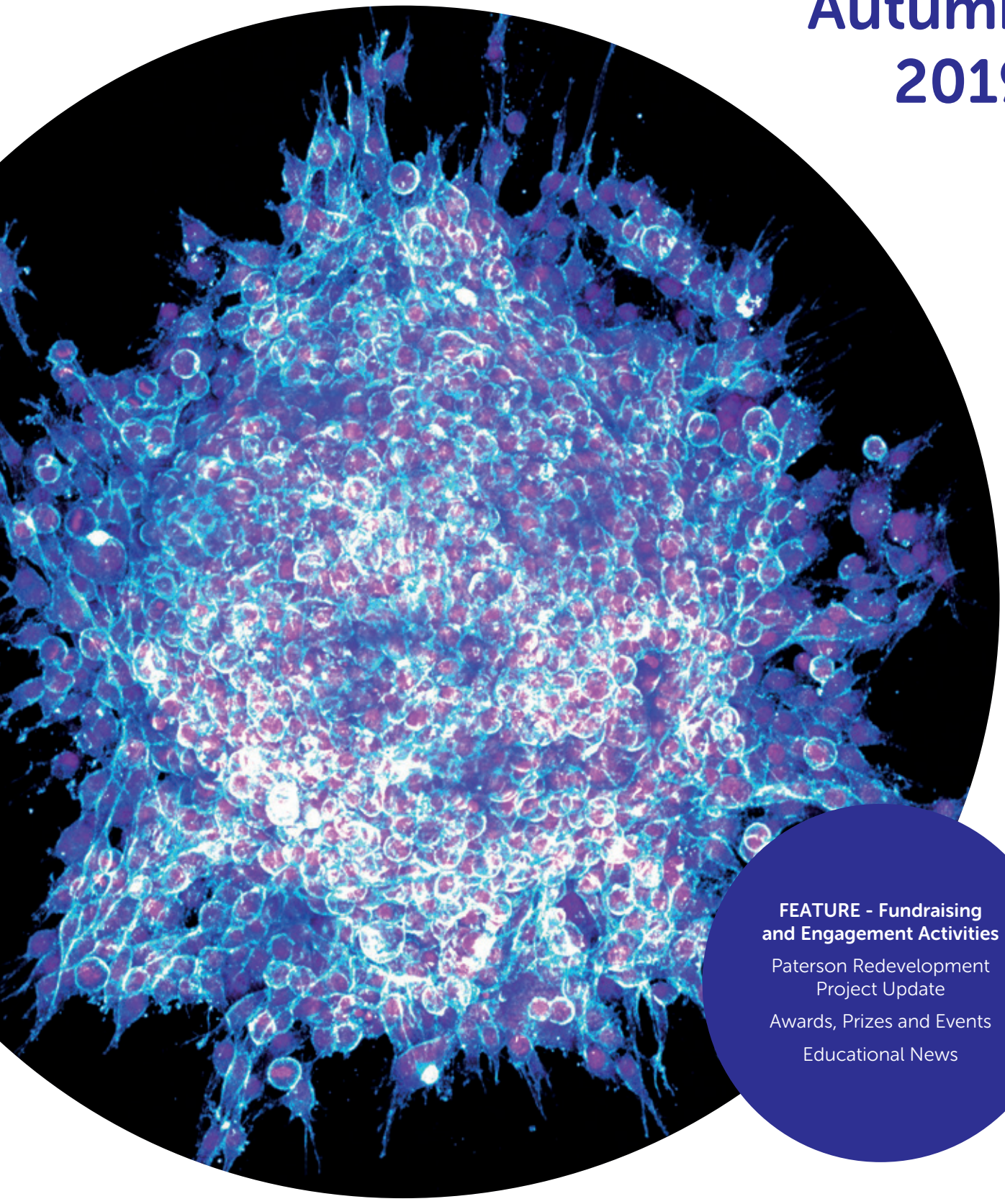
Newsletter

CANCER RESEARCH UK | MANCHESTER INSTITUTE

Autumn 2019



FEATURE - Fundraising and Engagement Activities

Paterson Redevelopment Project Update

Awards, Prizes and Events

Educational News

MANCHESTER 1824
The University of Manchester

Director's Introduction

Over the last nine months we have watched our old home the Paterson Building being dismantled to make way for the new building. Progress has accelerated of late and we are all pleased that the planning application for the new building was approved in August.

I am also delighted that the Research England UK Research Partnership Investment Fund is supporting this project with an award of £25 million and the campaign to raise the remaining vital funds needed to build our new research home is now live. The new facility will bring our scientists and clinicians back together, allowing us to continue to consolidate the critical partnerships that are pivotal to discovery, translational and clinical cancer research. I want to express special thanks to all donors who are supporting this exciting project that will allow us to reach our ambition of creating one of the five top cancer research centres' in the world here in Manchester.

Meanwhile, research at our temporary home in Alderley Park thrives. In April, Institute Deputy Director Caroline Dive and her Cancer Biomarker Centre underwent a successful quinquennial review of their research programme. I am delighted that Caroline and her team achieved an "Outstanding" rating for both their past work and future plans and I want to congratulate them on this impressive result.

Integral to the Institute are our excellent core facilities, so it is great to report that Biological Mass Spectrometry now boasts a new, state-of-the-art spectrometer. The facility, headed by Duncan Smith and ably supported by Yvonne Connelly, was hit very hard by the fire and it took several months and concerted effort to build a suitable environment to house the recovered instruments. Despite attempts to repair the old mass spectrometer, it eventually failed and the replacement, a much upgraded Orbitrap Lumos, was finally installed and service resumed earlier this year. Then the existing Sciex 6600 QToF was brought back to life in April, and I want to thank Duncan and Yvonne for their patience and hard work during this challenging period.

We have integrated well into our new environment, exemplified by our annual 3Rs event, which we now run jointly with AstraZeneca and Agenda Life Sciences. This year's event was another success, celebrating the tremendous commitment to animal welfare of our staff and students and sharing our 3Rs initiatives. I wish to congratulate all the prize winners.

Developing our early career researchers is also an essential part of our research strategy, so I am pleased to welcome several new guest editors who have helped write the scientific articles in this edition. The ability to convey our science to a broad audience is an important part of being a successful scientist and this opportunity will help our PhD students and post-docs to develop their communication skills. My thanks go to Charlotte Bell, Richard Rebello, Hasse Bossenbroek, Alexandru Suvac and Andrew Porter.

This summer our Institute was represented at a number of national and international meetings, with many of the prizes going to our young researchers. Post doc Lucas Trucco in my own group received the AACR Scholar-in-Training Award to attend the prestigious AACR Annual Meeting, while Brian Lee from Systems Oncology was awarded a poster prize at the BACR Tumour Microenvironment meeting. A number of our PhD students attended the International PhD Student Cancer Conference in Amsterdam, with two of our students winning poster prizes – Max Schenk and Chris Bromley. Congratulations to you all.

Our junior researchers also continue to apply for funding to advance their career. Post doc Victoria Pelly from Cancer Inflammation and Immunity was awarded a CRUK Research Travel Award, which gave her the fantastic opportunity to spend several weeks in the group of Ton Schumacher at the NKI. I congratulate Victoria for her success and look forward to hearing about her visit in our next newsletter.

Our more established researchers were also recognised for their scientific contributions. MCRC Director and Senior Group Leader Rob Bristow was elected Fellow of the Academy of Medical Sciences for advancing medical science through his outstanding contributions towards understanding the prostate cancer genome and championing translational science to significantly benefit patients.

Caroline Dive was named Researcher of the Year by The University of Manchester for her transformative and world leading biomarker research that is changing the paradigm of cancer care. Caroline also received the 2019 Heine H. Hansen Lectureship Award for Small Cell Lung Cancer in recognition of her long-standing discovery research in the field. I would like to congratulate all our award winners for their achievements.

In September, we held our annual colloquium, bringing together researchers from across the institute to share their science and build collaborations. It is also a great opportunity to introduce our new PhD students to the Institute and to meet their new colleagues. I would like to welcome all our new students and wish them a successful and enjoyable four years. You can read all about them and the colloquium in the next edition of our newsletter.

Our external funding is regularly boosted. Georges Lacaud was awarded a grant from Bloodwise, Santiago Zelenay secured funds from the Manchester Academic Health Science Centre (MAHSC) Cancer Domain, and Caroline Dive and Andrew Hughes won a CRUK Accelerator Award to digitise clinical trials. I wish to congratulate them all on their success.

Collaboration is critical to advancing science and making a real impact with research. I would like to thank members of the Institute for their contribution towards the success of two major consortia – the new CRUK multimillion-pound funded International Alliance for Cancer Early Detection (ACED) and RadNet – the next generation radiotherapy network. Well done also to everyone involved on the renewal of the Belfast-Manchester Movember Centre of Excellence for Prostate Cancer for a further five years.

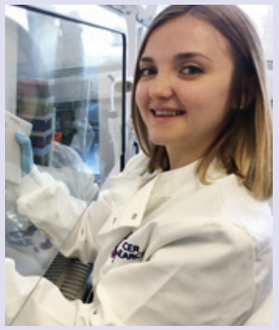
And finally, I am delighted to announce that the Cancer Research UK Manchester Institute has been invited to present an exhibit at the prestigious Royal Society Summer Science Exhibition in 2020. This is a great achievement and an excellent opportunity for the Institute to engage with the public and showcase our work. I wish to congratulate our winning team of Andrew Porter, Steve Bagley, Joanna Kelly, Chris Bromley, Charlotte Bell, and Gill Campbell and wish them all the best for the show. I look forward to seeing their ideas develop over the next few months and I am sure we will all get behind and support them in this exciting initiative.

Professor Richard Marais
Director, Cancer Research UK Manchester Institute

Cover Image: A melanoma spheroid embedded in a 3D collagen matrix (representing the tumour microenvironment), showing cells invading into the surrounding collagen, as a model to study cancer cell metastasis. Cells are stained for markers of the actin cytoskeleton (cyan) and cell nuclei (magenta).

Image supplied by Andrew Porter (Cell Signalling) and Tim Budden (Skin Cancer and Ageing)

Fundraising and Engagement activities



Charlotte undertaking her PhD cancer research studies

Charlotte joins CRUK Sponsor a PhD Scheme

Third year PhD student, Charlotte Bell has been selected to be part of CRUK's Sponsor a PhD fundraising scheme.

The scheme allows supporters to make regular or one-off donations in return for personal updates from chosen PhDs who are part of the scheme. Donations are allocated to the charity's central PhD research funding system.

Charlotte, from Santiago Zelenay's Cancer Inflammation and Immunity group, said: "It's great to be able to help support CRUK's fundraising efforts in any way I can. Since the charity receives no government funding, it relies on donations to fund life-saving cancer research (like mine hopefully will be!)"

Duncan Smith joins IronFran

Francis Benali, former professional footballer at Southampton FC, took on his third and definitely toughest final challenge in a bid to hit his £1m fundraising target for Cancer Research UK. The superhuman was to complete seven Ironman Triathlons in seven days - a daily 3.2 mile swim, 112 mile cycle and 26.2 mile run.

On Day 1 of the challenge, Duncan Smith, head of our Biological Mass Spectrometry facility, joined Fran on the cycle from Manchester to Nottingham. An enthusiast, or in Duncan's words, "a man who cycles", equipped with a reasonable cyclo-cross bicycle, faced a challenge of his own up against Fran and his team of professional cyclists on their super light bicycles – the leader was using the same bike on which Chris Froome won the Tour de France, a Pinarello Dogma. At a gruelling pace of 20 miles an hour, Duncan dropped back after 50 miles and let them steam ahead without him. This was a fantastic effort from Duncan, who completed the ride in his own time and found the pace over the first 50 miles tough.

By Day 5 of the challenge and physically exhausted, Fran was pulled out by his medical team. Duncan, who had been determined to run with Fran that day, was instead invited to run with Fran's team. Self-classified as 'not a runner', Duncan joined at mile 5 fully intending to run for 5 miles. But the pace was relaxed and before he knew it, mile 18 was upon them. With only 8 miles to the finish, he was not going to stop now. Incredibly, Duncan crossed the finish line; the furthest he had ever run before and without training. Consequently, he could not really walk afterwards and spent the next three days living on the ground floor of his house, not able to go up or down stairs.

By Day 7 Fran was back and completed his final ultra-endurance challenge, raising well in excess of his £1m goal. Fran has an incredible mental ability to push through and complete more and more arduous challenges, observed Duncan.

In his first challenge in 2014, Fran ran between every Premier League grounds, covering over 1,000 miles and running for 21 consecutive days. Then in 2016, his second challenge saw him running and cycling to every Premier League and Championship football club covering an incredible 1400 miles in just 2 weeks, running a marathon then cycling at least 75 miles every day. Our Duncan had joined Fran then on a 72 mile cycle from Manchester Etihad to Old Trafford, then to Liverpool and Anfield and Goodison Park, and finally to the grounds of Wigan Atheletic.

Duncan celebrates with Fran after finishing his 112 mile cycle ride.

Images left to right: David and his vegan cake bake, David proudly displays his CRUK running vest for the Manchester 10K, and David's lucky dip. **Below:** Valentine's Day bake sale special.

David Does it Again

Following another busy year of baking, sourcing and selling, long-time supporter of CRUK and MI Purchasing Officer, David Jenkins reflects on the activities that led to raising over £580 this year:

"It's 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 a Purchasing Officer, I'm 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." My bake sales, known as "David's Great British Bake Off" are also always a hit; home-baked products taste so much better than shop-bought and are greatly appreciated by staff!

My fundraising for this year's Great Manchester Run started with a Valentine's themed bake sale. This was very popular and raised just over £200. Next up was "David's Lucky Dip". I had a lot of great prizes donated to me, which helped this to be a success and raise £152. My next fundraiser was a new event – "David's Great British Bake-Off Vegan Special." This involved a lot of research (as I'm not vegan) and was slightly more stressful as people seem to be highly suspicious that vegan cakes can taste nice! The feedback was really positive and I raised another £120.

I completed the 10k in 1hour, 5 minutes and 35 seconds, raising a total of £588.50!

My motivation to keep on fundraising is because I see the great work the scientists do here at CRUK MI and I want the life-saving research carried out here to continue and grow."

Loose Change Buskers Celebrate at Alderley Park

Friends of the MI, the Loose Change Buskers community fundraising group visited Alderley Park in February to celebrate their £500,000 fundraising milestone.

The dedicated group have been raising money since 2010, through their busking performances in and around Manchester, on shopping high streets, and at food and craft markets, performing over 100 times in 2018.

Their visit to AP, hosted by Caroline Wilkinson, was an opportunity for the charity and MI scientists to thank them for their continued efforts; the group were invited to visit the Molecular Oncology lab with Denys Holovanchuk and met Garry Ashton's team in Histology.

The group are motivated by the losses they have suffered through many of their family and friends. In September 2017 a key member of the group, Tommy Stott sadly passed away from oesophageal cancer.

Another key member of the group, Bernard Dolan's mantra is to always keep fundraising as "it's never enough money!"

Loose Change Buskers celebrate their impressive fundraising milestone

Relay for Life Stockport 2019

Stockport Relay for Life – Manchester team members

Another successful year of fundraising for the Manchester Scientists' team culminated in a sunny celebratory weekend at this year's Relay for Life Stockport.

The team, made up of scientists from across the MI and the Division of Cancer Sciences at The University of Manchester, raised over £2,000 for this year's 24-hour walking event, contributing to the £40,000 total across all the Relay teams.

Relay for Life Stockport is the only Relay event in the country which features a team of CRUK-funded scientists. Captained by Steve Lyons since the event's inception in 2005, the team not only put a huge amount of effort in to fundraising in the lead-up to the event but also take the opportunity to engage Relay participants with science research through interactive activities.

This year, the team helped translate some of CRUK's key research and health messages through the charity's immersive Escape the Lab game.

Steve said: "Taking part in Relay isn't a walk in the park. You need to build a team, get commitment from everyone to engage in fundraising throughout the year, plan our science activities and then walk around a track for 24 hours at the end of it all!
"It's really rewarding though and important that the organisers and participants all know how much we appreciate their support.

"We're hoping to reach a total of £600,000 overall for the event once we've completed this year's fundraising; any support we can get from the research community along the way is gratefully received."

Rob Bristow Celebrates £1m Milestone for CRUK Volunteer Fundraisers

Professor Rob Bristow celebrated with CRUK's Nelson and Barrowford Volunteer Fundraising Committee in May, where he thanked them for 60 years of determined fundraising and on reaching an incredible £1million milestone.

Rob shared with supporters and guests the impact their fundraising efforts make to patients' lives and the latest research progress happening in Manchester.

Following Rob's address, a member of the committee – who are all over 80 years old – commented that whilst they often think of stepping down, they now felt inspired to keep on fundraising.

Rob said: "Visits like this make all our research worth it, on behalf of these exemplary citizens and fundraisers."

Nelson and Barrowford Volunteer Fundraising Committee celebrate their staggering fundraising milestone

Arts and Research Collaboration at Science and Industry Museum

Visitors to the Science and Industry Museum's Arts and Health late event in March took part in a range of creative activities as they learned about health research happening across the city.

Scientists from the MI and the Division of Cancer Sciences represented local CRUK-funded research, allowing visitors to create their own cell badges and take histology images with their smartphones, in the shadow of "Cancers", the artwork created by Alice Thickett in collaboration with MI scientists and using images from the OCRB laboratories.

The event was organised to coincide with the World Healthcare Congress Europe 2019, taking place in Manchester.

Visitors create their own cell badges, taking histology images with their smartphones, and Tim with artist Alice Thickett

Selected Publications

New method to identify drugs effective for lung cancer

Researchers in the CRUK Manchester Institute Cancer Biomarker Centre have developed a new method for identifying drugs which could treat patients with small cell lung cancer (SCLC).

SCLC is a type of lung cancer which affects around 15% of lung cancer patients. This disease type rapidly progresses and usually spreads to other organs earlier than other types of lung cancer. After chemotherapy the majority of patients relapse and become resistant to treatment, therefore there is an unmet need to understand better how SCLC can be treated.

Obtaining tumour biopsies from the lung is invasive and challenging, meaning limited samples are available for research. This lack of tissue is overcome by developing a new cell culture method using circulating tumour cells (CTCs) commonly found in the blood of SCLC patients and avoiding the need for painful procedures. In previous work from the group, patient CTCs injected into mice have been shown to form tumours (known as CTC derived tumours or CDX) which closely mimic the donor patient's response to chemotherapy.

The group now shows that when CDX tumours are removed from mice, the extracted tumour cells can live in culture for short periods of time. They found that CDX-derived cells are genetically comparable to the donor CDX tumour and show similar responses to chemotherapy drugs. The group were also able to predict the effectiveness of other treatments in the mouse CDX models based on how the cultures had responded.

This novel method offers a way of identifying drugs which may be effective for SCLC patients, especially in patients which have become resistant to chemotherapy. The cultures maintain patient characteristics and drug responses and therefore can be used as a tool to understand how patients become resistant to treatment and ultimately how resistance could be overcome with the use of other drug treatments.

Lallo A, Gulati S, Schenk MW, Khandelwal G, Berglund UW, Pateras IS, Chester CPE, Pham TM, Kalderen C, Frese KK, Gorgoulis VG, Miller C, Blackhall F, Helleday T, Dive C. (2019) Ex vivo culture of cells derived from circulating tumour cell xenograft to support small cell lung cancer research and experimental therapeutics. *British Journal of Pharmacology* 176(3):436-450.

MRI scans insufficient to decide treatment path for prostate patients

Research led by Esther Baena and Richard Marais revealed that patients with tumours in their prostate could be mistakenly given insufficient treatment following MRI scanning.

Prostate cancer affects over 45,000 men per year in the UK. A key issue is distinguishing between patients who need treatment, and those who can remain on active surveillance – avoiding the unpleasant side-effects of therapy and surgery. Clinicians make this decision by analysing a patient biopsy, where a small sample of the prostate is collected using a thin needle. Hospitals also give patients MRI scans, which are non-invasive. Recent studies propose these scans alone could be used to decide which patients are at low risk of their cancer spreading and therefore put on active surveillance.

Researchers from the Institute and the Christie NHS Foundation Trust compared MRI scans and biopsy samples collected from six patients.

They revealed two patients had tumours large enough to be detected by MRI, but examination of the whole prostate found additional, smaller tumours. One patient did not have any tumours detected by MRI scan, but examination of the prostate found aggressive tumours missed by the scan. From this detailed study the researchers conclude that MRI scans alone are insufficient to decide whether a patient needs treatment. They recommend clinicians continue to combine information from scans and multiple biopsy samples to decide the correct treatment for individual patients.

Parry MA, Srivastava S, Ali A, Cannistraci A, Antonello J, Barros-Silva JD, Ubertini V, Ramani V, Lau M, Shanks J, Nonaka D, Oliveira P, Hambrock T, Leong HS, Dhomen N, Miller C, Brady G, Dive C, Clarke NW, Marais R, Baena E. (2019) Genomic evaluation of multiparametric magnetic resonance imaging-visible and -nonvisible lesions in clinically localised prostate cancer. *Eur Urol Oncol.* 2(1):1-11.

Strategic targeting of PARG in ovarian cancer

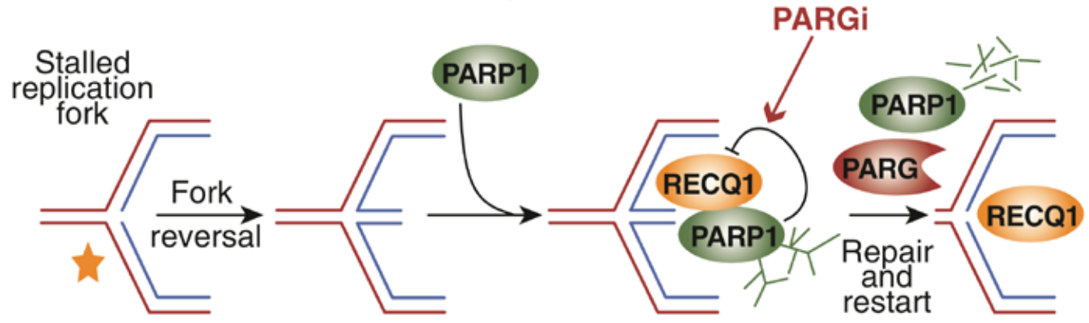
A study recently published in *Cancer Cell* and led by Stephen Taylor from the Division of Cancer Sciences at The University of Manchester, demonstrates that Poly(ADP-ribose) glycohydrolase (PARG) inhibition is an effective strategy for the treatment of non-BRCA1/2 mutant ovarian cancer, which represents a majority of cases.

DNA damage triggers the activity of Poly(ADP-ribose) polymerase which facilitates branched PAR chain assembly, allowing repair factor recruitment to the damage site, a necessary process in DNA damage repair. PARG plays an important role in the DNA damage response in mediating PAR chain liberation and degradation.

The team, which includes members of our Drug Discovery Unit, showed that certain ovarian cancer cells are killed following PARG activity inhibition. A screen for synthetic sensitivity to PARG inhibition revealed an essential role for genes involved in the replication stress response, a vital process in DNA repair.

Furthermore, cancer cells with inherent replication stress due to defects in these genes were sensitive to PARG inhibition. Insensitive cells when co-treated with a CHK1 inhibitor become sensitised to PARG inhibition. This was exemplified further in primary patient-derived ex vivo culture models of high grade serous ovarian cancer (HGSOC). Taken together, this study supports PARG as an attractive drug target in an aggressive molecularly distinct group of ovarian cancer.

Pillay N, Tighe A, Nelson L, Littler S, Coulson-Gilmer C, Bah N, Golder A, Bakker B, Spierings DCJ, James DI, Smith KM, Jordan AM, Morgan RD, Ogilvie DJ, Foijer F, Jackson DA, Taylor SS. (2019) DNA replication vulnerabilities render ovarian cancer cells sensitive to Poly(ADP-Ribose) Glycohydrolase inhibitors. *Cancer Cell* 35(3):519-533.



Schematic showing how PARGi reinforces PARP1-mediated inhibition of RECQ1, thereby suppressing fork restart

UV-associated melanoma mutations linked to better clinical outcome

It has been widely publicised that getting sunburnt - excessive exposure to ultraviolet (UV) radiation from the sun or sunbeds - is a risk factor for skin cancer.

Researchers from the Molecular Oncology group have now found a link between UV-associated genetic faults, called mutations, and melanoma, an aggressive form of skin cancer. The presence of these mutations could help clinicians determine the prognosis of melanoma patients more accurately.

Too much UV radiation can damage the genetic material, or DNA, in your skin cells. Over time, this process can lead to skin cancer. The researchers focused on a mutation pattern known as signature 7, commonly found in UV-associated skin cancers. They studied the effect of this pattern in melanoma patients and found that those with signature 7 had a better clinical outcome than those without, remaining disease-free for longer after treatment and surviving longer overall.

The study showed that melanoma patients with a signature 7 pattern of mutations had a better prognosis. Because patients with a better prognosis are often treated differently than those with a poorer prognosis, this finding could have important implications for the treatment of melanoma patients.

Trucco LD, Mundra PA, Hogan K, Garcia-Martinez P, Viros A, Mandal AK, Macagno N, Gaudy-Marqueste C, Allan D, Baenke F, Cook M, McManus C, Sanchez-Laorden B, Dhomen N, Marais R. (2019) Ultraviolet radiation-induced DNA damage is prognostic for outcome in melanoma. *Nature Medicine* 25(2):221-224.

Understanding treatment-resistant prostate cancer

The latest research from Esther Baena's lab points to a specialist population of cells in the prostate that might be resistant to treatment before it ever begins.

Prostate tumours rely on a hormone called androgen to grow and a common first line of treatment is androgen deprivation therapy (ADT). While this works very well at the start, a large proportion of patients see their tumours return, a result of the tumour developing "castration resistance."

How castration resistance arises has had scientists perplexed for decades. In this study, the authors postulate that intrinsically resistant cells are always present and rise in number following ADT, much in the same way we think about "survival of the fittest."

Whilst investigating luminal and basal cells, the two predominant cell types in the prostate, their search uncovered a subpopulation of luminal cells in mice that express a cell surface molecule called LY6D. Cells expressing this molecule were shown to increase in number upon ADT, have the ability to give rise to various other cell types, and were better at growing into organoids - mini organs - compared to cells that did not express this molecule. Together, this finding suggests that this cell surface molecule can be used to identify resistant prostate cancer cells and possibly predict for development of prostate tumours. When looking at the impact of LY6D on patients, it was linked to poorer outcome in prostate cancer.

Overall, the presence of LY6D could in the future be used to predict which patients are at risk of developing a tumour and could potentially be used to predict which patients will relapse from primary treatment.

Barros-Silva JD, Linn DE, Steiner I, Guo G, Ali A, Pakula H, Ashton G, Peset I, Brown M, Clarke NW, Bronson RT, Yuan GC, Orkin SH, Li Z, Baena E. (2018) Single-cell analysis identifies LY6D as a marker linking castration-resistant prostate luminal cells to prostate progenitors and cancer. *Cell Reports* 25(12):3504-3518.

A molecule designed to reduce breast cancer metastasis in mice

The Drug Discovery Unit have found a number of powerfully active molecules that stop the function of an enzyme that has an important role in allowing the growth of tumour cells.

The enzyme lysyl oxidase (LOX) is produced by tumour cells to cross-link collagens and elastin fibres, creating a "mesh" for spreading tumour cells to grow. Here we make a comparison to the spider (picture LOX) spinning a web – if the spider is killed and no webs are formed then there will be nowhere for flies (or roaming cancerous cells) to stick.

In preventing LOX from doing its job, then it is possible that tumour cells released from the main cancer site will have no 'web' to attach to in order to colonise and grow. Finding molecules that inhibit LOX's function could be a useful tool in stopping the spread of cancer.

An aminomethylene inhibitor targets lysyl oxidase (LOX) resulting in breaks in the collagen cross-links – shown figuratively as the disintegrated spider's web and targeting of the spider representing inhibition of cancer and metastases.

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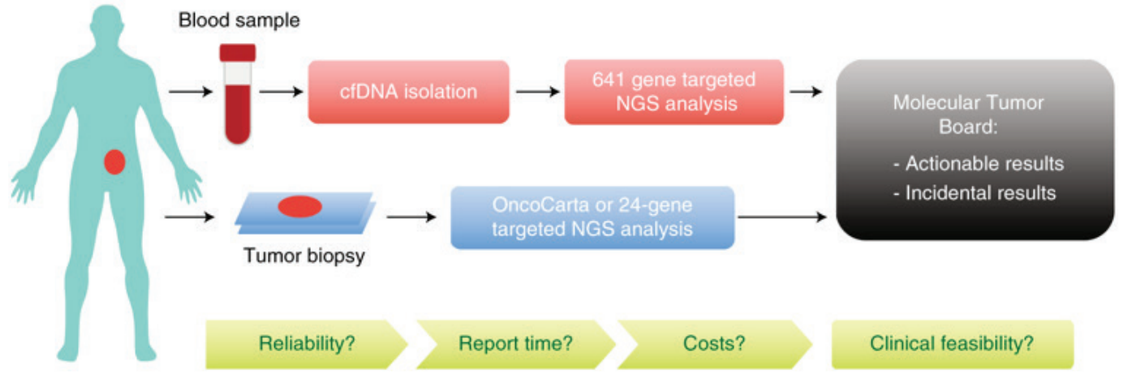
The team discovered several molecules that inhibit LOX. Overcoming significant structural challenges, they optimised these compounds so that they are safe for oral delivery. They found one of the LOX inhibitors reduces the growth of spontaneous breast tumour lung metastasis in a mouse model, suggesting that this compound is a promising drug candidate in future research.

Leung L, Niculescu-Duvaz D, Smithen D, Lopes F, Callens C, McLeary R, Saturno G, Davies L, Aljarah M, Brown M, Johnson L, Zambon A, Chambers T, Ménard D, Bayliss N, Knight R, Fish L, Lawrence R, Challinor M, Tang H, Marais R, Springer C. (2019) Anti-metastatic Inhibitors of Lysyl Oxidase (LOX): Design and Structure-Activity Relationships. *Journal of Medicinal Chemistry* 62(12):5863-5884.

Blood samples to help select the right early phase clinical trials for cancer patients



Outline of the approaches used for ctDNA and tumour analysis in the TARGET study

Cancer patients with no other treatment options are matched to clinical trials with experimental medicines by profiling the molecular alterations in the circulating tumour DNA (ctDNA) from a sample of their blood, according to research published in *Nature Medicine*.

Manchester researchers and colleagues have demonstrated in their feasibility study that a blood test can be carried out and analysed in a timeframe that can help clinicians select a matched, targeted treatment. Currently, enrolment to trials depends on a patient's type of cancer or genetic data obtained from an invasive tumour biopsy, which is often months or years old and may not represent a patient's current disease due to their tumours' evolutionary changes over time.

Our scientists from the CRUK Manchester Institute Cancer Biomarker Centre showed that a small volume of blood can contain up-to-date genetic information about a patient's cancer to inform treatment choices. In this feasibility study of the first 100 patients, 11 were enrolled onto an available and molecularly matched clinical trial.

In the first of the two-part trial, called TARGET (Tumour chARacterisation to Guide Experimental Targeted therapy), the researchers were able to collect, process and analyse blood samples from 100 patients in the Manchester area.

The researchers now hope the second part of TARGET, which is already underway, will show how often the blood test is successful at matching patients to early phase clinical trials and the impact this has on their overall survival. Overall, TARGET shows the feasibility of using ctDNA to successfully guide a subset of patients to specific treatment regimens in early-phase clinical trials.

Rothwell DG, Ayub M, Cook N, Thistlethwaite F, Carter L, Dean E, Smith N, Villa S, Dransfield J, Clipson A, White D, Nessa K, Ferdous S, Howell M, Gupta A, Kilerci B, Mohan S, Frese K, Gulati S, Miller C, Jordan A, Eaton H, Hickson N, O'Brien C, Graham D, Kelly C, Aruketty S, Metcalf R, Chiramel J, Tinsley N, Vickers AJ, Kurup R, Frost H, Stevenson J, Southam S, Landers D, Wallace A, Marais R, Hughes AM, Brady G, Dive C, Krebs MG. (2019) Utility of ctDNA to support patient selection for early phase clinical trials: the TARGET study. *Nature Medicine* 25(5):738-743.

Paterson Redevelopment Project update

Image of the new world-class cancer research building at the former Paterson Building site which has now been approved by Manchester City Council

Following the fire in 2017 that destroyed our research building and displaced over 300 scientists and support staff, we launched plans to build a new world-class cancer research centre on the original site.

This project is known as the Paterson Redevelopment Project and is led by The Christie NHS Foundation Trust on behalf of the partnership between The University of Manchester, Cancer Research UK and The Christie – the Manchester Cancer Research Centre (MCRC).

Whilst the fire was devastating for us and for our partners, we capitalised on the destruction and seized the unique opportunity for Manchester to co-locate the researchers, clinicians and key allied health professionals within one building that is connected to The Christie hospital.

Co-locating researchers and clinicians is essential to the translational research approach, delivering better research outcomes for patients. The Paterson Redevelopment Project will make an even greater contribution to the treatment of cancer in Manchester and globally.

In May 2019, a planning application for the Paterson Redevelopment Project was submitted to Manchester City Council.

On 22 August, Manchester City Council's Planning and Highways Committee approved the planning application, which will see the future of cancer research take place in a new, one-of-a-kind facility built at the site of the fire-damaged Paterson Building.

We are also pleased to report that the Paterson Redevelopment Project will be supported by an award of £25 million by the Research England UK Research Partnership Investment Fund (UKRPIF).

Demolition of the fire-damaged building is progressing well and during the six-week 'cooling off period' following the approval of our plans, the construction team will mobilise and start early works on the new building.

As well as housing the Cancer Research UK Manchester Institute, the new development will be a major step forward in realising the MCRC's ambition of becoming one of the world's top five centres for basic, translational and clinical cancer research by 2025. The new facility will attract the best scientists from around the world and help deliver our vision of the way cancer is diagnosed and treated in future.

Demolition of the Paterson Building in progress

Latest stage of the demolition process

Meet the latest members of the Institute

Alastair Kerr

Alastair joined the Institute in March to lead the Bioinformatics and Biostatistics team for Caroline Dive's Clinical Experimental Pharmacology group.

His team will collaborate in the myriad of diverse projects that are planned and already underway to provide guidance with experimental design and engage in a wide range of data analysis activities.

He has two degrees in genetics, a BSc [Hons] from the University of Edinburgh and a PhD from University of Nottingham. Unusually for that time, his PhD was purely computational, and involved comparative studies between some of the first sequenced genomes. This fast-developing field, now called bioinformatics, led him to the USA for his first postdoctoral position where he studied the biochemical properties and protein sequence conservation of paralogous protein families. This post was funded by both Merck and NASA (under its astrobiology programme), and provided insights into the mechanisms that change the function of proteins since their divergence from the Last Universal Common Ancestor - cenancestor - of cellular life. In 2000, Alastair joined Cereon Genomics, a biotech firm in Cambridge, USA, that was the flagship of Monsanto's efforts to determine suitable transgenes and genetic biomarkers for plant breeding using the latest technologies: Sanger based capillary DNA sequencing and microarrays. When the biotech bubble deflated in 2002, he moved to a pharma company in Scotland to lead several bioinformatics projects in their drug target identification pipeline.

Over the last 15 years, Alastair founded and developed the Bioinformatics Core Facility in the Wellcome Centre for Cell Biology at the University of Edinburgh. The Centre hosts leading scientists in the field of cell and molecular biology and is headed by the current director Professor David Tollervey, who took over from Professor Sir Adrian Bird at the end of the last quinquennial centre grant. There Alastair gained many insights into aspects of the cell and cell cycle regulation (including epigenetics) and is a co-author on many key publications.

Alastair brings to the post a culture of open source software and an enthusiasm for enabling reproducible research. He manages an expanding multidisciplinary group in the fields of genomics, statistics, mathematical modelling and health economics.

Carlos Garcia-Lopez

Carlos undertook his PhD at the University of Murcia in Spain with a scholarship awarded by the Ministry of Science and Technology.

His PhD work focused on the role of polyamine metabolism during pregnancy using in vivo models. These enigmatic molecules have a very bad reputation as some of them are produced during putrefaction. However, he found that the less odorous polyamines - spermidine and spermine - are indispensable in the process of normal placental formation.
After completing his PhD, he obtained a postdoctoral fellowship to join the laboratory of Doug Winton at the CRUK Cambridge Institute. There, he investigated adult stem cell dynamics in the intestinal epithelium using an in vivo lineage tracing strategy to monitor the size of the clones arising from the crypts. This project involved a fruitful collaboration with Ben Simons, a physicist who pioneered applying statistical methods to biology. This collaboration forced Carlos to learn a whole new language of intricate terms in the boundary between mathematics and biology.

Then, Carlos joined the laboratory of Charles Swanton at the CRUK London Research Institute, which after some years and £millions later, became part of The Crick – so it was a very busy time for him. There, he also developed a project on colon cancer, but this time more closely related to translational research. They found that loss-of-function alterations in BCL9L were frequent in aneuploid colorectal tumours, where it regulates aneuploidy tolerance by p53-dependent and independent mechanisms.

Now Carlos has decided to change tack and join the world of lung cancer, a field with abundant research opportunities and an urgent need to improve patient outcomes. During his time here in the CRUK Manchester Institute Cancer Biomarker Centre, he intends to use the human cells-of-origin of lung cancer to investigate the role of major genetic drivers in the initiation and progression of this disease, as well as exploit the knowledge they will obtain to explore potential early detection strategies.

Outstanding review for the CRUK Manchester Institute Cancer Biomarker Centre

The CRUK Manchester Institute Cancer Biomarker Centre team

Our Group Leaders are core-funded by Cancer Research UK and every five years they undergo a rigorous review by a panel of international experts to assess the quality and impact of their research programme.

The CRUK Manchester Institute Cancer Biomarker Centre had their latest quinquennial review in April this year. Being such a large group, with over 70 people, the review process took two days.

There were seven talks and a vibrant lunchtime session with 10 posters on show to a panel of ten international experts in lung cancer and cancer precision medicine, chaired by University of Cambridge's Gerard Evan.

In the opening session, Centre Director Caroline Dive CBE presented the strategic build and vision for her Cancer Biomarker Centre within the CRUK Manchester Institute.

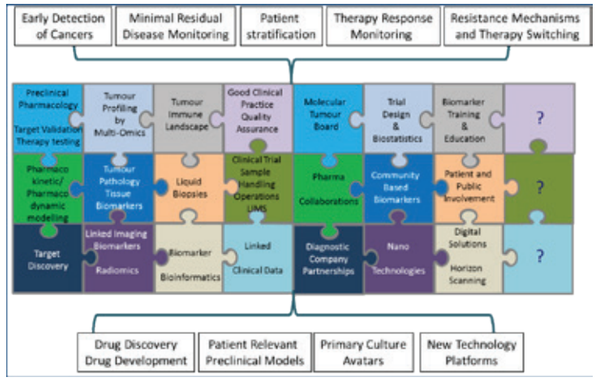
The mission of the Biomarker Centre is to improve outcomes for cancer patients via translation of tumour biology to clinic ready biomarkers for the earlier detection of cancer and optimisation of cancer treatment.

Caroline argued that biomarker-informed patient management is critical in cancer precision medicine to maximise benefit and reduce harm. Biomarkers arising from discoveries in basic science and reverse translation - from the clinic and back to the lab - are important for all aspects of a cancer patient's 'journey', from the pre-disposition and early detection of cancer through to best care in advanced disease.

However, biomarker discovery, assay validation to appropriate regulatory standards followed by implementation in clinical trials and clinical qualification is especially challenging. Overcoming these challenges demands a number of essential elements:

- a range of dedicated facilities and specialised skill sets
- integration of different disciplines
- access to large and appropriate patient cohorts
- extensive early phase clinical trial activities
- access to innovative technology platforms - with high sensitivity and specificity
- dedicated and sustainable biobanking
- organised analytical, management and reporting processes compliant with regulatory authorities
- partnerships for biomarker commercialisation enabling entry to the NHS and routine clinical use

With this long list of 'must haves' simply not feasible in all CRUK centres, Caroline advocates that a different solution is required – the driving force behind the development of our Biomarker Centre. Since 2013, Caroline has been building the Biomarker Centre and now all the pieces of the 'jigsaw of Biomarker Sciences' are in place.



The Biomarker Centre 'Jigsaw'

Joining the activities across eight research teams is integral to realise the vision of the Biomarker Centre, which plans to deliver three key priorities in the next five years:

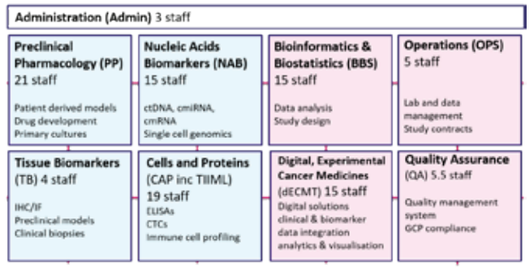
i. develop digital clinical trials (funded with a CRUK Accelerator Grant of £4.5M) led by Andrew Hughes
ii. expand the Bioinformatics and Biostatistics Team led by new recruit Alastair Kerr
iii. merge the new Tissue Biomarkers Team with the Academic Pathology Unit at the Christie NHS Foundation Trust

The Biomarker Centre interacts with the CRUK Experimental Cancer Medicine Centres across the country, and Caroline highlighted the developing multiple international partnerships with leading scientists as well as with pharmaceutical and diagnostic companies.

In terms of Caroline and her team's own international reputation in liquid biopsy development and clinical implementation, this was exemplified by their high impact publications over the past five years, particularly the landmark studies of lung cancer circulating tumour cells (CTCs) and circulating tumour DNA (ctDNA) profiling applied to Phase I trial selection – both published in *Nature Medicine*.

Past Research and Future Plans

Their programme of research was divided into five workstreams, described to the panel of experts by the Biomarker Centre Team leads.



The joined up activities across eight research teams

Lung Cancer

Basic and translational research on small cell lung cancer (SCLC) – led by Kris Frese and Kathryn Simpson in partnership with Fiona Blackhall from the Christie – has capitalised on their previous discovery that CTCs from a 10ml blood draw from a patient can grow in mice and provide new models to study this aggressive disease. The CRUK Manchester Institute Cancer Biomarker Centre now have the largest panel of these CDX models worldwide, and have used them to test new therapies, study metastasis and vasculogenic mimicry – the intriguing process where SCLC cells form their own blood vessel.

In exciting translational research led by Ged Brady and Dominic Rothwell, CTCs and ctDNA have been used as blood tests to monitor SCLC patients in clinical trials.

Research into non-small cell lung cancer (NSCLC) – partnered with thoracic physician Phil Crosbie and CRUK Lung Cancer Centre of Excellence UCL-lead Charles Swanton – focused on earlier detection of the disease. Critically, early interventions are more likely to produce durable patient benefit or cure.

Integrating a comprehensive sample collection protocol within community-based lung health checks to take blood samples from individuals at high risk of lung cancer has been a step-change in managing this disease. Together with low dose CT 'scan in vans' in local supermarket carparks with full clinical follow up, these blood samples provide a unique opportunity to develop sensitive and specific liquid biopsies for early detection.

Biomarkers

Their clinical trials portfolio, overseen by Jonathan Tugwood, includes two flagship biomarker studies across tumour types:

(i) the ctDNA profiling in the TARGET trial for patients entering the Phase I clinic assists in trial selection - led from the clinic by Matthew Krebs

(ii) longstanding studies with Gordon Jayson on circulating predictive and response biomarkers for angiogenesis targeted therapies

A quick tour of the Centre's collaborations in biomarker sciences with colleagues across Manchester featured melanoma, extra thoracic pulmonary cancers, cancers of the prostate, pancreas and colon, cancers of unknown primary and links with our Drug Discovery Unit. Particularly exciting is their decision-making ctDNA analysis in the CACTUS melanoma trial and the progress made on ctDNA analysis in the national PRECISION PANC consortium.

Next, they described their new approaches to increase the sensitivity and specificity of liquid biopsies. Of great importance in this area is the patented workflow for ctDNA developed by Biomarker Centre Deputy Director Ged Brady, and their 'Cancer Moonshot' partnership with Peter Kuhn at the University of Southern California to install and implement the high definition single cell analysis (HDSCA) platform that captures both epithelial and mesenchymal CTCs. They were also proud to present the development of the new Tumour Immunology and Inflammation Monitoring Laboratory led by Elaine Kilgour and the biomarker toolkit that can now be applied to trials of immunotherapeutics.

In a summary of their ambitions and vision for the future of biomarker research in 30 years' time, they suggested that with the prevalence of cancer increasing, community based screening for cancer with liquid biopsies will become commonplace and digital approaches would emerge alongside home based tests.

At the conclusion of the site visit the team were awarded 'Outstanding' for both past research and future plans. The Institute is extremely proud of their achievements and success.

CRUK MI Biological Resources Unit's transgenic mouse capability

Transgenic Breeding team members.

Much of our research depends on the use of transgenic – genetically modified – mice and we maintain an internal breeding colony of over 130 lines with different genotypes to provide our research groups with an immediate source of animals.

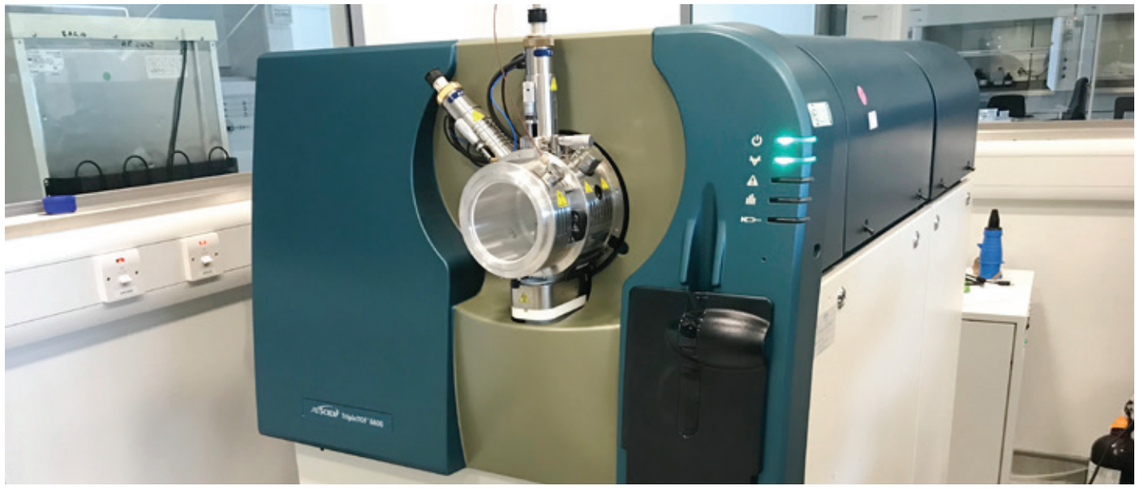
The CRUK MI colony is housed in the Incubator Building at The University of Manchester, where it was relocated over five years ago because of space limitations at the Paterson Building. This new location became a fortunate circumstance in the aftermath of the fire and meant that our supply of mice remained intact throughout. The colony is managed by Dr Jennifer Hughes supported by a team of 12 animal technologists.

Maintaining sufficient breeding pairs of mice and offspring for each of the 130 lines translates into the production of nearly 25,000 mice annually and approximately 2500 cages to care for in the facility at any one time. The production of transgenic mice through breeding programmes is unfortunately an inefficient process because only around 15% of animals may have the required genotype or phenotype.

Initial breeding steps when combining different genotypes are intrinsically inefficient and researchers studying diseases such as breast and prostate cancer will only be able to use animals of a single sex. The rise in the use of transgenic mice worldwide means that mice in breeding programmes such as this account for nearly half of all animals used in scientific research and comprises the majority of mice used within CRUK MI. It is vital, therefore, that researchers and the Transgenic Team critically and continuously review how many lines and animals are bred, and the efficiency of production. This task involves working with meticulous records of breeding and genotyping; as well as the successful production of research animals, all transgenic animals must be accounted for under UK law. Previously these data were collected and managed using numerous Excel files but last year, after evaluation of several providers and a tendering process, specialist software Tick@lab[R] was selected and went 'live' in February. Currently, the system is being used for keeping detailed animal stock records, including breeding details and genotype results, tracking health problems and for sending and reporting on completion of tasks. We are currently moving over to the system for semi-automated transfer of genotyping results and other functionality may be explored. One major advantage of moving over to the new system has been that mouse details are much more easily searchable across all lines, allowing easy identification of subsets within the population. Similarly, tasks can also be tracked or searched, allowing both researchers and technicians to track progress more easily. Although edits can be made to data on the system, changes are tracked and viewable within the history functionality, leading to both a greater transparency and security.

Animals required for research are transported from the Incubator Facility to the Alderley Park site twice each week after confirmation of genotype and health status by the team. Rigorous attention to all the ~ 6300 animals in the colony is very labour intensive, each cage of animals requiring inspection every day to ensure high standards of care and welfare. One of the welfare improvements introduced recently has been to ensure that any male mice which are the only mouse of interest in their box, and which would otherwise be housed singly, have a 'buddy' male companion where possible. There is also a move to cryopreserving mouse sperm rather than mouse embryos as archive material for the colony (which is required as a back-up for lines which may be lost or not currently required); this greatly reduces the numbers of animals required to produce the archived material.

Example of a transgenic mouse.



Sciex 6600 QToF resurrected

The return of Mass Spectrometry

By Duncan Smith

Duncan Smith and Yvonne Connolly run the MS facility.

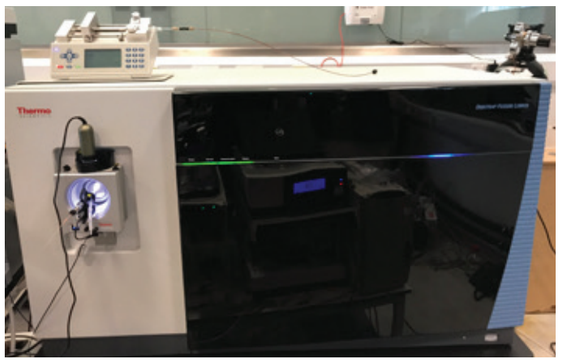
The devastating fire at the Paterson Building, followed by instrument storage in cold damp warehouses and then relocation to another lab, was a huge challenge for the Mass Spectrometry (MS) lab.

We set up a sample prep lab in the Oglesby Cancer Research Building in May 2017 and outsourced the MS data acquisition until we were able to re-establish both the environment and hardware capability of the Paterson Building main MS lab.

2018 was to be a year of challenge and change in the facility. In addition to running services – with the outsourced data acquisition – we needed to establish an appropriate environment at Alderley Park (AP), which would allow us to assess the systems we retrieved from storage. We moved into our new laboratory space during January and February last year. We were forced to write-off our Orbitrap Fusion after extensive attempts to repair it eventually failed in June 2018. The tender progressed resulting in an impressive upgrade to the latest Orbitrap Lumos, which was installed in December 2018. The Lumos has the same architecture and functionality as the Fusion it replaces, however the Lumos has a much brighter source and an advanced segmented quadrupole that means we generate far greater ion numbers (from any given amount of protein) and transmit them at much greater efficiency. This adds together to make the Lumos much more sensitive than the Fusion's capabilities. After a hiatus of 21 months of outsourcing data acquisition, we were pleased to launch the MS service onsite again in January 2019. We were delighted to take back control finally of the service and to be in the exciting position of providing a far more superior hardware capability to support the needs of our research groups. We wasted no time optimising the workflows previously available in a way that exploited the massive improvement the Lumos offers.

With our existing Sciex 6600 QToF, we had to wait until autumn 2018 for it to be installed at AP. Again, the system required multiple visits and repairs before its pre-fire performance was achieved in a reproducible manner. The robust 6600 was returned to service in April 2019, the only mass spectrometer to survive the ordeal intact.

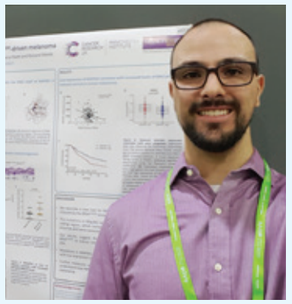
We are delighted to be supporting the Institute's research groups with world-class proteomics capabilities again. The sensitivity and quality of MS workflows available are now much improved from those in the Paterson Building. We would like to thank everyone for your patience and understanding – now it is science full steam ahead!



The latest Orbitrap Lumos

Awards Prizes and Events

Our researchers travel to the AACR annual conference on awards



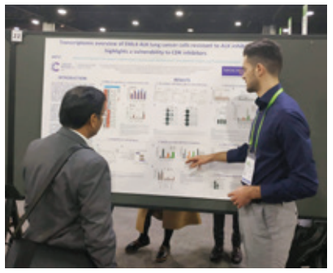
Lucas presents his award-winning poster at the AACR conference.

Lucas Trucco

Scholar-in-Training Awards recognise early-career scientists and enable their participation at the AACR Annual Meeting.

I was pleased to learn of my selection for this award that provided me with the opportunity to participate in this international meeting for the first time. It has been a highly enriching experience, allowing me to meet renowned experts in the field and to attend exceptional talks about all aspects of cancer. It has also permitted me to share and discuss the latest results of my studies with other researchers and clinicians.

I was also invited to a reception honouring awardees and funders where I had the chance to meet and share experiences with other recipients of the prize, and to thank the Pezcoller Foundation committee who sponsored my award.



Sakis explaining his research during the poster session at the AACR conference.

Sakis Paliouras

Seeing your scientific role models in person, networking with key leaders in the field and sharing your results with the community are all possible at top-notch international conferences.

With the support earned from a University of Manchester Doctoral Academy Graduate Society conference award and a BACR-CRUK student travel award, I was able to attend one of the most important translational cancer research conferences, the 2019 AACR in Atlanta, US.

The first day started with the opening ceremony, with various awards being given followed by a number of scientific presentations. The pace of the meeting remained intense, with multiple presentations taking place simultaneously throughout the day. During the next day, poster presentations commenced. We had four hours during which we could browse hundreds of posters, talk to the presenters or visit company booths. The scientific highlight was listening to the Nobel laureate James Allison, as well as three other scientists who were instrumental to the development and testing of immunotherapies, share stories explaining how these discoveries were made.

For my poster presentation, I had the opportunity to interact with a large number of scientists from all levels, PhD students, postdocs, group leaders as well as industrial employees. I had stimulating discussions, received interesting feedback and even a career opportunity offer. All in all, the meeting set a strong focus on the trends for the upcoming years of cancer research. This was undoubtedly the best conference I have attended and I am glad I decided to apply for travel funding.

BACR Tumour Microenvironment Meeting Poster Prize

Brian and fellow poster-prize winners at the BACR Tumour Microenvironment meeting.

Postdoctoral fellow Brian Lee from the Systems Oncology group attended the British Association for Cancer Research Tumour Microenvironment meeting in July and won an award for his poster.

Tumour growth and metastasis are critically dependent on the interaction between tumour cells and their surrounding environment. Cancers require a vascular supply, a lymph drainage, immune escape, evasion from growth suppression and pro-apoptotic signals coming from their environment and an ability to move through the surrounding stroma to metastasise.

Good science relies on a combination of factors, but the opportunity to present, discuss and interact are key to getting the best out of meetings. Brian certainly made the most of this meeting with his award-winning poster focusing on the effect of macrophages on tumour microenvironment and tumour cell signalling in pancreatic cancer.

Santiago talks about his latest research

Julie and Paul with their prizes

Manchester Phase 1 meeting

The "Phase 1: Where Science Becomes Medicine" conference, organised by the Manchester Cancer Research Centre (MCRC) and the Experimental Cancer Medicines Centre (ECMC), was an opportunity to further celebrate Manchester's position in scientific research.

This event, which brought together a diverse range of industry professionals for three days of presentations discussing early phase clinical research, was a great success. Attendees included representatives from across the world from diverse backgrounds covering healthcare bodies, academic researchers and other early-phase clinical trials specialists.

From our Institute, Santiago Zelenay gave an excellent talk describing his group's work on the prognostic value of a Cox2 associated inflammatory signature across a range of cancers, while Caroline Dive CBE enthralled the audience with a fantastic presentation on the TARGET trial, describing the pan-Manchester effort to test the feasibility of ctDNA profiling to match patients to targeted therapies in phase 1 trials.

Over 30 posters were also presented, covering a range of topics including digital technologies for oncology, immune-oncology, radiotherapies and more. We would like to congratulate two members of our digital Experimental Cancer Medicine Team (digital ECMT) Julie Stevenson and Paul O'Regan, who were jointly awarded prizes for their posters on eTARGET - a digital solution for the Manchester Molecular Tumour Board.

The digital ECMT is part of the Cancer Biomarker Centre at the CRUK Manchester Institute and is closely aligned with the Experimental Cancer Medicine Team at The Christie. They lead the way in health technology, applying digital science to transform decision-making in early clinical trials and the patient's role.

Professorship announcement

Ged Brady

Ged Brady was awarded a Professorship by The University of Manchester in recognition of his outstanding work in nucleic acid research.

Professor Brady is Deputy Group Leader of the CRUK Manchester Institute Cancer Biomarker Centre at the Institute, where he also leads the Nucleic Acids Biomarkers Team.

Ged has a strong background in innovation and biotechnology and is renowned for developing advanced molecular biological methods to further our understanding of the processes behind cancer progression.

His most significant contributions recently have been in the genomic profiling of single circulating tumour cells (CTCs), advancing precision medicine for patients with lung cancer. He plays a critical role in the CRUK Manchester Institute Cancer Biomarker Centre and is the driving force behind biomarker-supported clinical trials at The Christie NHS Foundation Trust.

The Institute is incredibly proud of Professor Ged Brady for this tremendous achievement.

2019 Researcher of the Year Award

Researcher of the Year medal presented by Nancy Rothwell

Deputy Director Caroline Dive CBE was recently named the Faculty of Biology, Medicine and Health's Researcher of the Year at The University of Manchester's 2019 Distinguished Achievement Awards.

The awards recognise outstanding performance and significant contribution to the University, with Caroline recognised for transforming the field of biomarker research, and her commitment for nurturing the next generation of clinical and non-clinical cancer researchers in Precision Medicine.

Caroline is internationally renowned for her pioneering work on the development of liquid biopsy methods which use biomarkers circulating in the blood, such as circulating tumour cells and cell-free tumour DNA, to diagnose and monitor cancer. She has revolutionised research in lung cancer and is continuing to make important contributions to the advancement of medical science and in particular personalised medicine for cancer patients.

She was presented with the medal by University of Manchester President Professor Dame Nancy Rothwell, at a ceremony on 1 July.

Suppliers' exhibition fair features communication workshop

Cancer Research UK Manchester Institute in conjunction with Alderley Park Ltd brought the return of the popular biannual suppliers' exhibition fair "Suppliers A Go Go" on 15 November 2019. David Jenkins, our Purchasing Officer at the Institute, presents this fun and informative suppliers' day, which includes 25-30 scientific laboratory suppliers.

"Workshops A Go Go"

Headlining this November is Jamie Gallagher, an award-winning scientist and science communicator. Jamie spends his days sharing his love of science and helping others to do the same. His work has taken him around the world, from the skyscrapers of Hong Kong to tents in the African bush. As well as speaking live to thousands of people each year, he has had work published in 19 different counties and has contributed to a number of television shows, radio programs and museum exhibitions.

The workshop started with talks from the Institute's STAy group, run by junior scientists and brings together early-career students, postdocs and scientific officers in order to network, share ideas and discuss topics of scientific relevance.

Academy of Medical Sciences elects Professor Rob Bristow as Fellow

The Academy of Medical Sciences has elected 50 of the UK's leading figures within biomedical and health sciences to their esteemed Fellowship.

We are pleased to announce that amongst those 50 was the MCRC Director and Senior Group Leader at the CRUK Manchester Institute Professor Rob Bristow.

New Fellow Rob was selected for his outstanding contributions to advancing medical science, cutting-edge research discoveries, and translating developments into benefits for patients and wider society.

A leading clinician scientist and world-expert in prostate cancer, Rob champions translational science; combining innovative laboratory research on the tumour microenvironment with deep clinical understanding that significantly benefits patients. To distinguish which men diagnosed with prostate cancer are at high risk of cancer recurrence after treatment, he led an international team that developed a genetic test that can identify patients who need more aggressive treatments. Crucially this test provides better options for personalised therapy in high-risk prostate cancer patients, while avoiding over-treatment for patients with less aggressive cancers.

The Academy of Medical Sciences is the independent body in the UK representing the diversity of medical science. Their mission is to advance biomedical and health research and its translation into benefits for society.

STAy update

Members of the STAy Committee

The STAy committee have had a busy first half of 2019. The centrepiece was our well-attended "Behind the Labels" event on World Cancer Day, 4 February.

This brought together researchers, clinicians and patients with the aim of going from those broad labels to finding out about the real people living with and working against cancer. The evening included public tours of the Oglesby Cancer Research Building and interactive exhibits illustrating aspects of cancer research. From our speakers we heard about cutting-edge developments in research, the value of international partnerships, the work of the Biobank, and how childhood inspiration led to a career as a research nurse. The evening ended with moving descriptions from two women living with breast cancer, who gave us an insight into their day-to-day experiences. As a team we benefited from input from Clare Dickinson, CRUK Senior Nurse Manchester, and Jo Taylor, who acted as our patient advocate for planning as well as speaking at the event. We look forward to putting into practice what we learned from running this evening in our next public-facing event.

In May we hosted a science media workshop at the Institute, run by two members of the CRUK Science Media team. This gave PhD students, post-docs and group leaders the opportunity to learn how science stories are reported and what factors influence which stories are taken up by media organisations. There was opportunity to practice writing media comments on research, as well as training in broadcast interviews. Participants left more aware of the background to science reporting, and this practical training was very useful for all who are involved in science communication and promotion of our work at CRUK MI.

June saw the STAy team organise and run a seminar on grant writing, where we drew on the combined experiences across the Institute, hearing from Gill Campbell as Grants Advisor, and Iain Hagan and Caroline Dive on the perspective of grant reviewers (and with many helpful tips on good writing!). Kiran Batta told us about his transition to independence as Principle Investigator, and Stuart Williamson took us through the process by which he was awarded a Fulbright scholarship. With strong attendance and good feedback, we look forward to coordinating similar events to gain from the insight of other institute members, as well as further training on grant writing.

As well as running several socials and another speed networking evening, we also hosted our first two external seminar speakers – Prof Massimiliano Mazzone (VIB) and Prof Rene Bernards (NKI) – invited from a shortlist drawn up by the STAy committee. Alongside their scientific presentations, we asked them to speak about their career paths and to give some advice for early career researchers, something we plan to continue with future invited speakers. We also learnt about the process of hosting and coordinating a visit, and will use that to help shape upcoming visits from Prof Clare Isacke (ICR) and Prof Madelon Maurice (UMC Utrecht).

Committee membership is open to all PhD students, post-docs and scientific officers, and we always welcome feedback and ideas. We are currently part of the steering group for a business innovation summit to be held in the autumn, and we have a growing list of ideas for future events, so watch this space!

DETECTION awarded

We are pleased to announce that CRUK have funded a Phase III trial called DETECTION (Circulating tumour DNA guidEd Therapy for stage IIB/C mElanoma after surgiCal resection).

The aim of the study is to test whether survival of patients with stage IIB/C melanoma is improved through early treatment of ctDNA-detected relapse with immune therapy. This is based on research performed in the Molecular Oncology group showing that minimal residual disease or early disease recurrence (molecular relapse) can be identified by detection of ctDNA in patients with early stage melanoma and is predictive of survival. Professor Paul Lorigan and co-investigators Professor Richard Marais, Professor Caroline Dive, Dr Rebecca Lee and Jackie Mitchell will lead this ambitious project. It will open in 20 UK sites, recruiting 1050 patients and is expected to test over 16,000 blood samples.

DETECTION trial logo

Modulating Tissue Immunity Innovation Workshop

By Victoria Pelly

As an immunologist working in the area of cancer immunotherapy, I am increasingly interested in uncovering mechanisms of immune dysregulation common to autoimmunity and cancer immunotherapy and how they relate to treatment response.

Earlier this year, a call was released for applications to attend a "sandpit-style" workshop co-organised by Cancer Research UK and Versus Arthritis entitled *Modulation of Tissue Immunity*. The remit of this workshop was to bring together a multi-disciplinary and diverse group of researchers to address challenges in immunology that could lead to advances in our understanding of cancer and of arthritis and related musculoskeletal (MSK) disorders. I was selected to attend as one of 25 participants ranging from early career to more established researchers from multiple universities and institutes across the UK. This seemed like the perfect opportunity for me to expand the scope of the work I am currently performing as part of my postdoc at with Santiago Zelenay, and to develop innovative proposals and collaborations with immunologists around the country.

The workshop was comprised of three intensive, highly interactive days spent in residence in the Jubilee Conference Centre. The workshop was led by the esteemed Professor Fiona Powrie and Professor Kevin Maloy from The University of Oxford and facilitated by a dynamic team Know Innovation (www.knowinnovation.com). Doreen Cantrell (Dundee) and Sergio Quezada (UCL) were invited to give talks on the first day to stimulate thinking. Subject guides including researchers (David Samsom (UCL) and Awen Gallimore) and two patient representatives were present throughout the workshop to guide interactions, conversations and project ideas. By the end of the second day, with the help of Know Innovation exercises and many hours spent interacting with other participants over coffee, six groups of mixed sizes and expertise were organically formed around themes ranging from the tumour microenvironment, metabolism and immunotherapy. Each team was asked to prepare a seven-minute pitch and a one-page proposal and initial feedback was received that night in the form of a practice interview with the selection panel (made up of the workshop leaders, subject guides and patient representatives). Finally, we presented our exciting proposals to the panel and the rest of the workshop attendees on the third and final day. After a gruelling two hours of deliberation, the panel voted to fund three of the six projects for a feasibility period of 1 year (and up to £40,000), starting in October 2019. I look forward to seeing what emerges from these collaborations and strongly recommend keeping an eye out for any other CRUK-led sandpits to everyone at CRUK MI.

Education News

International PhD Student Cancer Conference goes to Amsterdam

International PhD students at the IPSCC at the National Cancer Institute

The 13th IPSCC organised annually by students for students at top cancer research institutes, took place at the National Cancer Institute in Amsterdam on 12-14 June.

We are delighted to announce and congratulate Maximilian Schenk from CRUK Manchester Institute Cancer Biomarker Centre, who was awarded the overall prize for best oral presentation showcasing his work on "Dissecting chemoresistance in small cell lung cancer"; and Christian Bromley based in the Cancer Inflammation and Immunity group, who was awarded the prize for one of the top 3 poster presentations "Combining cancer-promoting and cancer-inhibitory inflammation signatures to predict cancer patient outcome".

The Institute was represented by 23 students and the conference was attended by over 100 students from CRUK and cancer research participating institutes from the UK (Beatson, Cambridge, Crick, Oxford), Germany (Berlin, Heidelberg) and The Netherlands. There were 16 panel-selected student talks and 94 posters scheduled over the two and half days. Students enjoyed keynote lectures from Dr Andrea van Elsas, Aduro Biotech; Prof Karin de Visser, NKI; Dr Nicholas Navin, MD Anderson Cancer Center; and Prof Ben Feringa, Rijks Universiteit Broningen.

The social events during the conference included a pub quiz, networking social event and a walking dinner with a guided tour around Amsterdam, which were all well received. As always, the IPSCC provided a unique opportunity for PhD students to present their work and network with some of Europe's best cancer research institutes. The event was a great success - especially for our Institute.

Chris (left) and Max (right) receiving their poster prizes

Fabrizio addresses the audience at the BACR PhD Student Conference he helped organise

PhD student co-organises national conference

We are proud to announce that PhD student Fabrizio Simeoni helped organise the first BACR PhD cancer conference that took place in December last year.

Fabrizio is in his third year in the Leukaemia Biology group led by Tim Somervaille studying the role of the transcription factor FOXC1 in Acute Myeloid Leukaemia (AML) and trying to unveil the molecular mechanism by which FOXC1 is able to block monocyte lineage differentiation, accelerating leukaemia onset.

As one of the six who formed the BACR PhD Student Conference Organising Committee, Fabrizio helped put together an exciting programme of talks by leading cancer scientists, including Mina Bissell of University of California Berkeley and Carlos Caldas of Cancer Research UK Cambridge Institute, attracting over 100 participants from across the UK.

The conference 'organised by students for students' aimed to expose PhD students to the newest trends in cancer biology and cutting-edge research presented by highly acclaimed speakers, enabling them to interact with the invited speakers and obtain valuable advice on career options and opportunities. They would also benefit from great networking opportunities with other students from diverse cancer-research-linked disciplines.

Being involved in organising a big national conference was a fantastic opportunity for Fabrizio, who also helped put together the grant application earning the committee £5000 from CRUK to help fund the event.

Staff News

Another successful Suppliers a Go Go

David Jenkins (Purchasing Officer) hosted a new Suppliers a Go Go event on 17th May, with the participation of Alderley Park Ltd. There were 25 suppliers showing their products to the scientists and GE Healthcare also offered a workshop about a new on-site Laboratory set to open soon.

The event was a great success and it even had a few upgrades: new logo and promo posters, as well as free lunch, including delicious science themed dishes like Summer berry posset petri dish, Pimms test tube jelly, wine and dark chocolate test tube and summer berry mocktails.

"As NASA will be celebrating the Apollo's 50th Anniversary of the moon landing, I thought it would be fun to have a life size cardboard cut-out of Buzz Aldrin, which was perfect for taking selfies with for your Instagram, Facebook or Twitter, and as if that wasn't enough, I also organised Mr Whippy ice cream van to pull up outside the Alderley Park Conference Centre selling ice creams at lunch time, my next Suppliers A Go Go will return in November", said David.

25 suppliers exhibited on the Alderley Park Conference Centre

Two of our own at the London Marathon

Sarah Craig, from our Skin Cancer and Ageing Group, ran the London Marathon this year raising over £1300 for Cancer Research UK.

"I've always wanted to run the London Marathon and after 5 years of applying, I finally got a ballot place for 2019! Of course CRUK is a very worthy cause and I wanted to do my bit. It took me 4hrs 48mins and I raised £1330 so thank you to all that donated!", said Sarah.

Sarah, exhausted but very happy after finishing the marathon

On his third marathon, Max raised an amazing £386 for CRUK

After running the Manchester Marathon 2017 and the Hamburg Marathon 2018, Maximilian Schenk (CRUK MI CBC) thought it was time to take on another challenge for CRUK: The Virgin London Marathon 2019. "It was a great experience to cross Tower Bridge and to finish the race at Buckingham Palace which led me to run my personal best of 03:20:09 hrs. Again, it was incredibly motivating to see all the support from people of CRUK MI, friends, and family!", said Max, who thanked everyone for their encouragement and donations.

He also congratulated Kathryn Simpson (CBC), who won a European Hamper for guessing his time ahead of the race! "Thanks again to everyone for believing in me and now I am looking forward to running next year´s Brighton Marathon!", concluded Max.

Wedding Bells!

Huge congratulations to Belen Conti (EA to the Senior Management Team), who got married to Cian Vyas on March 28th in Nottingham.

The great British weather was actually great on their wedding day, and was the perfect complement for a fantastic day with family and friends. In fact, they enjoyed it so much that they are doing it all over again in Belen's home country of Argentina in October, before setting off for their honeymoon in South America.

The happy couple, Cian and Belen Conti Vyas

Aishwarya Payapilly (postdoc in our Cell Signalling lab) tied the knot with her partner Dan on April 27th.

They enjoyed a lovely ceremony with their friends and family in Wales. Huge congratulations to this great couple!

The newlyweds, Aisha and Dan

10K and delicious fundraising events

As if Suppliers a Go Go wasn't enough of a challenge, David Jenkins also did a great job running the Manchester 10K on May 19th.

He raised an amazing £588.50 for Cancer Research UK, thanks to online donations and some of his famous events such as David's Great British Bake Off (Valentine's Day Special), David's Lucky Dip and the brand new David's Great British Bake Off Vegan Special!

"On the day of the 10K run the weather was perfect, a bit cloudy and not too cool which helped make running easier. I managed to do it in 1hour, 5minutes and 31 seconds, which was 3 minutes faster than the last time I did the 10K in 2017", celebrated David. Well done!!

The Cancer Research UK Relay for Life Stockport, Manchester Scientists Team organised a very successful Breakfast Bake and Fresh Juice Sale at the Oglesby Cancer Research Building. They raised almost £400 ahead of the Stockport 24 hours Relay for Life, which this year took place on the 13th & 14th July at The Kingsway School (Broadway Site) in Cheadle.

From left to right: Natalia Moncaut, Suzanne Johnson, Samantha Littler, Kim Acton and Stephen Lyons

Follow the Paterson demolition live

Live footage of the Paterson Demolition on July 1st

In June we finally saw the walls of the Paterson Building starting to come down. Saying goodbye to this building fills us with mixed emotions: sadness to see it go, but also excitement for what's to come.

If you want to view the progress of works in the site, you can follow this link to a live CCTV footage that updates every 10 minutes: https://bit.ly/2FLxDRM

In the spotlight with Julie Edwards

Julie Edwards is our Postgraduate Education Manager and has worked at the Institute for 20 years. Julie manages our 4 year PhD programme, from running the annual recruitment of our PhD students, supporting the assessment process throughout, and providing pastoral care and support for each student during their four year stay with us. She also leads the Education Committee, which acts for postgraduate students and monitors the students' progress and projects ensuring that the proposed plan of research is suitable, and that progress is made consistently throughout the course of the studentship. Julie also enjoys getting involved with the annual International PhD Student Cancer Conference (IPSCC) and supporting our student's attendance.

1. What is your favourite part of the UK?
Wales, lots of happy memories

2. What was your best ever holiday and why?
Florida – family Christmas holiday – 11 theme parks, swimming with dolphins and burgers for Xmas lunch. It will never to be forgotton!

3. Which website do you always check, and why?
BBC Weather - forewarned is forearmed!

4. What is your favourite film?
The Shawshank Redemption and Harry Potter Film series

5. What is your favourite band/ singer?
Jeff Lynne of ELO

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

7. What is the most important lesson that you have learnt from life?
Learn while you are still young

8. Name three things you would take with you to a desert island?
A hammock, plenty of champagne and sun cream

9. What is your greatest fear?
Flying

10. How would you like to be remembered?
If someone remembers me with a smile and a laugh, or makes them feel proud that will do for me!

11. If you could change one thing in your past what would it be?
Listen to and trust my own instincts

12. What is your signature dish to cook?
Roast dinner with all the trimmings

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

14. What is your idea of perfect happiness?
Healthy family, gourmet food, good wine and laughter, preferably in warmer climates!

15. What keeps you awake at night?
Indigestion

Editorial Team:
Steve Bagley
Gillian Campbell
Belen Conti
Tim Hudson
Steve Royle
Caroline Wilkinson

Cancer Research UK Manchester Institute
The University of Manchester
Alderley Park
SK10 4TG

e: enquiries@cruk.manchester.ac.uk
www.cruk.manchester.ac.uk
twitter.com/CRUK_MI

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

The University of Manchester
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