really well and is loved very much by her big sister, Eadie.

Conference participation

Ali Raoof, from our Drug Discovery Unit, attended the Concept Life Conference at Alderley Park last October.

This chemistry/medicinal chemistry conference at AP attracted nationwide scientists from both industry and academia. We were very proud to have Ali representing our DDU and presenting one of their programmes.



Ali Raoof

In the spotlight with Patricia Muller

Patricia Muller is one of our Institute Fellows who joined us in May 2017. Hailing from the Netherlands originally, she came to us from the MRC Toxicology Unit at Leicester, where she was working on the function of mutant p53 in chemoresistance. She now leads the Tumour Suppressors group here at the Institute where she continues to pursue her interest in p53, the most frequently mutated gene in human cancers. In particular, she aims to investigate further the function of mutant p53 proteins and whether novel therapeutic strategies to target mutant p53 expressing tumours can be developed.

1. What is your favourite part of the UK?
Scotland (despite all the rain)

2. What was your best ever holiday and why?
Porto in Portugal- lovely city, sun, beautiful surroundings, sea and Port

3. Which website do you always check, and why?
Dutch news to make sure I can keep up with my mum

4. What is your favourite film?
Many, but the last film I remember I got quite emotional from was Selma about a march for equal voting rights in Alabama

5. What is your favourite band/ singer?
REM

6. If you had to change careers tomorrow, what would you do?
A professional painter of landscapes or portraits (not a chance that that will happen anytime soon, but nice to keep dreaming about)

7. What is the most important lesson that you have learnt from life?
Try to find the positives in what you are doing and enjoy the small things. The gloomier you are about things, the harder it is to get it done

8. Name three things you would take with you to a desert island?
When I went on a training course for interviewing candidates for jobs, this was quite a loaded question. This question was meant to gain insight into the personality of the applicant. Do they come up with practical things, family or friends or something else? Can someone think on their feet and answer an out-of-the box question at all? I was (and am) not a fan of this question, it has to be said. Other than the obvious boyfriend Ian and most importantly my cat Suki, I am struggling to not come up with another cheesy answer like an emergency boat to get the hell out of there

9. What is your greatest fear?
Scorpions-two weapons on the front and the back

10. How would you like to be remembered?
Cheerful? At times serious, but mostly fair?

11. If you could change one thing in your past what would it be?
My dad passed away a few years ago and I only found out afterwards how much of a sacrifice he once made for me. My biggest regret is that I never really had the guts to talk to him about this and to simply thank him

12. What is your signature dish to cook?
Risotto- but I am not sure it will hold up to Italian scrutiny

13. You've just won the lottery and have £5 million pounds to spend. What do you buy first?
As I just bought a house I am currently saving up to replace my car. It has decided to fail me a few times in the last few months so I would love a new one- a nice electrical one with a long range

14. What is your idea of perfect happiness?
A nice cup of tea or coffee, no worries, lovely sunset with good company and nice food (preferably all together)

15. What keeps you awake at night?
The computer programmer-levels of caffeine in my bloodstream.

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