Newsletter

CANCER RESEARCH UK | MANCHESTER INSTITUTE

Autumn 2020

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Fundraising and Engagement activties

Events, Awards and Prizes

Staff News

MANCHESTER 1824
The University of Manchester

Director's Introduction

This edition of the Cancer Research UK Manchester Institute Newsletter sees us in unprecedented and challenging times as we face the COVID-19 pandemic and cope with the impact on our research. Like all universities and research institutes, we closed our doors in March to all non-essential access to prevent the spread of the virus and protect our staff.

Throughout this period our priority has been the safety and wellbeing of our staff, so everyone worked from home except those required for business-critical activity, which included ensuring the welfare of our animals, ensuring that our vital experimental materials were protected, and that our infrastructure was maintained. We are extremely grateful to the staff who came in to support these essential functions and I personally want to thank them for their exceptional commitment and dedication during this time.

As our own research was paused, we used our skills to support the nation in the fight against the virus. A national COVID-19 testing hub was established at the Alderley Park Lighthouse Laboratory – led by the Medicines Discovery Catapult – and we developed a working partnership with the diagnostic facility. I was delighted that so many of our scientists volunteered to help with this effort, supervised by Dr Dominic Rothwell from the CRUK MI Cancer Biomarker Centre. We were amongst the first to undergo training and start testing samples from front-line NHS workers, whose negative results allowed them to return to patient care. Additionally, we loaned key equipment, including PCR machines to get this vital work going as quickly as possible and to help expand the testing capacity within the lighthouse. I am proud of our volunteers and staff who made this possible, and for the part we played in this magnificent effort.

Our scientists also found other innovative ways to support front line NHS workers. Responding to the lack of PPE for the nation's frontline staff, Steve Bagley – head of our Visualisation, Irradiation & Analysis service – used our specialist 3D printer to create plastic headbands for protective face masks. We provided over 200 of these face masks to hospitals across the North West, including The Christie NHS Foundation Trust in Manchester. Well done Steve for your vital support.

Alongside our homeworking, several our staff and students found time to undertake fundraising challenges to raise money for CRUK. Initiated by the Drug Discovery Unit, I joined the team for the CRUK MI Race for Life at Home challenge, where we each ran, cycled or undertook other exercise, to individually cover 25 miles (the distance between the old Paterson Building to Alderley Park and back). Together we raised over £3,000, an impressive achievement so well done everyone. Also, fundraising champion Steve Lyons and the 'Manchester Scientists' raised money for 'Stockport relay for life' by selling their rather lovely hand-made face masks. A great effort that will help support Cancer Research UK since the charity is likely to lose around 25% of its income over the next financial year, partly due to having to cancel mass participation events such as the Race for Life.

During the COVID-19 lockdown it was important that we remained connected and supported each other. I led weekly updates to inform staff of the progress and ever-changing situation as well as provide an opportunity to share other news and to take questions. It also became more important than ever to hear about research from our colleagues – both from within the Institute and further afield. We therefore took our external seminar series online, and I am grateful to all of our invited speakers for committing to give talks despite the strange conditions. We formed an Education and Engagement group to find ways of motivating staff whilst working from home. This resulted in several online training sessions that were a great success. I would especially like to thank our STAy Committee for their ideas and for boosting morale with their Quarantine Quizzes. I am extremely proud of how everyone responded in the face of adversity and stuck together in this difficult time.

The pandemic has also changed how we share our science with other scientists around the world. Large international meetings such as those organised by the AACR and EACR also went virtually this year. PhD student Denys Holovanchuk in my own group was awarded two separate travel grants to attend the AACR this year to present a poster. Although the virus meant there was no longer a meeting to travel to, Denys was able to share his research via an audio guide attached to an electronic version of his poster and still obtain that all-important feedback from his peers.

Of course, we have overcome challenges before as an Institute. We are still in the recovery phase from the 2017 Paterson Building fire and consolidating our interim base at Alderley Park.

The Paterson Building has now been demolished and good progress is being made on the plans for its replacement. I was pleased to announce that the project received a significant boost last year through a £25m award from the Research England UK Research Partnership Investment Fund and towards the end of 2019, the Rewrite Cancer campaign was launched by the project's partners to raise the final £20m required for the build.

As 2020 proceeds, we look forward to finalising the design and watching the new facility start to emerge and take shape.

Despite the challenges, I am pleased that we continue to make notable contributions and achievements. A key study from our Cancer Biomarker Centre was published in *Nature Medicine* describing the prediction of non-small cell lung cancer (NSCLC) relapse through pulmonary venous circulating tumour cells. Prof Caroline Dive's team is partnering with Lloyds Pharmacy in Greater Manchester, where phlebotomists will take blood samples from patients following lung cancer surgery with the aim of using these "liquid biopsy" approaches to detect relapse at an early stage. The TARGET trial, another exciting development for the CBC, together with clinical colleagues at the Christie NHS Foundation Trust, is a ctDNA-driven selection phase I clinical trial being run across Experimental Cancer Medicine Centres in the North and was also published in *Nature Medicine*. The trial will now be expanded to assess patient survival. It is very pleasing to see how well the CBC has recovered from the fire.

Other recognised contributions include a publication by Angeliki Malliri and her team in the *Journal of Cell Science*, revealing their discovery of a new regulator of mitotic spindle orientation through the interaction of the calcium/calmodulin-dependent serine protein kinase (CASK) with the tumour suppressor Dlg1. The Leukaemia Biology group led by Tim Somervaille continue to develop their programme on the potential AML target Lsd1 and have identified mTORC1 inhibition as a synergistic therapeutic approach. These are just some of the examples that demonstrate the quality and breadth of our ongoing research.

The Cancer Research UK Manchester Institute was invited to showcase our research at the prestigious Royal Society Summer Science Exhibition. This is a wonderful achievement and I am very proud of our team and all the hard work they put into the winning application and their work since on designing the exhibit. Originally planned for July 2020, the event was unfortunately postponed due to the COVID-19 pandemic, but we look forward to our team displaying their virtual exhibit on the theme of the Institute's work on the tumour microenvironment next summer.

A number of our staff and students have also received awards and prizes. Congratulations go to Junior Group Leader Santiago Zelenay, who received the inaugural BIAL Prize in Biomedicine, along with former mentor Caetano Reis e Sousa from The Francis Crick Institute. This new award recognises significant achievements in biomedicine published over the past decade. During his time at the Crick, Santiago discovered a mechanism used by cancers to escape detection by the immune system, which has the potential to be exploited therapeutically. This work has formed the basis of several clinical trials exploring the combination of anti-inflammatory drugs with immunotherapy in a range of cancers and is underpinning the research programme of Santiago's Cancer Inflammation and Immunity group.

Each year the Institute awards its own prize to recognise the most outstanding achievements by a young scientist. Named after a former Institute Director, the 2019 Dexter award was presented jointly to Mark Williams and Alice Lallo. During his time as a Clinical Research Fellow in the Leukaemia Biology group, Mark uncovered the molecular mechanism underpinning up-regulation of the drug efflux pump ABCB1, which is a key driver of chemoresistance in acute myeloid leukaemia. His work, published in the *Journal of Clinical Investigations*, suggested a potential therapeutic approach to overcome this form of resistance and enhance the activity of ABCB1 inhibitors. Mark is set to pursue a career as a clinician scientist in the field of stem-cell transplantation, and we look forward to welcoming him back to CRUK MI this year, through a University of Manchester Presidential Fellowship.

Alice Lallo's work in the CBC focused on characterising DNA damage response deficiencies (DDR) in small cell lung cancer using cell lines and circulating tumour cell derived explant (CDX) models. Her research has supported translation of the combination of two DDR inhibitors to the clinic and resulted in a first author publication in *Clinical Cancer Research*. A critical part of her study involved the use of ex vivo CDX cultures to screen for drug efficacy as well as investigating molecular mechanisms of drug response. In 2019, Alice published her second first author paper in the *British Journal of Pharmacology*, in which she described the development and characterisation of her CDX ex vivo culture system.

I have learned that it is through adversity and challenge we discover new and possibly better ways to conduct our research and interact with each other. During the pandemic, I was constantly reminded how resilient we are and I am impressed at how the Institute has not only coped with this difficulty, but continued to thrive. We have reopened our laboratories, albeit with some restrictions due to reduced occupancy and social distancing, but I am proud to see our dedicated staff back at work and pursuing their projects with so much renewed vigour.

Finally, this will be my last Director's Newsletter, as after 9 years at the helm, I have decided to step down as Director in March 2021. This is an exciting time for the Institute as we look to the move into the new building in Spring 2023. The move will provide opportunities to build and expand the Institute in new directions, and so I have decided to stand aside early so that a new Director takes on the task of creating that exciting future.

It has been a privilege to run the Institute and while I am sad to be moving on, I am proud of the Institute that I shall be handing over.

Professor Richard Marais
Director, Cancer Research UK Manchester Institute

Cover Image: Zoom is our new communication tool – for now it has replaced all our face to face meetings. Zoom screen shot showing participants in Molecular Oncology lab meeting.

Fundraising and Engagement activities

Committee Celebrate 60 Years of Fundraising at Alderley Park

The Blackburn and Ribble Valley Fundraising Committee celebrated raising more than £3million for CRUK in the last 60 years, with a special event hosted by the CRUK Manchester Institute at Alderley Park.

The group spent their day visiting research labs and core services, discovering how far their fundraising goes to help research progress.

They were welcomed by Millie Jones, Andrew Porter, Duncan Smith and Steve Bagley before enjoying an exclusive afternoon tea celebration, where Head of Volunteer Fundraising at CRUK, Trudy Stammer presented the committee with an engraved trophy to recognise their achievement.

CRUK Local Fundraising Manager, Leah Mitchell said: "We don't have many committees who have shown such outstanding dedication and have raised such an amazing amount of money for Cancer Research UK so we are truly very grateful for all that the volunteers do."

Duncan explains the role of mass spectrometry in cancer

The Blackburn and Ribble Valley Fundraising Committee

Revealing Research: CRUK Manchester Open Morning

Staff from the Institute joined together with other researchers and nurses from The University of Manchester and The Christie NHS Foundation Trust to welcome over 60 CRUK supporters to an Open Morning at the Oglesby Cancer Research Building.

After an overview and welcome from Chief Laboratory Officer Stuart Pepper, groups were able to visit the OCRB laboratories, take part in CRUK's Escape the Lab challenge and informally chat to scientists over a cuppa in the Researcher Café.

CRUK's Research Engagement Manager in Manchester, Tim Hudson said: "The open day allowed us to bring together a range of dedicated supporters and volunteers from the local area, celebrating their achievements and allowing them to engage with the research they have helped to fund.

"We're always grateful to all our funded researchers and scientists, including those at the Institute, for their commitment to thanking our supporters and giving an inspiring insight in to their work."

CRUK supporters learn what goes on in our labs

Images left to right: Poster gallery; Joanne presents her work at the public event

Research Spotlight: Manchester's Early Career Researchers

Before the outbreak of SARS-CoV-2, students and early career scientists at the Institute were given a chance to present their work to the public at an event organised by the early careers researchers' Committee (STAy), in collaboration with Cancer Research UK.

Over 60 members of the public, including local CRUK supporters, attended the mini scientific conference at the Oglesby Cancer Research Building, where they heard about the latest work happening at the Institute through presentations, posters and informal networking.

The event also included a keynote presentation by Institute Fellow, Patricia Muller.

Callum Hall, a PhD student in the Tumour Suppressors group and part of the STAy Committee who helped to organise the event, said: "We wanted to give younger scientists the opportunity to present to a lay audience and showcase their great work, as well as practise their poster presentation and speaking skills for future scientific meetings."

Drug Discovery Unit Lead Fundraising at Home Challenge

Being locked-down at home hasn't stopped Institute scientists doing their own fundraising for Cancer Research UK, who took on the charity's Race for Life at Home challenge, raising £3,000.

Megan proudly displays her fundraising tools

Led by Cinzia Bordoni and her colleagues in the Drug Discovery Unit, staff from the DDU, together with MI Director, Richard Marais, challenged themselves to raise £2,600 for CRUK as the charity's flagship sporting event went indoors. Each of the team walked, ran, cycled or exercised the equivalent of 25 miles: the distance between the old Paterson building, Alderley Park and back again.

CRUK is likely to see a drop of around 20-25% in income over the next financial year, in part due to having to cancel the Race for Life mass participation events, which themselves would have raised at least £30million.

Megan Mylrea, a PhD student in the DDU said: "You only have to see the amazing research that's going on in our institute and understand the impact that could have on thousands of patients to grasp how vital that money is.

"Cancer won't stop just because funding stops. That's why we wanted to do our bit to support that work.

"Without the funding that comes from events such as Race for Life we would not be able to continue our lifesaving work. I've never been a runner but it's been nice to focus on a positive challenge during lockdown.

"I've lost several immediate family members to cancer so it's good to be able to see first-hand the exciting research being done to improve cancer survival rates, all of which is made possible through generous donations."

David Jenkins fundraises with his edible treats

"I started off my fundraising for the Manchester 10K in support of Cancer Research UK with a Valentine's Day themed bake sale and a chocolate hamper Raffle on 14 February."

"My bakes included the ever-popular Chocolate and Caramel Cupcakes, Red Velvet and Jammy Dodger Cupcakes, Chocolate Fudge Cake, Dundee Cake, Gingerbread Men and much more! I also raffled off a 'Hotel Chocolat' Hamper kindly donated by one of our suppliers, Becton Dickenson (BD). The event was a big success and quickly sold out, raising £317.26 towards my £500 target, which was a great start. Due to the pandemic, the Manchester 10K has been postponed, so I now have more time to achieve my target. When we get back up and running I am hoping to organise a "David's Lucky Dip" event, a guaranteed prize every time – tombola is always a winner."

David and his 'lovely' raffle

New CRUK Video featuring MI scientists

CRUK's Research Engagement team have collaborated with scientists from across the UK to produce a new video, highlighting how CRUK-funded researchers have responded to the COVID-19 pandemic.

The new video, available to watch and share on the charity's YouTube channel, features scientists and nurses at all levels describing how they have continued to progress their work and support people affected by cancer during lockdown: https://youtu.be/owDs7JHZc5k

The video features Institute Director, Richard Marais and Head of Visualisation, Irradiation and Analysis, Steve Bagley.

Although reduced access to the labs means CRUK haven't been able to deliver face-to-face events and activities, the Research Engagement team remain in close contact with researchers in each location, helping to keep CRUK supporters engaged with funded scientists and their life-saving research via digital content.

COVID-19 research video participants screenshot

Selected Publications

Understanding drug resistance in acute myeloid leukaemia

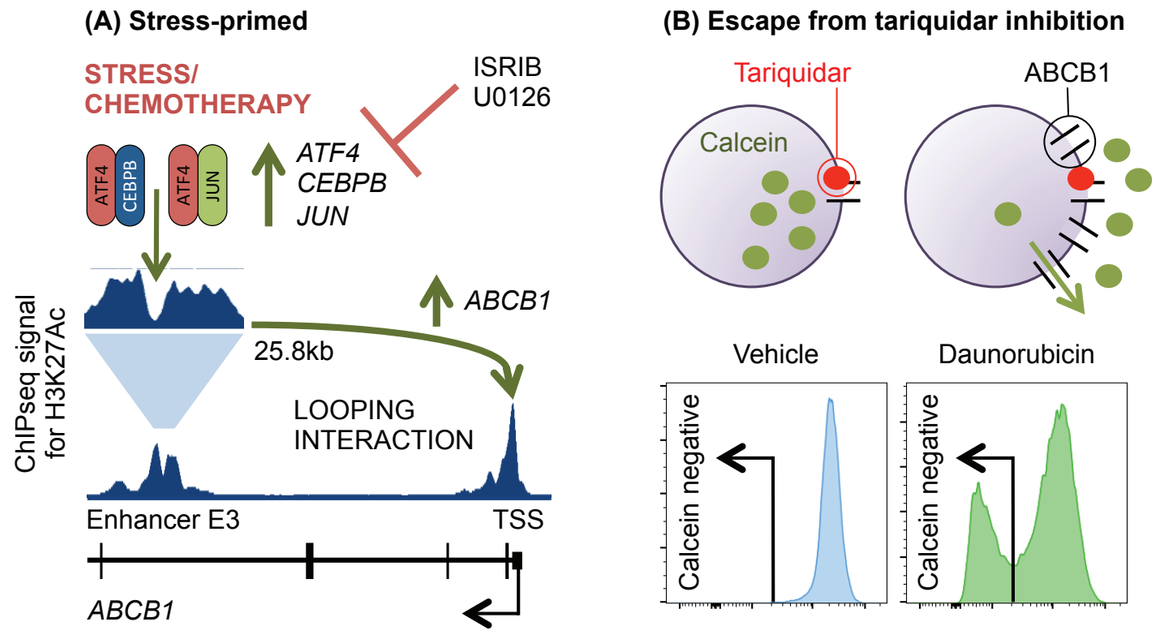
Acute myeloid leukaemia (AML) is a debilitating disease with various chemotherapy drugs developed against it. However, it is known that the drugs can fail and the cancer persists. It is also known that a protein called ABCB1, which is a drug pump, is one of the culprits behind these resistance mechanisms.

To understand how ABCB1 is regulated and thus understand the mechanisms responsible for the removal of a drug from cells and AML resistance, the Leukaemia Biology group investigated its transcriptional network (how a gene is expressed in the cell).

They found that when treating with a common chemotherapy drug (daunorubicin), the network would get activated, with the cell manufacturing more ABCB1 and exporting the drug out of the cell. To make matters worse, if cells were treated for long periods of time and daunorubicin was removed, after re-introducing the drug it resulted in rapid ABCB1 production, suggesting that the cells were able to "remember" the drug and how to react to it. Tackling the ABCB1 protein head-on proved unfruitful as it was able to escape direct inhibition if the cells were challenged with daunorubicin. However, when treating with other drugs such as U0126, alone or in combination with ISRIB, they were able to stop the cells from sending the signals from the daunorubicin-activated network and successfully reduce the amount of *ABCB1* gene expression.

The importance of this work is two-fold. First, it is a possible or partial explanation for the failure of ABCB1 inhibitors in clinical trials. Secondly, it shows the potential of a treatment strategy where U0126 +/- ISRIB are provided together as adjuvant therapy before ABCB1 inhibitors.

Williams MS, Amaral FM, Simeoni F, Somervaille TC. (2020) A stress-responsive enhancer induces dynamic drug resistance in acute myeloid leukemia. *Journal of Clinical Investigation* 130(3):1217-1232.



Stress induces *ABCB1* (ATP binding cassette subfamily B member 1) expression in leukemic blasts and permits escape from targeted ABCB1 inhibition. (A) Enhancer 3 (E3) is primed by chronic stress. Recurrent stress or chemotherapy induces an Integrated Stress Response-like transcriptional program that includes the transcription factor (TF) genes *ATF4, CEBPB* and *JUN*. The TF proteins bind E3 and drive increased *ABCB1* transcription. Stress-induced upregulation can be mitigated by inhibitors of stress signaling (U0126 and ISRIB). (B) Upregulation of *ABCB1* increases cell surface protein density and allows drug efflux to occur in the presence of pharmacologic doses of tariquidar (red dot). A calcein-negative population is observed following daunorubicin exposure despite concomitant tariquidar treatment (bottom panel). H3K27Ac, histone H3 lysine 27 acetylation; TSS, transcription start site.

Identifying response to immune checkpoint blockade therapy in melanoma

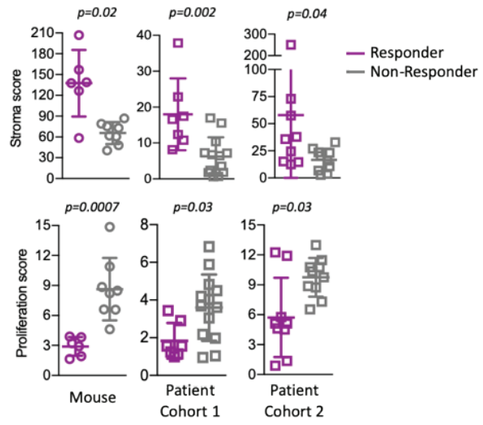
Immune checkpoint inhibitors (ICIs) have considerably improved treatment outcomes for advanced-stage melanoma patients. Understanding how these drugs can change the composition of tumours is key to further improve patient responses to ICI therapy.

Identifying changes in a tumour that indicate a response in humans is difficult because factors such as the patient's genetic background, lifestyle, previous treatment history and location of metastasis can all affect how a patient responds. Researchers from the Molecular Oncology group have used a mouse model of melanoma, with comparable genetic features and ICI response to human disease, in order to control these variables and gain a clearer insight of important changes occurring during response to ICI therapy.

By comparing non-responder mice to those with a continued response, they found a set of genes more highly expressed in responder mice and a number of genes that were downregulated. The 10 highest expressed genes were related to cancer-associated fibroblasts and incorporated into a 'stroma score'. Downregulated genes were related to cell division and growth, and from these 7 genes were used as a 'proliferation score'. Importantly, the expression of these gene scores were able to distinguish responders from non-responders in two independent patient cohorts treated with ICI therapy.

This research highlights the potential to identify early changes in tumour biology associated with response in patients through measuring the expression of a small number of genes. This could allow for personalised treatment, by predicting which patients are likely to progress on ICI therapy and benefit from combination treatments. Equally, patients likely to have a durable response can be spared further therapy which may risk toxic side-effects.

Galvani E, Mundra PA, Valpione S, et al. (2020) Stroma remodeling and reduced cell division define durable response to PD-1 blockade in melanoma. *Nat Commun* 11, 853.



Stroma remodelling and reduced cell division define durable response to therapy with anti-PD-1 in melanoma. Top: Stroma score defining the level of expression of the 10-gene signature identified in our mouse model (left) and validated in two independent human cohorts (middle, right); Bottom: Proliferation score defining the expression of the 7-gene panel identified in our mouse model (left) and validated in two independent human cohorts (middle, right).

Liquid biopsies for small cell lung cancer

Tissue biopsies and serial biopsies pose a significant challenge in small cell lung cancer (SCLC) as they are typically of poor quality or unavailable for research. Several targeted therapies have now entered clinical trials and analysis of circulating free DNA (cfDNA) is a minimally invasive approach for disease monitoring and stratification.

The Cancer Biomarker Centre developed a molecular profiling and disease monitoring liquid biopsy workflow to support targeted treatment of SCLC. They examined genome-wide copy number aberrations (CNA) and targeted mutation analysis of 110 SCLC associated genes, including those within DNA damage repair pathways.

CBC applied this workflow to pre-treatment cfDNA from patients with extensive-stage (ES) or limited-stage (LS) SCLC to establish sensitivity. Tumour-related changes (CNAs and/or somatic mutations) were detected in >93% patients with potentially targetable mutations in >50% cases. In multivariate analysis, CNA analysis and mutation number significantly associated with disease stage. They explored utility of cfDNA analysis for disease monitoring and CNA profiles showed dynamic changes through therapy to disease relapse. The liquid biopsy approaches reported here are promising and may have potential to become a routine patient-monitoring tool in the clinic.

Mohan S, et al. (2020) Profiling of circulating free DNA using targeted and genome wide sequencing in patients with small cell lung cancer. *Journal of Thoracic Oncology* 15(2):216-230.

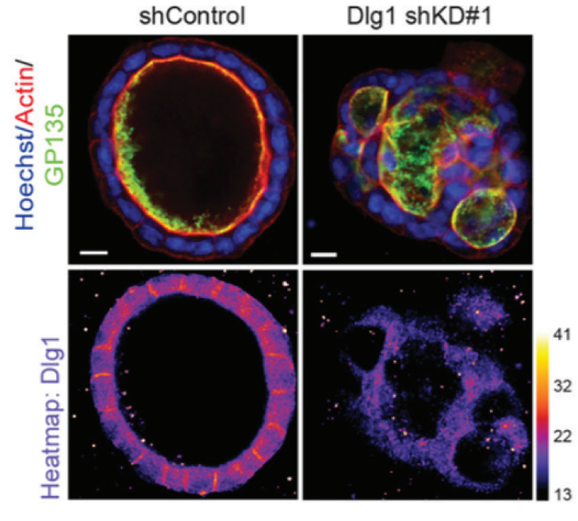
An essential interaction to maintain normal epithelial structures

A study published in the *Journal of Cell Science* led by Andrew Porter and Angeliki Malliri from the Cell Signalling group demonstrates that normal epithelial organisation is maintained by the interaction between tumour suppressor proteins – Dlg1-CAS – and their depletion or dysfunction leads to mitotic aberrancies and loss of epithelial lumen integrity in 3D culture. This is now believed to have an impact on tumour suppression within mammalian epithelium.

Development and maintenance of normal epithelial structures require the correct positioning of the mitotic spindle. Therefore, new cells from a cell division must be integrated properly to maintain existing structural architecture. A set of proteins are thought to regulate mitotic spindle orientation and stability known as LGN and NuMA proteins. Correct localisation of these proteins must be directed by a yet unelucidated set of protein-protein interactions.

Porter and colleagues now show that Dlg1 plays an essential role in orienting the mitotic spindle and LGN-NuMA proteins along an apical-basal axis to maintain normal lumen structures and additionally identify an essential Dlg1 protein interaction with CASK for normal Dlg1 activity. By inhibiting these interactions, they were able to demonstrate that an interruption in this process during mitosis will result in multi-lumen structures, a characteristic often seen in human epithelial neoplasms.

Porter A, et al. (2019) The interaction between the CASK and tumour suppressor Dlg1 regulates mitotic spindle orientation in mammalian epithelia. *Journal of Cell Science* 15;132(14) jcs230086.



Dlg1 regulates epithelial lumen formation and mitotic spindle orientation: Confocal images of MDCKII cysts grown in collagen I, constitutively expressing non-targeting shRNA (shControl) or shRNA targeting Dlg1 (Dlg1 shKD#1), stained for the indicated proteins to show lumens (upper panels) or Dlg1 levels (lower panels; heatmap of expression levels, arbitrary units), showing multilumen structures after Dlg1 depletion.

Circulating cell-free DNA assay makes marker for pancreatic cancer

Using serial biopsy of pancreatic ductal adenocarcinoma (PDAC) to chart tumour evolution presents a significant challenge. The Cancer Biomarker Centre examined the utility of circulating free DNA (cfDNA) as a minimally invasive approach across a cohort of 55 treatment-naïve patients with PDAC; 31 with metastatic and 24 with locally advanced disease.

Somatic mutations in cfDNA were detected using next generation sequencing in 15/24 (62.5%) and 27/31 (87%) of patients with locally advanced and metastatic disease respectively. Copy number changes were detected in cfDNA of 10 patients of whom seven exhibited gain of chromosome 12p harbouring *KRAS* as well as a canonical *KRAS* codon 12 mutation. In multivariable Cox Regression analysis, they show for the first time that patients with *KRAS* copy number gain and *KRAS* mutation have significantly worse outcomes, suggesting that this may be linked to PDAC progression. The simple cfDNA assay the team describe will enable determination of the presence of *KRAS* copy number gain and *KRAS* mutations in larger studies and clinical trials.

Mohan S, et al. (2019) Analysis of circulating cell-free DNA identifies KRAS copy number gain and mutation as a novel prognostic marker in pancreatic cancer. *Scientific Reports* 9(1):11610.

Non-small cell lung cancer relapse risk prediction by pulmonary vein CTC number at surgery

Approximately half of patients with early-stage non-small cell lung cancer (NSCLC) who undergo surgery to cure their cancer will relapse within five years. Determining which patients are most at risk of recurrence could allow increased monitoring for residual disease after surgery.

Circulating tumour cells (CTCs) – individual cancer cells which have broken free of the primary tumour – are thought to be the direct cause of metastasis in NSCLC. Scientists at the CRUK Manchester Institute Cancer Biomarker Centre had previously shown that counting the number of CTCs in a patient's blood was indicative of the course of the disease. This larger study of CTCs from 100 patients enrolled in the TARGET (Tumour chARacterisation to Guide Experimental Targeted therapy) trial sought to look in more detail at those CTCs.

First, the researchers confirmed the prognostic value of CTC number, showing patients with very high CTC number isolated from the pulmonary vein during surgery highly likely to relapse. They also identified which other factors should be determined to increase the sensitivity of the test in a clinical setting.

For one patient they were able to compare the DNA of the primary tumour to that of individual CTCs and also a secondary tumour which developed after the initial surgery. Remarkably, they showed that the CTCs contained mutations more in common with the secondary tumour than the primary tumour from which they originated, indicating that CTCs are indeed the source of metastasis. Some of those mutations were in genes known to increase cancer growth, suggesting that sequencing the DNA from CTCs may allow for precise characterisation and targeting of a patient's future tumours.

Chemi F, et al. (2019) Pulmonary venous circulating tumor cell dissemination before tumor resection and disease relapse. *Nature Medicine* 25(10):1534-1539.

Monitoring early changes in blood T cells can predict response to immunotherapy

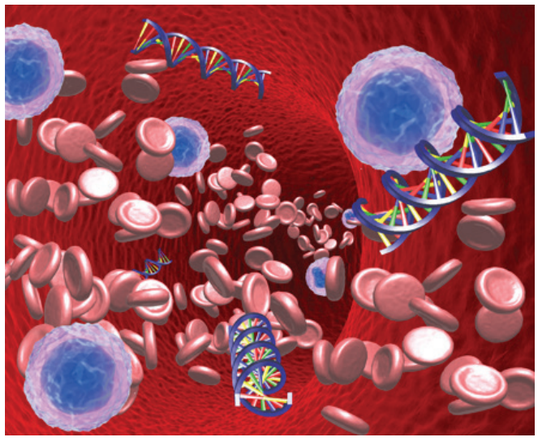
Research into how immune checkpoint inhibitors (ICIs) affect the systemic immune system, rather than inside the tumour, is currently limited. In a study led by Sara Valpione and Professors Richard Marais and Paul Lorigan, T cell populations circulating in the blood of metastatic melanoma patients were analysed after one cycle of ICI therapy to identify early on treatment changes.

The study used T cell antigen receptor (TCR)-sequencing in parallel with analysis of paired cell-free DNA (cfDNA) to analyse blood samples before treatment and 3 weeks after treatment. Increased turnover of T cells and the presence of more productive TCR sequences were found to correlate with a patient response to ICI therapy.

The researchers also identified a memory effector cytotoxic T cell subset which they called TIE cells. The expansion of these cells was seen to be higher in patients who responded to ICIs.

Importantly these events can be detected from a blood sample, occur early after starting treatment and can predict a patient's likelihood of responding to ICI therapy. This research could therefore help clinicians to make more effective treatment decisions for patients with metastatic melanoma on ICI therapy.

Valpione S, Galvani E, et al. (2020) Immune-awakening revealed by peripheral T cell dynamics after one cycle of immunotherapy. *Nature Cancer* 1(2), 210–221.



The Molecular Oncology group identified an immune signature of response to anti-PD1 drugs analysing peripheral blood T cells and the T cell receptor DNA sequences in cfDNA of cancer patients receiving immunotherapy.

Maintaining connectivity at the Institute during Covid-19 lockdown

During the lockdown period it was critical that we remained connected with our colleagues and support each other in this challenging time.

Institute Director Richard Marais gave weekly updates where he addressed the Institute from his home via Zoom. Here he reassured staff, kept everyone up to date with the developments in relation to Covid-19, and provided an opportunity for everyone to ask any questions. These updates were an important source of contact with each other and helped us feel united against the impact of the virus.

We also continued with our programme of internal seminars online as well as inviting several external speakers to give talks. We are extremely grateful to everyone who gave their time to share their research with us.

Education and Engagement Group

An education and engagement group was established to discuss, plan and deliver a programme of events that would keep our people engaged and connected as the Institute closed its doors during the months of lockdown.

The creative team was comprised of a mix of senior scientists, members from our Operations department, Education Committee and the STAy Committee. Together, they worked hard to assess the needs of everyone with surveys and formulated a variety of interesting seminars, training sessions and courses in response.

The training sessions were popular and included 'Introduction to Photoshop' by Yannick Von Grabowiecki, 'Beginners Introduction to R' led by Simon Pearce, and a 'Crash statistics course' run by Sara Valpione.

The group also formulated a series of seminars to be delivered by internal and external lecturers via Zoom to engage our staff and students. The successful 'Underpinning Elements of Cancer Research Talks' involved a series of lectures from cancer researchers and clinicians from the University and the Christie NHS Foundation Trust. This was a prime opportunity for our scientists to take part in discussions on varying and widening key topics. These well attended sessions offered insight into the concepts of other fields such as pharmacodynamics/kinetics, pharmacology, drug discovery, radiation biology, hypoxia and carcinogenesis. We would like to thank all those who took part.

The group was also concerned about the wellbeing of our staff during these difficult times and the impact of lockdown on mental health, whether it be coping with social isolation for those living alone, or balancing caring commitments and home-educating children with working from home. With this in mind, we circulated the webinar 'Wellbeing for Managers – supporting your staff during Coronavirus' ran by Gemma Dale, Wellbeing and Engagement Manager at the University of Manchester. This one-hour session introduced the subject of wellbeing at work and the roles and responsibilities of people managers. It looked at the specific actions that managers can take during the current situation to enable and support the wellbeing of individuals and teams. We also regularly posted advice and resources to help staff cope and manage their wellbeing during this time.

The STAy Quarantine Quiz!

The STAy Committee, in the spirit of keeping our whole research community connected, hosted fortnightly quizzes for everyone on Friday evenings.

Teams were assigned at random and prizes were given to the winning teams. STAy also hosted coffee mornings before seminars to give staff and students an opportunity to chat and catch up. Both these events were very popular and played an important role in connecting us all with our colleagues across the Institute.

Communications support

By David Stanier

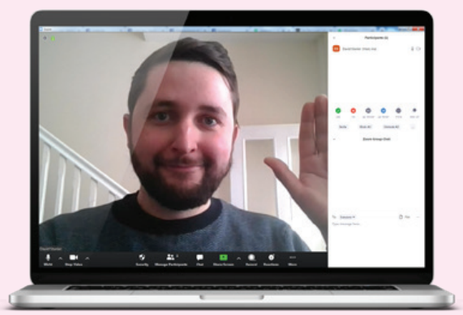
The Operations team have been continuing our seminars using online streaming. These have included our usual Internal Seminar Series and talks from external speakers, as well as additional talks from our Core Facilities staff and weekly updates from our Director.

Our team has already had quite a bit of experience in streaming seminars online. While we wait for our new building, the majority of our staff are located at Alderley Park, however some groups are currently at the OCRB or elsewhere, and so for the past three years we have been streaming seminars using Zoom.

But now rather than between the two lecture theatres, everyone joins the streaming from their homes via Zoom, with audiences reaching over 250 of our staff. Speakers are shown how to share their presentations, questions are taken in the 'Chat', and some talks are recorded for later viewing.

We held a useful online session to teach anyone who needed to learn how to use some of the different options available on Zoom, such as sharing documents and the various settings when scheduling meetings.

It's nice to see familiar names logging on each time and friendly faces even if they are currently through a webcam.



David supporting our communication platform

How the Institute supported the national effort in SARS-CoV-2 testing

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CANCER RESEARCH UK MANCHESTER INSTITUTE

As COVID-19 disease in the UK escalated, and the Cancer Research UK Manchester Institute along with the rest of The University of Manchester shut its doors, our senior management immediately started to think how to best support the urgent national need to expand SARS-CoV-2 testing.

We first planned to establish a testing facility within CRUK MI, but when the government announced that a national testing hub would be developed at the Alderley Park site, our home base, it was clear that this initiative should be where we would focus our efforts and support. Many of our research staff, whose laboratory skills are especially well suited for the task of SARS-CoV-2 testing in a regulated laboratory environment, were keen to volunteer. Institute Director Richard Marais and Caroline Dive contacted Peter Simpson, CSO at Medicines Discovery Catapult, and Director of the Alderley Park Lighthouse Laboratory, to offer our support. We developed a working partnership between CRUK MI and the Lighthouse Laboratory and our staff were amongst the first to undergo training and to get started testing samples from front-line NHS workers, whose negative results allow them to return to patient care.

Dominic Rothwell, lead of the Nucleic Acids Biomarker team in the CRUK MI Cancer Biomarker Centre, supervised lab staff within the Lighthouse Laboratory. He has been impressed with the speed at which testing sample numbers increased in a period of just a few weeks. The Institute also loaned key equipment to the Lighthouse Laboratory that will underpinned the rapid further expansion of testing capacity. We are proud of our volunteers and our part in this magnificent effort.

Institute Deputy Director Caroline Dive is continuing to support the COVID-19 efforts by being part of the Leadership Team of the Lighthouse Laboratory, working with a small group of talented individuals from the diagnostic and pharma industries and from academia, who are busy developing the strategy for future proofing the Alderley Park laboratory to ensure testing capacity meets ongoing demand.

CRUK MI scientists on the frontline at coronavirus mega-lab

Sophie

Three of our scientists were part of a group of highly qualified Cancer Research UK volunteers who are testing thousands of patient samples each day for coronavirus at the new Lighthouse Lab at Alderley Park in Cheshire, led by Medicines Discovery Catapult.

CRUK volunteers are involved in part of the testing process – including debagging nose and throat swabs delivered daily from across the UK, extracting genetic material from the samples, and running tests which identify presence of the SARS-CoV-2 virus.

With many laboratories shut down for the time being, our scientists are using their expertise in the national and global effort to beat Covid-19.

Dominic Rothwell, senior scientist in the Cancer Biomarker Centre, led the group of CRUK volunteers working alongside industry partners at the mega-lab.

His usual work at the Institute includes examining how circulating tumour DNA – a substance released from cancer cells into the bloodstream – can develop better treatments for patients.

Dominic said: "I'm proud to be playing my part in the fight against coronavirus. I'm normally based at Alderley Park, so I'm very familiar with the location and the facilities on site.

Dominic

Isabelle

"The techniques and approaches used by cancer researchers for decades are the same disciplines being used to track, understand and defeat this virus – so when the opportunity came up, I knew I wanted to get involved.

"Research on cancer is still our priority, but the virus must be tackled too. By helping the global effort of tackling Covid-19, we hope we can get back to beating cancer as soon as possible."

Amongst those who volunteered alongside Dominic were Sophie Richardson and Isabelle Thompson, both scientific officers based in the Cancer Biomarker Centre.
Sophie said: "When I heard that the new lab was looking for volunteers, I put myself forward right away. I'd only been in my role at the Manchester Institute for a few months before lab work was paused in March, but I wanted to put my skills to good use in the meantime.

"It's a really supportive environment in the labs and it's amazing to see how everyone's pulled together to make this happen at such speed. What we're doing here is part of history and it feels good to know I'm helping the country beat this virus."

Isabelle said: "As scientists, we have a really important part to play in the fight against the coronavirus, and I'm proud to be a part of the work at Alderley Park. As soon as I heard about the opportunity to volunteer, I knew I had to sign up straight away.

"In the cancer lab we handle biological samples every day and have many of the skills needed to deal with coronavirus samples too. Each part of the process is meticulously done, from unpacking the samples through to testing them and quality controlling them, which suits the way most scientists work.

"I'm normally based at Alderley Park so, while our labs on site are temporarily closed, this a great opportunity to come together with industry and academic volunteers from across the site in one big collective effort. Everyone is really supportive of one another and the morale feels really positive."

Testing Minister Lord Bethell said: "Many extraordinary people are playing a vital role in the national effort to fight coronavirus and rapidly increase testing.

"I'd like to personally thank Dominic, Sophie and Isabelle for volunteering to work at the Lighthouse Lab in Alderley Park. They are part of what is now the biggest network of diagnostic testing facilities in British history – a phenomenal achievement, helping to make sure anyone who needs a test can get one."

Prof. Peter Simpson, Chief Scientific Officer, Medicines Discovery Catapult and Director, Alderley Park Lighthouse Lab, said: "The Alderley Park Lighthouse Lab has been set up at an unprecedented pace and scale to respond to an urgent national need.

"This would not be possible without the hard work and dedication of all the scientific volunteers from research charities, universities, and industry, who have stepped forward to collaborate and utilise their skills in the fight against COVID-19. The volunteers from Cancer Research UK have been instrumental in progressing testing, and we can't thank them enough for their continued commitment."

The Lighthouse Lab at Alderley Park is part of what is the biggest network of diagnostic testing facilities in British history, testing coronavirus samples from drive-through test sites across the country. Similar mega-labs have been set up in Glasgow and Milton Keynes.

As well as volunteers, Cancer Research UK has also loaned specialist equipment to the Alderley Park Lighthouse Lab. This includes seventeen polymerase chain reaction (PCR) machines, which are used in cancer research to examine DNA in tumour samples. These machines have been repurposed to examine DNA from nose and throat swabs to look for signs of viral genetic material left behind by the coronavirus.

Cancer Research UK has seen a heroic surge of activity amongst its research community to tackle Covid-19. As cancer scientists, its highly skilled workforce a have a range of specialist skills needed for this kind of work.

The new Lighthouse Labs have been created through a partnership with the Department of Health and Social Care and Medicines Discovery Catapult with UK Biocentre and the University of Glasgow. They are being closely supported by both NHS and Public Health England. The Alderley Park facility is hosted by the Medicines Discovery Catapult, working closely with AstraZeneca.

Institute scientist determined to teach cancer a lesson

Steve at his day job in the lab

One of our scientists, who during lockdown with his three children, added a new activity to the home-school timetable.

Steve Lyons is a senior scientific officer at the Institute based at the OCRB, where he works in the Translational Oncogenomics group exploring new ways of understanding how prostate cancer develops so that new treatments can be created.

He has been working for the Institute for over 20 years and is a familiar face to many of us, known widely for his commitment to fundraising and public engagement. But when lab work was temporarily paused due to the pandemic, Steve continued his research from home while also entertaining his children with a boredom-busting initiative from Cancer Research UK's Race for Life Schools.

Equipped with eggs and spoons the young competitors helped to launch the charity's free resource kit full of tips, ideas and materials for holding a DIY sports day. The siblings have been competing against each other in a range of traditional events in their back garden, including sack races, bean bag races, and of course an egg and spoon race.

The family wanted to do everything they could to ensure that the fight against cancer can continue during these unprecedented times. Steve lost his mother Sue to bowel cancer in 2008 and is determined to play his part in beating the disease.

Steve said: "As scientists we are not immune to cancer – it affects us too. Our research is so important, because cancer affects a massive number of people. And not just those with the cancer, but also everyone around them.

"That's what drives our fundraisers and that's what drives scientists. So many families are affected by cancer, so I hope others will help the cause.

"Charities like Cancer Research UK will be hit hard by the current situation, but we can all play a part – no matter how big or small – in supporting life-saving work right now.

"Lockdown isn't easy for any of us, but the kids had really good fun creating their sports day at home, and it was all the more meaningful to know we were doing it for a good cause."

Cancer Research UK's Race for Life, in partnership with Tesco, is an inspiring series of events which raises millions of pounds every year to help beat cancer. Last year, the charity was able to spend over £30 million in the North West on some of the UK's leading scientific and clinical research.

To get involved, visit www.raceforlife.cancerresearchuk.org/about-our-events/race-for-life-schools/do-your-own-sports-day

As reported to the Oldham Evening Chronicle on 27 May.

CRUK MI PhD student shares experience of COVID-19 lockdown

Zoe Lee

Lockdown due to Covid-19 is affecting scientists and their research all over the world. The Royal Society Blog has featured stories from a number of scientists in their Science in Lockdown series, where they describe the impact of the current situation on their research.

Zoe Lee, PhD student in the Cell Division group at the Institute, was invited to share her story and here is what she had to say about her experience during the lockdown.

"My PhD project combines genetics, biochemistry and molecular biology to study phosphatases in fission yeast. Due to the current coronavirus pandemic, CRUK MI has temporarily closed. Whilst in lockdown, I was really keen to use my laboratory skills to help out with COVID-19 testing in order to do what I can to help and aid the reopening of CRUK MI so that we can return to fighting cancer as soon as possible. Eager to resume my work in cancer research, I immediately signed up to the call for volunteers to help out with COVID-19 testing at the Alderley Park Lighthouse Lab, which is led by Medicines Discovery Catapult. On my first day at the Lighthouse Lab, I was shown around the different workstations which link together from receiving the swab sample up until analysing the sample for the presence or absence of the virus. After I met everybody on the different workstations, I received thorough training at my workstation and got stuck straight in. The smoothness of the workflow is incredible and everybody is very motivated to push out increasing numbers of tests.

The diversity amongst the volunteers from different companies and the army, all coming together for a single goal, has made the experience very rewarding. The atmosphere on site is extremely uplifting and the team have made volunteering a real pleasure. I'm looking forward to the future weeks and I'm delighted that I am able to be a part of the Alderley Park Lighthouse Lab. I am striving to get things back to normal to address this dreadful pandemic and then get back to my important work in the CRUK MI Cell Division lab where we are pushing back the boundaries to find new and better cancer therapies."

The original piece was featured in the Royal Society Blog edited by Helen Eaton.

Institute cancer scientist returns to hospital wards treating patients with both cancer and coronavirus

Victoria in full PPE

Victoria Foy is a PhD student at the Institute where she works on ground-breaking lung cancer research. Part of our Cancer Biomarker Centre, she is exploring how circulating tumour DNA – a substance released from cancer cells into the bloodstream – can help develop better treatments for patients with the disease.

When her academic work was paused due to the pandemic, Victoria – who has a degree in medicine from the University of Liverpool –returned to the NHS as a frontline doctor.

She worked full time at The Christie NHS Foundation Trust in Manchester, where her work includes treating hospital patients with a diagnosis of both cancer and Covid-19. The specialist cancer centre is providing care for a small number of cancer patients whose illness and treatment is complicated by an episode of the Covid-19 infection.

Victoria said: "With the research lab shut down for the time being, I had a feeling that I should be doing something to support the national effort on the NHS frontline. I am registered to practise as a medical doctor, so I felt determined to play my part in supporting vulnerable patients.

"In my first week, I was asked to work on a ward with Covid-19 cancer patients at The Christie.

"It was a bit daunting at first as I was given full protective equipment to wear, including a mask, face visor, apron and gloves. But the ward feels very calm and under control – and I feel like I'm able to contribute and make a real difference.

"It's tough enough for patients to deal with treatment for cancer and all that entails, but to add an additional diagnosis of Covid-19 is particularly challenging. It's a really difficult time for patients as visiting is significantly reduced at the hospital and family contact isn't so readily available.

"But the teams at The Christie are doing a great job."

As well as her work with Covid-19 cancer patients, Victoria also cared for patients who had routine cancer treatment at The Christie for bone and tissue sarcoma – a rare form of cancer that normally affects younger people.

She said: "I'm very proud to be part of the team providing direct patient care and making sure that cancer patients continue to get the treatment they need. Many of these patients have young families of their own, and it's really important to offer support and care for them at what can feel like a very daunting and isolating time."

Victoria continued working at the hospital until she could resume her PhD studies after the Covid-19 pandemic restrictions eased.

She said: "We must not forget that researching cancer is such a critical part of improving long term outcomes for patients. The sooner we can get back to the labs, the sooner we can start beating cancer again and saving even more lives."

Anna Taylor, north west spokesperson for Cancer Research UK, said: "Cancer doesn't go away during or after Covid-19, but we're incredibly proud of our community of scientists who have been very quick to respond to the crisis, using their kit, skills and talent to support the NHS.

"Victoria is a shining example of the heroic efforts our scientists are making to support the global effort of tackling Covid-19, and helping us get back to beating cancer as soon as possible."

As reported to the Warrington Guardian on 22 April.

CRUK MI scientist manufacturing PPE against COVID-19

Steve Bagley is the head of our Visualisation, Irradiation & Analysis service at the Institute. He normally works with microscopes and X-ray machinery to analyse cancer cells, but became increasingly aware of the lack of PPE for the nation's frontline staff. Steve said, "I saw that there was a need for more protective equipment for those working in the NHS, so I wondered how I could help."

While our labs at Alderley Park were temporarily closed for research, Steve had been tasked with the job of looking after and maintaining the specialist lab equipment, including a 3D printer.

"I'm very familiar with the 3D printer, as it's a piece of kit we use regularly to create parts for microscopes and other lab equipment," says Steve. "And it occurred to me that I could use this to create plastic headbands for protective face masks."

Once Steve had worked out a template, with correct dimensions for the headbands, he began a mini production line, printing the plastic headbands in the lab.

So far, Steve has produced over 200 protective face masks for frontline healthcare staff. The PPE will be distributed to hospitals across the North West, including The Christie NHS Foundation Trust in Manchester.

"I really wanted to do something to support all those who are working so hard on the frontline in the battle against Covid-19. And the sooner we beat this virus, the sooner we can return to beating cancer."

The Institute is proud of Steve for using his ingenuity and time to support our NHS staff at the frontline.

Steve with his 3D printer and one of the protective face masks he produced

From the lab to the living room - transitioning cancer research during a pandemic

Eve Oliver, part of the Manchester Cancer Research Centre Operations team, interviewed two of our 2nd year PhD students, Alexandru Suvac and Jack Ashton, who both work in Prof Robert Bristow's lab based in the OCRB Building, for her MCRC blog on 26 May.

Has Covid-19 impacted your current research project/projects? Are you able to continue any of your research in some format?

I don't think there is a scientist whose work has not been impacted by the current pandemic. Some are hit harder than others. Generally, the current situation is disrupting "dry" lab scientists (bioinformaticians, statisticians) much less than "wet" lab (molecular biologists, those in charge of animal facilities). Although this has placed a dam on my novel data flow it has also liberated me to analyse my backlog of data and gives me time to reassess old results and place them in the bigger context of my project.

I am also putting my efforts into reading more papers on my topic and taking the time to think about new techniques and to brainstorm the applicability of the project. In short, this is a fantastic time for generating ideas!

What responsibilities have you and your lab said 'goodbye for now' to?

Any experimental work – which was a big proportion of my day-to-day work.

What have you and your colleagues been doing to virtually encourage work-cohesion and morale?

The same as everyone else – virtual meetings and group chats. We stay interacting with each other, cracking jokes, chatting about serious issues, updating each other on our lives – the same as before lockdown. We are trying out online quizzes and party games in an effort to socialise. The work group chat has been a lot more alive and vibrant, putting a smile on my face that face-to-face jokes would have before.

Has working from home benefitted your team in any way?

It certainly has! It allows us to share ideas and think about them at a slower tempo. It has opened up time for more lab meetings and more journal clubs which keeps us stimulated with fresh ideas and exciting research.

Are you currently having to juggle working from home with other responsibilities, e.g. being a new 'teacher from home' or a primary carer for family?

I am very lucky with respect to this point. As a 23-year-old living alone in a studio flat my only responsibility is myself. This has just turned into one long weekend that I have to work through.

Has Covid-19 impacted your current research project/projects? Are you able to continue any of your research in some format?

My research involves investigating the role of hypoxia and genomic instability in prostate cancer progression, with a primary focus on hypoxia induced DNA repair vulnerability. The primary goal of my research is to facilitate better risk assignment and treatment decisions for patients who present with both tumour hypoxia and highly unstable genomes. While it was tough adjusting to social distancing and lab closures, I feel our lab team are making the best of the situation. We're a close-knit bunch, so it's been a big miss not being able to crack jokes in our tissue culture room and catch up each lunch time. Nevertheless, we have been conducting regular lab meetings through zoom, giving us more time to discuss experiment progress, as well as future projects, hypotheses, and plans for when we return to the lab. Alongside this we have also been meeting for weekly journal club sessions and have even maintained our Friday beers tradition once the clock strikes 5pm, virtually now of course!

On a personal note, like for many people it has been quite an anxious period given the time limited nature of working towards a PhD and not being able to generate data as I move into a key phase of the project. However, the Cancer Research UK Manchester Institute has been fantastic in reiterating support for their current PhD students, both through ensuring stipend security in the short term and also relating to potential PhD extensions if necessary. The Institute Director also holds weekly Zoom meetings to field questions and update us on the Institute's response to the crisis, which helps us stay informed about how the other groups are doing and how the situation is progressing.

Has working from home benefitted you or your team in any way?

I have used the downtime away from the lab to focus on image analysis using the HALO platform and have also started teaching myself R. The institute is organising additional online training in these areas, as well as a regular seminar series, both of which are keeping the community scientifically engaged. The image analysis algorithms I develop on HALO will be vital for an upcoming project assessing the relationship between hypoxia and homologous repair in patient samples, while I also hope to translate my learnings in R to genomic based analyses in a separate project.

Since late April I have been volunteering at the Alderley Park Lighthouse Lab, one of the COVID19 national testing centres. I perform the RNA extraction step of the testing process and it has been great to use my lab skills to play a part in the pandemic response effort.

Educational News

We welcomed nine new PhD students and one clinical research fellow to the Institute in September 2019, with their inauguration to CRUK MI at the Colloquium.

Naseer Basma

Hello, my name is Naseer. I was born in Lebanon and have lived in Manchester since my early teens. I have recently joined the Leukaemia Biology group led by Tim Somervaille. Prior to this move, I completed an undergraduate degree in Pharmacology at The University of Manchester, then an MRes in Biomedical Sciences at the University of Liverpool. During the latter, I worked in a lab focusing on acute myeloid leukaemia where I researched the role of inflammation in this disease using the CRISPR-Cas9 gene editing system.

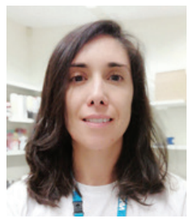
I subsequently undertook an internship within the Epigenetics of Haematopoiesis group at the OCRB where I also worked closely with the Leukaemia Biology group. The area of science covered by both groups, studying the molecular mechanisms driving haematological malignancies, and my fond interactions with lab members convinced me to pursue a PhD here. I am now fortunate enough to be working in the Leukaemia Biology group, where I will investigate the origin of inflammation in a blood cancer called myelofibrosis and determine how inhibition of a histone modifying enzyme called LSD1 alleviates this inflammation. Having lived close to the former Paterson Building for most of my life, I am very proud to be working at CRUK MI and am tremendously excited to be part of the CRUK family. Outside of work, I am an avid gym-goer and dedicate a lot of time to fitness. I am also a huge Manchester United fan so there isn't a better place to be for me than here!

Cath Felton

Hi, I'm Cath. I grew up in a small village in Surrey, just south of London. I spent the last four years studying Cell Biology at The University of Manchester. During my undergraduate studies I completed a 9-month placement at the Fred Hutchinson Cancer Research Center in Seattle, USA where I first discovered a love of single cell technologies and there I focused on utilising single cell RNA sequencing to explore cell type composition of myeloproliferative neoplasms with a view to identify rare cell types. Upon my return to Manchester, having realised I had more of an interest in solid tumours, I focused my final year project on the role of adhesion signalling in mammary epithelial tissue transformation. Bringing together an interest in cellular signalling and single cell perspectives, I am excited to join Systems Oncology led by Claus Jørgensen. The aim of my project is to explore the role heterogenous signalling in pancreatic tumour cells plays in therapeutic resistance. Outside academia I play hockey with City of Manchester Hockey Club, enjoy hiking in the Peak District and sampling some of Manchester's best food, craft beer and independent coffee shops.

Mihaela Ficu

Hi, my name is Mihaela, and I am originally from Galati, a port city in Romania with the beautiful riverside scenery of the Danube River. I obtained my integrated MChem degree in Chemistry and Drug Design from the University of Sussex, Brighton. For my Master's project I worked in the Oncology team at the Sussex Drug Discovery Centre where I designed and synthesised small molecule inhibitors of a protein kinase as potential anti-cancer agents. Two weeks before my graduation, I joined the Early Drug Discovery team at Charles River Laboratories in Essex as an Associate Scientist and contributed to two medicinal chemistry projects as well as supporting the Analytical Chemistry team. After gaining experience in industry for over a year, I started my PhD in Medicinal Chemistry as part of the Drug Discovery Unit under the supervision of Caroline Springer. I am currently developing chemical compounds that have the ability to degrade a protein of interest with a role in cancer development by hijacking the natural machinery of the cells that regulate protein levels. By being part of the CRUK Manchester Institute, I have the opportunity to use an interdisciplinary approach to understand complex biological mechanisms and contribute to the discovery of potential new therapies. In my free time, I enjoy reading personal development books and science magazines as well as listening to podcasts, practising yoga, jogging or attending gym classes.



Melissa Frizziero

Hello, I am Melissa and I grew up in a small countryside village half way between two beautiful historical towns in the north of Italy; Verona and Mantova. I graduated in Medicine and Surgery in 2009 and specialised in Medical Oncology in 2015 at the University Hospital of Verona in Italy. My interest in digestive tract cancers and the desire to pursue a career in research led me to undertake a 2-year Clinical Research Fellowship in the Hepato-Pancreato-Biliary and Neuroendocrine Tumours (NET) Team at the Christie NHS Foundation Trust, under the supervision of Dr M. McNamara and Prof J. Valle. This unique experience at an internationally renowned Cancer Centre with high volumes of patients/clinical trials strengthened my ambition for an academic career. Here, I became eager to understand the biology behind the most aggressive and lethal NET subgroup, neuroendocrine carcinomas (NECs), which are rare and understudied diseases. I went on to secure grant funding to work for a year in the Cancer Biomarker Centre on a pilot project aiming to establish circulating tumour cell-Derived explants (CDX) of NECs of extra-pulmonary (EP) origin. The extraordinarily stimulating work environment of CBC motivated me to embark on a PhD programme which will allow me to expand my research in EP-NECs by exploiting the cutting-edge techniques and world-leading expertise in SCLC (a NEC from the lung) of CBC. About me? I am as Italian as you can imagine and I like going to music gigs.

Lucy Ginn

Hi, my name is Lucy and I'm from a small town in Rutland. Before joining CRUK Manchester Institute, I spent four years studying at the University of Sheffield. I completed my undergraduate degree in Molecular Biology and continued on to do a Masters in Translational Oncology, undertaking a 6-month research project investigating 'The Role of Matrix Stiffness in Breast Cancer'. Following the project, I was keen to continue translational based research and so I was delighted to accept a PhD in Michela Garofalo's Transcriptional Networks in Lung Cancer group. Here I will be investigating the role of a DEAD-box protein, DHX9, in non-small cell lung cancer, and I'm looking forward to the project and the opportunities available at the Manchester Institute. Outside of the lab, I enjoy sport and play hockey for Didsbury Northern Hockey Club. As I'm new to the city, I'm looking forward to exploring Manchester and all it has to offer.

Alexandra Hendry

Hello! My name is Alexandra, and I'm from Hong Kong. In 2015 I moved to the UK to study Biochemistry at the University of York. During my undergraduate degree I undertook a placement year at GSK in the Cell and Gene therapy department, where I worked to develop a CAR-T therapy to target solid tumours. For my final year project, I studied the effect of stem cell regulating genes on the development of prostate cancer. These research experiences developed my interest in cancer, and the role that the immune system plays in tumour development. Therefore, I was delighted to be able to join the Prostate Oncobiology group, led by Esther Baena. My PhD project will investigate the immune microenvironment of prostate cancer, and how different intra-tumoural mutations may affect the immune landscape of a tumour. In my free time I enjoy going to concerts, reading and doing pole exercise to keep fit. I'm really looking forward to experiencing more of Manchester's music scene, and exploring the Peak District.

Megan Mylrea

Hi, my name is Megan and I grew up in Staffordshire. I studied Chemistry with a Year in Industry at the University of Nottingham and graduated with my integrated Master's degree in 2019. As part of my degree I completed an industrial placement working for AstraZeneca in Cambridge. During this year I worked in oncology research and development on one of their live drug discovery projects. Having thoroughly enjoyed my time at AZ, I was delighted to be given the opportunity to join the institute to undertake my PhD research in the CRUK MI Drug Discovery Unit. As an organic chemist, my project is focussed on the development and synthesis of novel PROTAC degraders for cancer-causing proteins. This work will be used to provide alternative strategies to aid both target validation and drug discovery within the DDU and the wider Institute. When I'm not in the lab, I enjoy playing hockey and I love to cook. I am excited to be studying my PhD in Manchester and cannot wait to learn more about the fascinating world of cancer research from the experts themselves!

Julia Ogden

Hi, my name is Julia and I come from Edinburgh, Scotland. I originally studied Genetics at the University of Glasgow. I also completed an integrated year in industry with AstraZeneca within their translational oncology department and it was during this time that I completed my Master's thesis in cancer immunology. Following this, I spent two years working for a biotechnology company near Oxford which focuses on the development of bi-specific TCRs as immuno-oncology agents. Working in industry within a highly collaborative team was a very rewarding experience. However, during my time there I decided that I wanted the opportunity to lead a project and delve further into academic research. I am therefore delighted to have recently joined Caroline Dive's group where I will be working in the pre-clinical team supervised by Carlos Lopez-Garcia. I will be working on investigating lung squamous cell cancer progression using genetically engineered human basal cells. LUSC has been considerably neglected in comparison to other lung cancer types and is currently without targeted therapies. The primary aim of my project will be to generate a human model of LUSC progression to better understand the disease. Outside of work, I enjoy socialising, reading and cooking as well as exploring Manchester and the surrounding areas.

Bradley Revell

Hi, I'm Bradley and I have recently started my PhD here at the Institute. I grew up in a small town called St. Ives (near Cambridge not the coast!). Prior to starting at CRUK MI, I completed my four-year undergraduate degree in Veterinary Biosciences at the University of Surrey in 2018. This included a placement year at Texas A&M University where I was involved in looking at genetic and epigenetic targets of Angelman Syndrome, which really kickstarted my interest in research. Here at CRUK MI, I have joined the Leukaemia Biology lab led by Tim Somervaille and my project consists of deciphering the molecular mechanisms of two transcription factors, IRX3 and FOXC1, in Acute Myeloid Leukaemia. Outside of research, I am a huge fan of movies and cinema alongside American Football. On first impressions, I really like Manchester and I can't wait to explore the city and the surrounding area further over the next 4 years!

Josh Searle

Hi I'm Josh and I am the newest PhD student in Cell Signalling, having joined the Institute in October last year. I grew up in Gloucester – famous for cheese rolling (Google it) and not much else – and went on to study Biochemistry at the University of Bristol. I spent a year of my degree on an industrial placement, living in Cambridge and working for AstraZeneca in their Oncology Bioscience group. Here, I was mostly using biological mass spectrometry to run existing assays as well as bringing a novel, targeted assay in-house. I carried out my final year dissertation project in a different field to add some extra flavour to my degree, using EM to determine the structure and mechanism of the *E. coli* protein secretory machinery. I am very glad to have joined Angeliki Malliri's group here at CRUK MI and my project involves investigating the role of the E3 ubiquitin ligase HUWE1 in KRas mutant non-small cell lung cancer. Preliminary *in vitro* and *in vivo* data from the lab shows a requirement of HUWE1 for tumorigenesis in this setting, and I aim to determine the underlying mechanism by identifying the target protein of HUWE1 involved. Having grown up in the south it is nice to have now moved 'up north' and as a lover of getting outdoors into the countryside it is great to live in such close proximity to the Peak District, and not too far from the Lakes either!

Events, Awards and Prizes

This edition of the newsletter has been delayed due to the pandemic and so here we are also featuring some older events that we still want to share. This year we held a virtual event in place of our annual colloquium, but now we look back to the highlights of last year when we could all be together.

Maria and Andzhela receive their poster prizes

Colloquium 2019 highlights

Fabrizio receives the Lizzy Hitchman student prize

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 a bit more about what we do.

Opening the first session, Institute Deputy Director Caroline Dive gave an enthralling presentation on how an integrated biomarker sciences approach is critical to delivering effective precision medicine to patients. In the subsequent sessions over the science-packed two days, were a variety of interesting talks on both fundamental and translational research. We heard excellent presentations from our second year PhDs, who impressed the audience greatly with their professionalism and enthusiasm. We also welcomed to the event Oglesby Senior Leukaemia Research Fellow, Dan Wiseman from the Division of Cancer Sciences at the University of Manchester. Dan gave an interesting overview of his group's projects addressing the epigenetic, transcriptional and microenvironmental landscape of chronic myelomonocytic leukaemia – a disease of urgent unmet clinical need – and how they are seeking and validating novel therapeutic targets. New to the programme, Jutta Zimmer from the Cancer Research UK Research Careers team gave a useful overview of CRUK fellowships for early- and mid-career researchers, outlining the requirements and application process as well as critical tips about what makes a good application. Jutta also held a much-appreciated drop in session over lunch for our researchers to ask further career-related questions.

Each evening, a poster session took place. As always, it is a pleasure and challenge to select to select the best posters to receive one of two prizes. A clear winner for the Lizzy Hitchman student prize went to Fabrizio Simeoni for his PhD work on acute myeloid leukaemia. However, judging the best poster by a postdoctoral researcher or scientific officer was so difficult that two were awarded. The joint winners were postdoc Maria Roel from the Prostate Oncobiology lab for her research exploring the role of ETV1 in prostate cancer, and scientific officer Andzhela Abu Rashed from the Molecular Biology Core Facility for her work on cell line screening and other techniques.

European Network for Young Cancer Researchers launched in Manchester

Networking success for our young cancer researchers

On the 16 November, The Society of Spanish Researchers in the United Kingdom (SRUK/CERU) launched its European Network for Young Cancer Researchers by holding the first networking day in cancer research, bringing together world-leading scientists in the field.

The networking day, which was held at the Manchester Cancer Research Centre (MCRC), is the first of a series of seminars that will be held in the UK and Spain. With this, SRUK aims to build a European network of young researchers working in the cancer field as a platform to forge strong collaborations between research centres and promote scientific discussions.

The event brought together British, Spanish and German speakers and early career researchers to present their latest results and discuss the future of cancer research and was separated into three research fields: Metastasis, Cancer Metabolism and Tumour Microenvironment.

The networking day started with a discussion around Cancer Metastasis, and featured talks from Prof Laura Machesky (Cancer Research UK Beatson Institute), Dr Violeta Serra (Vall D'Hebron Institute of Oncology, Barcelona) and Dr Jacob Insua Rodríguez (Hi-STEM, Heildelbeg).

Cancer Metabolism was the topic for the second session, with talks from Dr Andrew Finch from the MRC Institute of Genetics & Molecular Medicine (Edinburgh), Dr Cristina Muñoz Pinedo (Bellvitge Biomedical Research Institute-IDIBELL, Barcelona) and Dr Alejo Efeyan (CNIO, Madrid).

In the last session, attendees heard about the latest advances in research on the tumour microenvironment from Dr Claus Jorgensen (Cancer Research UK Manchester Institute), Dr María Muñoz Caffarel (BioDonostia, San Sebastian) and Dr Fernando Calvo (Institute of Biomedicine and Biotechnology of Cantabria).

The event closed with a round table about diversity, equality and inclusion in academia using the results of the study on gender inequality in academia conducted by SRUK as starting point for discussion.

Throughout the day there were also interactive sessions about career development and funding and collaborative opportunities as well as opportunities to meet with speakers in one-to-one sessions.

In the words of Rocío Gaudioso, SRUK/CERU president "With these initiatives we seek to create a vibrant international network of collaborations to develop new ideas of how to strengthen ties between institutions and researchers to facilitate the advancement of science."

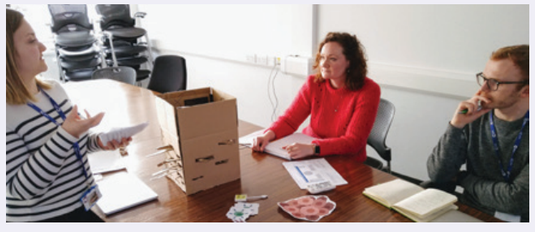
Exploring Cancer Landscapes at the Royal Society

The Cancer Research UK Manchester Institute has been invited to present an exhibit at the prestigious Royal Society Summer Science Exhibition. This is a great achievement and an excellent opportunity for the Institute to engage with the public and showcase our work in cancer research.

The winning team consists of Andrew Porter, Steve Bagley, Joanna Kelly, Chris Bromley, Charlotte Bell, and Gill Campbell. Together, with the support of volunteers from the Institute, they will be demonstrating to the public the complexity of cancer through a number of hands-on activities. Visitors will see that tumours are composed of a range of diverse cell types and how they interact effects tumour growth, immunity and response to treatment.

Accessible to all ages, the exhibit will help demystify these complex notions and allow for a general understanding of cancer growth and how this knowledge can help scientists and clinicians together form effective treatments. Crucially it will also highlight the power of multidisciplinary collaboration in scientific research. The team hope to motivate young people to study STEM subjects and inspire an interest in pursuing cancer research.

Due to the pandemic, the exhibition has been postponed until July 2021. Meanwhile, the Royal Society moved 'Summer Science' online from 13-17 July 2020, with a free digital programme of talks, quizzes and videos celebrating cutting-edge and historic science.



Royal Society Exhibit team discuss ideas for activities

Institute success at 3Rs poster event

We are delighted that members of the Cancer Research UK Manchester Institute were winners in all three prize categories at last year's 3Rs poster event.

Yannick and Callum's innovative approaches earn recognition

The joint event with AstraZeneca and Agenda Life Sciences takes place at Alderley Park every October. Here we celebrate the tremendous commitment to animal welfare of our staff and students, sharing our 3Rs initiatives - Replacement, Reduction and Refinement - with one another.

Twenty-seven posters displayed a wide variety of 3Rs topics, explaining development of methods that avoid or replace the use of animals, describing ways to reduce the number of animals used in each experiment, and incorporating refinements that help minimise suffering and improve animal welfare.

This time we invited members of the North West Animal Welfare & Ethics Review Body (AWERB) who helped judge and present the awards.

First to receive a prize was Lisa Doar from the Biological Resources Unit for Best Technical Development for her work refining injectable anaesthetic regimes to improve mouse welfare. Also acknowledged were the refinements and reductions in in vivo research on p53 mutations from our Tumour Suppressors group. Yannick and Callum received their well-deserved prize recognising their commitment and innovative approaches. And finally, making up the hat-trick was PhD student Christopher Below from our Systems Oncology group. We are proud of his 3Rs prize awarded for the development of an in vitro model to study pancreatic cancer. His amazing work was beautifully explained and with great enthusiasm.

Images left to right: Chris receiving student 3Rs prize for in vitro model, Lisa has improved mouse welfare

EACR Travel Fellowship

We wish to congratulate PhD student Colin Hutton on his successful application for an EACR Travel Fellowship.

Colin is based in the Systems Oncology group led by Claus Jørgensen and his project focuses on the pro- and anti-tumorigenic properties of the tumour microenvironment in pancreatic cancer, a dismal disease defined by a dysfunctional stroma, infiltrated by several different cell types including cancer-associated fibroblasts (CAFs), myeloid cells and T cells. While sub-populations of CAFs have been described, little is known of their function in the microenvironment.

Colin had planned to use this travel funding to visit the prestigious Taylor Jacks laboratory at the Koch Institute at MIT. Sadly, this visit was cancelled due to the pandemic.

Having made the novel discovery that lineage-restricted fibroblasts exhibit pro-tumorigenic or suppressive functions in vivo, Colin initiated the collaboration with this internationally leading group to further develop our understanding of these fibroblast populations.

2019 Dexter Awards

The Institute's Dexter Award for the Best Young Scientist of 2019 was jointly awarded to Alice Lallo from the Cancer Biomarker Centre and Mark Williams from the Leukaemia Biology group.

The prize recognises the most impressive scientific achievement by a student, post-doc or scientific officer and is named after a former Director of the Institute – Professor Mike Dexter. The judging panel felt that both Alice and Mark had achieved an extraordinary amount during their respective PhDs and therefore were both very deserving of the award.

Alice Lallo

Alice's thesis focused on characterising DNA damage response (DDR) deficiencies in small cell lung cancer (SCLC) using cell lines and circulating tumour cell derived explant (CDX) models. Her research led to a first author publication in Clinical Cancer Research in 2018, describing the combination of two DDR inhibitors olaparib and AZD1775, where the data has supported translation of this combination to the clinic. A critical part of this manuscript entailed the use of ex vivo CDX cultures to screen for drug efficacy as well as investigating molecular mechanisms of drug response. In 2019, Alice published her second first author paper in the British Journal of Pharmacology, reporting the optimisation and thorough characterisation of the new CDX ex vivo culture system. Her work systematically described the molecular and cellular aspects of SCLC patient-derived ex vivo models, including a detailed analysis of drift in culture and its reversibility in vivo. Her work significantly contributed to the field and has now been exploited by other world-leading SCLC groups that have cited her work in several high-profile manuscripts of their own. Her work made a significant contribution to the successful assessment of the Cancer Biomarker Centre (formerly CEP) in the quinquennial review co-ordinated by CRUK in 2019 where the international panel highlighted the SCLC programme.

Alice is currently contributing to a large collaboration with AstraZeneca in which a panel of clinical grade DDR inhibitors are being examined in 40 SCLC CDX models. Alice is adapting several DDR functional assays for CDX ex vivo cultures as putative predictive biomarkers. Although she will finish her thesis research before this task is completed, she has already identified promising drug combinations and candidate biomarkers and her work will be an integral part of the mechanistic dissection of response to this panel of DDR inhibitors leading to combination trials in SCLC.

Mark Williams

During his time as a Clinical Research Fellow in the Leukaemia Biology group, Mark has conducted an elegant study that was published recently in the Journal of Clinical Investigations, which uncovered the molecular mechanism underpinning up-regulation of the drug efflux pump ABCB1, which is a key driver of chemoresistance in acute myeloid leukaemia. His data also demonstrated that a form of epigenetic memory of prior drug exposure led to a rapid induction of ABCB1 upon subsequent drug treatment explaining failure of third-generation ABCB1 inhibitors. Through targeting the stress-induced up-regulation of expression of ABCB1 he was able to demonstrate a potential therapeutic approach to overcome this form of resistance and enhance the activity of ABCB1 inhibitors. He also has published a first author preview in Cell Stem Cell with another submission under review and a third in preparation. Mark is keen to pursue a career as a clinician scientist in the field of stem-cell transplantation and has been developing several projects in parallel with his PhD studies that will form the platform for his applications for a clinician scientist fellowship. He has designed a clinical research project called Precision Medicine for Stem Cell Transplantation (PM-SCT) the aim of which is to identify biomarkers to predict complications in patients undergoing this procedure. As well as conceiving this work, he has also secured funding to support it from the MCRC, the Christie Charity and the Manchester Biomedical Research Centre, produced the trial documentation and co-ordinated the various clinical activities that will underpin this study. It is set to open later this year. Further work has led to national collaborations with leaders in the stem cell transplantation field and the development of a valuable network that should prove to be highly advantageous to his future career.

FBMH Presidential Fellowship for Clinicians

In a string of successes last year, Mark was also awarded the prestigious FBMH Presidential Fellowship for Clinicians at The University of Manchester, which recognises creative and ambitious clinicians keen to develop transformative research. This is excellent opportunity for Mark to drive his academic career to a higher level.

He will be appointed as a Senior Clinical Lecturer for a period of two years where he will undertake research looking at the mechanisms underlying relapse following stem cell transplantation, whilst maintaining his clinical practice.

Mark passed his PhD viva on 20 January this year with no corrections, a remarkable result.

BIAL Prize in Biomedicine 2019

Congratulations to Santiago Zelenay, who has received the inaugural BIAL Prize in Biomedicine 2019, along with Caetano Reis e Sousa. Worth €300,000, this new award was created by the BIAL Foundation to recognise high quality, scientifically relevant research in the biomedical field published in the last ten years.

The award-winning study led by Caetano Reis e Sousa focused on a mechanism used by cancers to escape detection by the immune system, which could help lead to potential first-line treatments, including for several metastatic cancers which are resistant to chemotherapy.

Santiago was first author of the publication in the journal Cell whilst undertaking a postdoctoral position in Caetano's Immunobiology lab at The Francis Crick Institute. The ground-breaking discovery has inspired new clinical trials testing the combination of anti-inflammatory drugs, such as aspirin with immunotherapy, in a range of cancer types, including breast and colon cancers. This work has formed the basis for much of the current research undertaken Santiago's Cancer Inflammation and Immunity group.

The first edition of the BIAL Prize in Biomedicine was presented to Caetano Reis e Sousa and Santiago Zelenay by the President of the Portuguese Republic, Marcelo Rebelo de Sousa, in March 2019.
The BIAL Foundation was created in Portugal in 1994, to foster scientific study through a series of awards and grants.

Santiago and Caetano with the President of the BIAL foundation

Denys ready to present his virtual poster for AACR 2020

Double awards for Denys Holovanchuk

Denys Holovanchuk, PhD student in Molecular Oncology, was awarded both a BACR/CRUK Student Travel Award of £1000, plus a £600 Conference Travel Grant from Disease Models and Mechanisms to attend the annual AACR conference this year to present a poster.

Of course, the conference sadly could not go ahead as planned, but instead was held virtually with great success over two sessions held in April and most recently in June. Denys presented his virtual 'e-poster' on "Elucidating genes that mediate brain colonization by metastatic melanoma cells" on 22 June. This is what he had to say about his experience:

"It is always exciting to present your work to a wide audience and to be able to discuss your data with the best researchers in the field, especially when you are a final year PhD student. That's why attending AACR this year was a very important milestone for me. Fortunately, I was able to secure funding from two sponsors to fly to sunny Sand Diego and attend this meeting (British Association for Cancer Research and Disease Models and Mechanisms journal), but unfortunately, as we all know, the world had different plans for all of us this year.

"As an alternative, AACR organised two sessions of virtual meetings and I am presenting my work as a poster in the second session (22nd-24th June). This is a completely new experience for me, not only because I will not be "standing" next to my poster and meeting visitors, but also because I had to record a 5 minute "audio guide" for people to visit and press play. AACR tried to make these sessions as interactive as possible by introducing a discussion box for each poster, like a comment section on social media, which is exciting and frightening at the same time. Nevertheless, I like new challenges and I look forward to this new way of networking."

Funding

New CRUK Accelerator Award for Digital Clinical Trials to UpSMART Experimental Cancer Medicine Centres

We are delighted that Professors Caroline Dive and Andrew Hughes with the digital Experimental Cancer Medicines Team within the CRUK Manchester Institute Cancer Biomarker Centre, along with our EU colleagues, including those from Fondazione IRCCS Istituto Nazionale dei Tumori Milano and Instituto de investigación Oncologica de Vall d'Hebron, Barcelona have been awarded a CRUK Accelerator Award to enable SMART Experimental Cancer Medicine Trials

The ambition of this new programme, entitled "UpSMART", is to 'digitalise' experimental cancer medicine centres across the UK, Italy and Spain, providing clinical teams with digital tools for real-time access to a wealth of patient data allowing faster decision making.

The UpSMART programme will test existing digital tools within 23 Phase I Units that have joined this aspiring, timely programme. They will develop and provide all clinical sites with access to new technology approaches and improvements in trials enabling patients access to tomorrow's medicines today. The team have already developed and implemented digital healthcare products in The Christie NHS Foundation Trust, including REACT for interpreting clinical data and PROACT for giving patients a voice within their own trials. Their goal is for these and other digital products to be shared and implemented more widely with training in digital approaches.

International Alliance for Cancer Early Detection (ACED)

Our scientists are benefitting from significant funding from Cancer Research UK and partners that will develop radical new strategies and technologies to detect cancer at its earliest stage.

The University of Manchester, together with the Cancer Research UK Manchester Institute, is a partner in the new transatlantic research alliance to help more people beat cancer through early detection. CRUK is investing up to £40 million over the next five years into the International Alliance for Cancer Early Detection (ACED).

ACED is a partnership between Cancer Research UK, Canary Center at Stanford University, the University of Cambridge, OHSU Knight Cancer Institute, UCL and The University of Manchester. Contributions from the Alliance's US partners will take potential investment to more than £55 million.

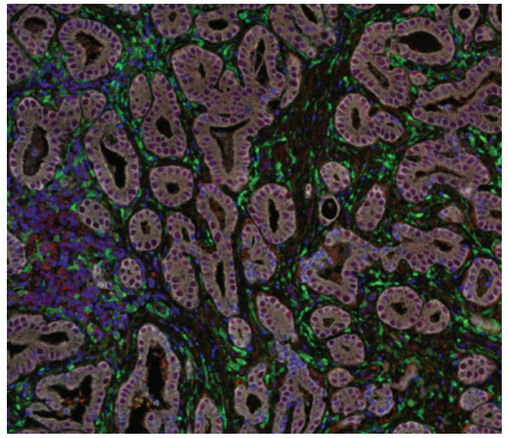
By combining the might of some of the leading research institutions in the world in early detection, ACED will accelerate breakthroughs, leading to quicker benefits for patients - a patient's chance of surviving their disease improves dramatically when cancer is found and treated earlier.

In Manchester, the funding will support scientists and clinicians to take forward new cancer screening projects in the city. As part of the Alliance, researchers will continue to develop a range of ongoing community early detection projects, including work to deliver lung health checks for people who could be at risk of developing lung cancer in some of the city's most deprived areas.

Regular funding rounds enable our researchers to apply for funding and to work with other high calibre scientists in the partnership.

£1.25m from Prostate Cancer UK and Movember Foundation to expand work in prostate cancer research

Researchers at the Cancer Research UK Manchester Institute have been awarded a part share of £1.25m funding from Prostate Cancer UK and the Movember Foundation to expand work being performed in prostate cancer research.



Prostate tissue showing cancerous cells

The grant, which is shared between The University of Manchester and Queen's University Belfast as part of the Belfast-Manchester Centre of Excellence (also known as FASTMAN), will help to expand current research programmes, drive the development of new clinical trials and answer some of the fundamental questions about the disease.

This latest funding injection builds upon an initial £5m investment from Prostate Cancer UK and Movember in 2014 to create the first regional Movember Centre of Excellence between Queen's University Belfast and The University of Manchester. Since its creation, researchers have developed new tests to identify high risk patients, and pioneered new basic and translational treatments in prostate cancer.

In Manchester, research will continue in three distinct programmes of work including: the identification of biomarkers linked to radiotherapy resistance; understanding the genetic and biological drivers of prostate cancer metastasis; and understanding of how novel imaging can predict success of radiotherapy in advanced disease. These programmes will be tackled across the Manchester Cancer Research Centre partnership, with basic research conducted by researchers in Molecular Oncology, Prostate Oncobiology and Translational Oncogenomics at the Institute being translated into the clinic at The Christie.

Funding to investigate potential therapy for blood cancer

We wish to also congratulate Georges Lacaud on receiving funding from the charity Blood Cancer UK.

Georges leads the Stem Cell Biology group and studies the role of transcription factors and co-activators together in blood development and maintenance in order to better understand how alterations of their functions might lead to leukaemogenesis.

This grant will further support investigations into the activity of histone acetyl transferase protein MOZ in leukaemia, with the aim of expanding the therapeutic application of MOZ inhibition.

Royal Society funding success

Congratulations to Institute Fellow Amaya Viros, who was awarded a Royal Society Research Grant.

Amaya is a Wellcome-funded Clinician Scientist who leads the Skin Cancer and Ageing group. Her studies focus on melanoma and squamous cell carcinoma (SCC), two forms of skin cancer that predominate in the elderly population and usually arise over skin that has endured sun exposure and/or ageing. In particular, her lab aims to understand what drives skin ageing and how these differences affect skin cancer onset, skin cancer progression and outcome.

In a fascinating new line of research investigating the sex bias in the molecular landscape of cutaneous squamous cell carcinoma, Amaya plans to use this funding to further explore why incidence of this disease is a striking 2-fold greater in men than women.

We look forward to hearing more from Amaya as this interesting project develops.

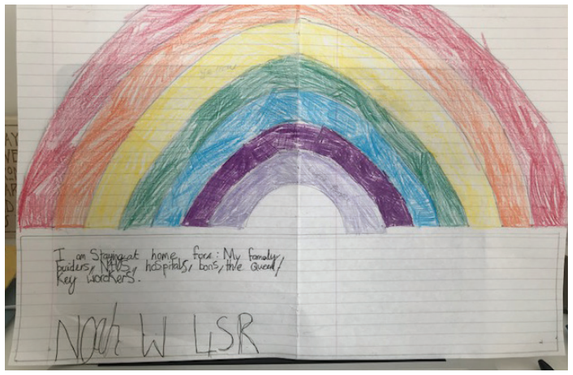
Staff News

Fun ways of coping with quarantine

From online choirs, to alternative ways of exercising and painting rainbows, CRUK MI staff have been getting creative when it comes to coping with the quarantine! These pictures are just some of the examples:

Daphne Brisard (Molecular Oncology) had to get creative when her favourite bouldering place had to close due to COVID 19. Don't worry, she is at a safe distance from the floor!

The 'Do Your Thing Community Choir' recorded a song to raise funds for NHS charities. If you look to the bottom right, you will spot our Jenny Ward (Digital ECMT)! Watch: https://bit.ly/36jVfJx



And the best rainbow award goes to: Noah Winterbottom! His mum Natalie (EA to the MCRC Director) proudly shared this beautiful drawing with us, which got Noah a diploma signed by the MCRC Director Rob Bristow. Congratulations!

Andrew Porter (Cell Signalling) and his son Benjamin took advantage of the lockdown to take part in a Software Carpentry course offered by the Institute. This was a good way of learning new skills while spending quality time together!

Getting to know CRUK MI

Our Institute is our people. We are very proud of everyone working with us and we wanted to share their stories with you. In January 2020 we launched a video series entitled "Getting to Know CRUK MI" in which we publish interviews with different members of our staff.

From scientists to administrative and support staff, everyone plays a vital role in our mission to beat cancer sooner. On these videos, you can find out not only about the work that they do, but also about what they enjoy most about their roles and their workplace.

To watch the videos: https://tinyurl.com/gettingtoknowcrukmi

If you would like to take part of this series, please email belen.conti@cruk.manchester.ac.uk.

Wedding bells

Huge congratulations to David Stanier, Admin Assistant and Information Governance Coordinator, who got married to Kris Stanier last Autumn! We wish you much happiness!

David and Kris, just minutes after they said yes

New arrival

Yannick Von Grabowiecki, from our Tumour Suppressors Group, and his girlfriend Yana welcomed a beautiful baby boy on December 2019. Julien arrived five weeks early, but is doing very well. Congratulations!!

Baby Julien, who is technically French, German & Bulgarian, enjoying playtime with dad

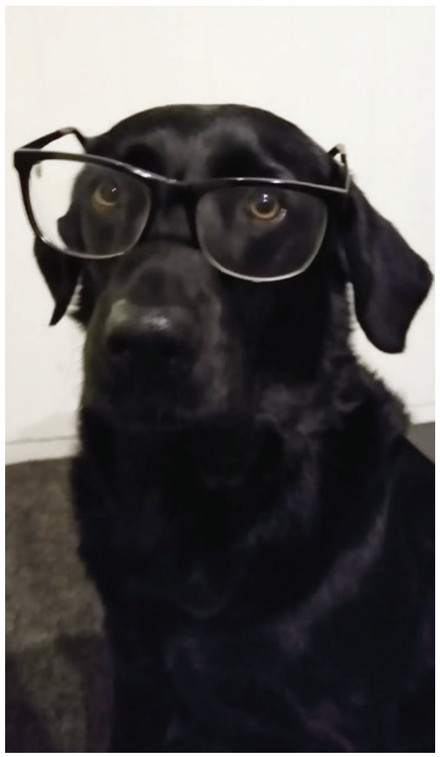
Pets working from home

When we had to shut our doors to help prevent the spread of COVID-19, working from home became the new normal. And many pets enjoyed seeing their owners more often, as these pictures shared by our staff attest!

Sara Valpione (Molecular Oncology) analysing data with some "help" from her cats

Patricia Muller (Tumour Suppressors) discovered that her cat Suki regularly poses in the window! She seems shocked to have been busted!

Georgina Binnie, MCRC Recruitment and Training Officer, has been enjoying extra cuddles from her rescue cats, Talula and Bugsy. Maybe not the most helpful when it comes to working, but certainly very cute!"



This is Poppy, the new office companion of Belen Conti Vyas (EA to the Senior Management Team)

In the spotlight with Belen Conti Vyas

Belen has certainly made some moves since she joined the Institute as Administrative Services Coordinator in January 2016. She started out in the Director's Office based in the Paterson Building, before moving to the Oglesby Cancer Research Building in 2017 and finally to Alderley Park in 2018. Belen put her media training background to good use managing our twitter account and other social media platforms. We also got to know Belen for her role in the external seminars, organising our social events, and more recently for putting together the online videos for the 'Getting to know' series – recording soundbites from our staff. Belen made another move; this time she changed roles and since September 2018 has been the Executive Assistant to the Senior Management Team, supporting the work Caroline Wilkinson and Stuart Pepper perform to facilitate the smooth running of the Institute.

1. What is your favourite part of the UK?
I really enjoyed the time when I visited Snowdonia, in Wales. A lot of nice walks and fun activities!

2. What was your best ever holiday and why?
Tasmania and Melbourne two years ago with my now husband. We really enjoyed the beautiful landscapes and wildlife, and we got engaged on this trip!

3. Which website do you always check, and why?
Reddit, because I always get a good glimpse of what's going on in the world in the different subreddits and the r/funny always makes me laugh.

4. What is your favourite film?
I have so many! Depends on the day and on my mood, but I will go for an Argentinian one that I really recommend: The secret in their eyes (El secreto de sus ojos) by Juan Jose Campanella.

5. What is your favourite band/ singer?
Again, I have so many! But I always loved Andrea Bocelli, so I will go for that one.

6. If you had to change careers tomorrow, what would you do?
Travel writer or maybe photographer/ video producer.

7. What is the most important lesson that you have learnt from life?
Things happen and you can't control everything. So think about what you can control and act on that. The rest will happen whether you worry or not, so don't keep obsessing about it!

8. Name three things you would take with you to a desert island?
A musical instrument (I would have time to learn to play it and then I would have music), a dog (they always keep me in a good mood) and my husband (am I allowed to take a person or am I cheating?)

9. What is your greatest fear?
Spiders, or any kind of creepy-crawlies to be honest.

10. How would you like to be remembered?
Laughing (and also making others smile).

11. If you could change one thing in your past what would it be?
Erm... I guess nothing, because everything led me to where I am now.

12. What is your signature dish to cook?
Milanesas (breaded steak) with chips. Simple but so tasty!

13. You've just won the lottery and have £5 million pounds to spend. What do you buy first?
A holiday with family and friends to somewhere with nice beaches and good adventure opportunities.

14. What is your idea of perfect happiness?
A walk with my husband on a deserted beach around sunset on a warm summer day. And maybe we can finish this with a nice dinner with some caipirinhas!

15. What keeps you awake at night?
Almost nothing! I'm finding it harder and harder to stay awake after midnight hahahah

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The University of Manchester
Royal Charter Number: RC000797