CANCER RESEARCH UK | MANCHESTER INSTITUTE

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The University of Manchester

Newsletter

Winter 2021

Director's Introduction

It is my great privilege to welcome you all to this latest edition of the Cancer Research UK Manchester Institute newsletter. It has been nearly 12 months since I became Interim Director of the Institute and I continue to be impressed by the quality of our research and the resilience of the Institute, despite the ongoing challenges.

I would like to thank you all for your flexibility in adapting to the changing situation in relation to the SARS-CoV-2 pandemic. Everyone's cooperation is keeping us safe while we continue to be as productive as possible. As always, the contents of this newsletter are a tribute to everyone's efforts.

In this edition, we highlight a selection of publications that showcase the breadth and quality of science that is being undertaken by our researchers at the Institute. The scientific digests have been written by some of our early career researchers, providing them with a great opportunity to develop their writing skills. Thank you all for your superb contributions.

There are several exciting studies featured but I am especially thrilled to see the first-author papers from Colin Hutton and Fabrizio Simeoni arising from their PhD studies, which were completed under the challenging circumstances of the Paterson Building fire and subsequent relocation as well as the COVID-19 lockdown and ongoing restrictions. I am delighted that Colin and Fabrizio passed their PhD examinations with flying colours and are now embarking on the next stages of their careers. Also recently passing their PhD examinations are Sarah Pearsall, Max Schenk, Eimear Flanagan, Ronnie Rodrigues Pereira, Matt Howell and Manuela La Montagna – many congratulations to you all.

A critical stage in the research pipeline is securing funding. It is with great pleasure therefore that I congratulate Carlos Lopez-Garcia on winning a grant from the UK's National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3RS). With this funding, Carlos has set up his own research group as an Institute Fellow, focusing on lung squamous cell carcinoma. Carlos was a valued member of the Cancer Biomarker Centre for the past two years, but I am delighted that he is establishing his own independent group.

Cancer Biomarker Centre Associate Scientist, Kathryn Simpson has also had funding success with an award from the Rosetrees Trust. She will lead on the study to investigate the early spread of small cell lung cancer to reveal new treatment strategies for this dismal disease. Many congratulations to Kathryn and her team.

Conferences are pivotal to scientific enterprise, enabling researchers to share their findings, exchange ideas, and to network for collaboration and career development. Internal meetings are also integral to the process of science, where we present new work to our colleagues to receive critical input that can help develop, clarify, and refine our research. So, I am delighted to say that the last few months have been packed with meetings.

This year's colloquium was a great success, boosted by hosting the event on virtual conference platform, Gather Town. Virtual meetings can challenge aspects of informal scientific communication, but here we enjoyed 'social spaces' that allowed more meaningful encounters with our colleagues. There were exceptional talks and posters from our scientists, and we were privileged to hear from Doug Lauffenburger, who joined us online from the Massachusetts Institute of Technology and spoke about how systems biology approaches can help explain the effect of immune cells in tissue microenvironments. The event was great fun, and I especially enjoyed seeing everyone connect through their personal 'avatars'.

After a delay of more than a year, our research was finally showcased at the prestigious Royal Society Summer Science Exhibition. In July, a team of researchers presented a plenitude of digital activities to help explain the complexity of cancer. I would like to thank our enterprising scientists for all their hard work, which was well received by the public.

Our annual 3Rs' poster prize event continues to be a great collaborative success with scientists from AstraZeneca and Agenda Life Sciences. We got together online to celebrate our commitment to animal welfare by sharing our 3Rs' initiatives. Congratulations to prize winner Bianca Blochl from the Cell Plasticity and Epigenetics group.

While we have successfully navigated our meetings using virtual platforms, it is hard to replace the joy of face-to-face encounters. So, it was with great pleasure that I opened the meeting to celebrate the remarkable life and scientific contributions of our first Director, Professor Laszlo Lajtha (1962-83) – a pioneer in stem cell biology and haematology. Joint with the Consul General of Hungary in Manchester, we got together to bring together Mancunian and Hungarian research and enjoyed a day of fascinating talks, posters and connecting with colleagues old and new. I hope this event will spark potential collaboration opportunities between researchers here in Manchester and Hungary.

In October, the cancer exhibition, 'Cancer Revolution: Science, Innovation and Hope' opened at the Science and Industry Museum in Manchester, where it will remain until March 2022. I am delighted that the Institute is featured in this excellent exhibition, and I hope that you will take the opportunity to visit. This fascinating world-first exhibition illustrates the revolution in science that is transforming cancer care.

Finally, I would like to welcome all new members of staff and our new PhD students. Even though many of us have not physically met each other, it has been enjoyable to meet many of you virtually. If you haven't had the chance to meet them yet, you can get to know more about some of them in the following pages.

Looking ahead, I am excited about the future of cancer research in Manchester. Next year the new building that replaces the Paterson Building will be handed over. Construction is progressing apace, and we are on track to move in and start our first experiments early in 2023. I was literally blown away standing on the top of the building, celebrating the 'topping out' milestone. But we would not be here without the generous gifts from donors and funders around the world, so I would like to express my enormous thanks for their crucial support, it really does make a difference.

Going on in the background has been an incredible amount of hard work planning the layout of laboratories and all our facilities that will make up the new building. I would like to thank those involved in this critical preparation for our move, which will facilitate the synergies in discovery translational research that relocating back to The Christie site will empower.

Rounding up, I would like to reiterate how much I have enjoyed my role as Interim Director over the past year. Despite the clear ongoing challenges, my role has been made much easier by everyone's commitment, motivation, and assistance.

I wish you all a wonderful festive break and hope you have time to reflect and refresh, ready for the new year ahead. I am looking forward to 2022 and working with you all to continue to advance our research and make a difference to the lives of people affected by cancer around the world.

Professor Caroline Dive, CBE., FMedSci.
Interim Director, Cancer Research UK Manchester Institute

Cover Image: The Cancer Research UK Manchester Institute contributed to the new cancer exhibition at the Science and Industry Museum, Manchester: 'Cancer Revolution: Science, Innovation and Hope'. The exhibition features work from the Cancer Biomarker Centre and Biological Resources Unit. *Photo credit: Science Museum Group © The Board of Trustees of the Science Museum, London*

Welcome to our new Research Engagement Manager

We are delighted to introduce our new Research Engagement Manager Iqra Choudhry, who took up her position with Cancer Research UK in July this year.

Iqra will be working closely with our researchers and clinicians here at the CRUK Manchester Institute, as well as with local fundraisers, to increase engagement and drive support for CRUK.

Iqra has had an interesting career path. She has an academic background with research interests in History of Science, Polar Studies, Science Policy, Science Diplomacy and Global Geopolitics!

She recently finished her PhD at The University of Manchester, where she had been studying the previously unseen SCAR Archive at the Scott Polar Research Institute in Cambridge, and its revelations regarding the histories of science policy, governance, scientific collaboration and diplomacy in Antarctica.

Iqra also has a Master's degree in Science Communication, is an experienced editor and writer and is passionate about communicating her research through public engagement projects.

As her role covers the north of England, Iqra plans to be based at the Institute one or two days a week. Although living in Newcastle, she has family in Manchester – which will make all the travelling between Manchester and Newcastle (and other research locations) much easier.

Iqra will be helping to develop high-impact events and experiences to connect Cancer Research UK supporters and the wider public to the life-saving research that it funds.

Her first major event was the launch of the 'Cancer Revolution: Science, innovation and hope' at the Science and Industry Museum, Manchester. Cancer Research UK worked closely with the curators, providing advice on content. CRUK MI scientists also contributed to the exhibition, and you can find out more in the following pages.

We are very happy that Iqra has joined us and wish her a warm welcome. We are all looking forward to working with her on future public engagement projects.

Black in Cancer Week 2021

By Julia Morris, Bioscientist, Drug Discovery Unit

In October 2020 I was absolutely enthralled by Black in Cancer Week. To see people who looked like me (I'm of Jamaican heritage) actively involved in the fight against cancer was both exciting and inspiring. I currently serve as a UK Director of Mentorship and Outreach at Black in Cancer. I was also privileged to be on the organising committee for Black in Cancer Week 2021, which took place from Sunday 10th October to Friday 15th October 2021.

For those of you who may not be aware, Black in Cancer is a transatlantic movement founded by Dr Henry J. Henderson (USA) and Sigourney Bell (UK). Its board of directors consists of a group of highly passionate and motivated individuals in the initial stages of their careers. We are on a mission to connect Black people who work in the cancer space, improve the understanding of cancer in the Black community (thus reducing cancer health disparities), and inspire the next generation of Black cancer researchers.

Due to the global reach of Black in Cancer, and the ongoing pandemic, all the events during Black in Cancer week took place online.

Here is a snapshot of how Black in Cancer Week unfolded:

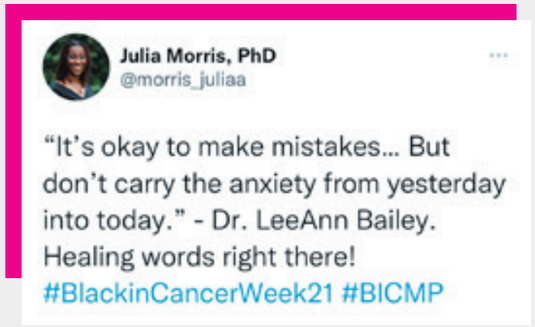
Day #1: We kicked off with the #BlackinCancerRollCall on Twitter. It was hugely inspirational to see a vast variety of scientists (including undergraduates, PhD students, research assistants, post-docs, professors, and principal investigators), engineers, medical doctors, patients, and professionals working in industry tweet about themselves. We had representatives from South Korea, South Africa, Australia, Burundi, Brazil, UK, and USA.

#BlackinCancerRollCall on Twitter

Day #2: The first panel event of the week was organised by my colleagues and I, entitled: "Elevate: Mentorship and Outreach." Dr Henry J. Henderson and Dr LeeAnn Bailey spoke about their experiences navigating their careers in academia, government and industry and offered many pearls of wisdom.

Day #3: On Tuesday we invited the OncoDocs (Dr Fiyinfolu Balogun and Dr Onyinye Balogun) to dispel some of the common myths surrounding cancer and COVID-19 that plague the Black community. Although the official statistics shared were USA-based, it was fascinating to see the similarities in the beliefs held by my own community here in the UK.

Day #4: We invited Dr Sam Merriel (a general practitioner and primary care researcher based in the UK) and Dr Morhaf Al Achkar (a family physician, associate professor, and stage 4 lung cancer patient) to discuss the best ways to support a friend or relative following a cancer diagnosis. This event provided a perspective I have never seen before. It was truly impactful and eye-opening.



Sound advice from Dr LeeAnn Bailey

Day #5: In collaboration with the National Cancer Research Institute (NCRI), "The Experience of Black People in Cancer Research" was held. I shared my experience as an early career researcher, Professor Dean Fenell spoke from his perspective as an established researcher and Ms Della spoke from her experience as a cancer patient. It was a very productive conversation for each of us. Amazingly, over 250 people were in attendance, which far exceeded my expectations!

Day #6 Event 1: We finished off the last of our public events with Dr Paula Hammond, Professor at the Massachusetts Institute of Technology, and the Head of the Department of Chemical Engineering, who gave the Keynote Address. She walked us through her fascinating science and then shared some sage advice from her own career experience. To top the week, the winners of the inaugural Black in Cancer Postdoc Awards, funded by the Emerald Foundation were announced.

The importance of mentorship

Day #6 Event 2: Finally, we finished off the week with a networking session with the mentees from our newly launched Black in Cancer Mentorship Program (BICMP). We have recruited a total of 26 Black undergraduate students (12 from the UK and 14 from the USA) who are currently studying at UK and US institutions. BICMP is part-funded by Cancer Research UK.

Black in Cancer Week 2021 was jointly funded by Fred Hutch Cancer Centre, Roche and Damon Runyon Cancer Research Foundation.

There are lots of more exciting things to come from Black in Cancer so please support us by visiting:

- www.blackincancer.com
- www.twitter.com/BlackinCancer
- www.instagram.com/blackincancer/
- vm.tiktok.com/ZM8x1RpLh/

The exhibition gives a rare snapshot into what cancer research using mice looks like

Cancer Revolution: Science, Innovation and Hope launches at the Science and Industry Museum

By Lisa Doar and Joanne Roberts, Biological Resources Unit

The Science Museum Group has just opened the first ever cancer exhibition, called 'Cancer Revolution: Science, Innovation and Hope'. The event will be at the Science and Industry Museum in Manchester from 22 October 2021 until March 2022, before moving to the Science Museum in London from summer 2022.

The focus of the exhibition is on exploring the revolution in science that has helped transfer cancer care over time, from some of the very early surgical methods used to remove tumours, right up to the cutting-edge technologies that have been developed in the present day to help both detect and treat cancer. There are also several individual stories from patients from different backgrounds and ages, which gives the exhibit a lovely personal touch.

The opening night was held on 20 October and was well attended by delegates from the sponsors and those involved in contributing to the exhibit. The evening started with welcome drinks followed by inspiring and some deeply personal speeches from several different people, including Michelle Mitchell (CRUK CEO) and Maureen Lipman (English theatre, film, radio, and television actress). This was followed by a sneak preview of the exhibition ahead of the public opening.

An insightful part of the exhibition in which the Biological Resources Unit (BRU) were able to contribute is a display of how mice are used in cancer research. The items include a high spec mouse cage complete with enrichment, which will be used in our new facility when we return to the Christie site. Also displayed is a handling tube used to reduce stress when moving a mouse to and from its cage, along with a set of callipers which the BRU technicians use to measure and monitor tumours on the mice. There is a screen showing video footage captured in our animal facility of experimental mice in their home cages, alongside which is a statement by Joanne Roberts describing the impact that animal technicians have on mouse welfare whilst they undergo procedures vital to cancer research.

It is fantastic to be able to give visitors a rare snapshot into what cancer research using mice looks like. The opportunity for the BRU to be involved in a national exhibit provides a visible platform to talk about animal research at the Institute – as signatories of the Concordat on Openness on Animal Research, we agree it is important to be more open about our use of animals in research.

The new cancer exhibition at SIM Manchester features patient stories, the science underpinning cancer and highlights some of the latest advances in research and treatment. *Science Museum Group © The Board of Trustees of the Science Museum, London.*

Other contributions to the exhibit from the CRUK Manchester Institute include the work of our Cancer Biomarker Centre and how they are developing tests known as 'liquid biopsies' to look for cells that have broken free from tumours and are circulating in the blood – circulating tumour cells. They have been studying these cells in lung cancer where traditional biopsies are challenging. In this disease, measuring CTCs can improve our understanding of how lung cancer changes over time and help predict which tumours are more likely to grow back when patients have undergone surgery. Also included in this section of the exhibit is a life-sized image of our very own Director Caroline Dive, highlighting how liquid biopsies can advance cancer treatment for patients.

Images left to right: Fantastic to see the work of Institute Director Caroline Dive and her team in the Cancer Biomarker Centre featured in the new cancer exhibition at the SIM Manchester; We are very proud of our Biological Resources Unit for their contribution to the exhibition with a display on in vivo research. *Science Museum Group © The Board of Trustees of the Science Museum, London.*

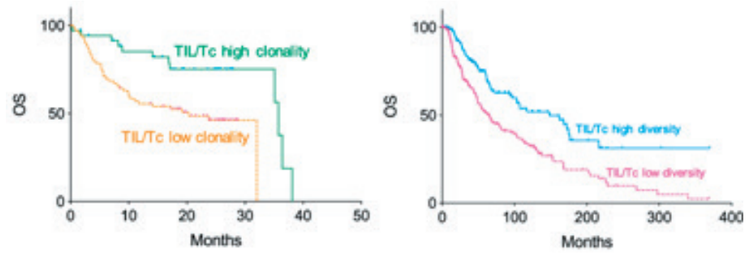
Using immune cells to predict response to therapy

By Molly Glenister-Doyle, Scientific Officer, CRUK MI Cancer Biomarker Centre

New research has shown that T-cells – a type of white blood cell – located in tumours can be used to predict the response of melanoma patients to therapy. The ability to stratify patients into responders and non-responders could allow clinicians to better tailor cancer therapy to an individual. This is an exciting step forward in the development of personalised therapy.

T-cells play an important role in our immune system by protecting our bodies from harmful substances, including cancer cells. Detection of these harmful substances relies upon proteins called receptors (TCR), which protrude from the surface of T-cells. Not all T-cells will have the same TCR, and it is the structural differences between these TCRs that give distinct T-cell populations the ability to detect different threats.

Scientists often gather information about T-cells by measuring TCR diversity and clonality. 'TCR diversity' is a measure of how many unique TCRs there are in a T-cell population. 'TCR clonality' is a measure of how many T-cells have the same receptor, and what proportion of the population they make up.



The use of T-cell TCR clonality and diversity in melanoma patients to predict response to immunotherapy (left) and indicate survival in the absence of immunotherapy (right). OS is overall survival.

Here, researchers in Manchester studied T-cells in the tumours of 16 melanoma patients and analysed previously published data to reveal that high TCR clonality correlates with a higher likelihood of melanoma patient response to immunotherapy.

Analysing published data from the 'The Cancer Genome Atlas' also revealed that high TCR diversity is associated with better overall survival in the absence of immunotherapy. This correlation was seen in patients with other types of cancer, such as breast, testicular, thymus gland, and specific types of lung and renal cancers.

Overall, this study is important as it puts forward two markers, TCR clonality and TCR diversity, which have the potential to identify patients who could better benefit from immunotherapy. The application of these markers is particularly relevant to melanoma patients where immunotherapy treatment is already approved for certain stages of cancer. Identification of patients who are unlikely to respond could spare them from unnecessary treatment-related toxicity.

Valpione S, Mundra PA, Galvani E, Campana LG, Lorigan P, De Rosa F, Gupta A, Weightman J, Mills S, Dhomen N, Marais R. (2021)
The T cell receptor repertoire of tumor infiltrating T cells is predictive and prognostic for cancer survival.
Nature Communications 12(1):4098.

Identifying biomarkers to improve chemotherapy responses in metastatic colorectal cancer

By Adesewa Adebisi, Scientific Officer, CRUK MI Cancer Biomarker Centre

In an exploratory study, Manchester scientists uncover the impact of chemotherapy treatments in cancer patients across a range of circulating and imaging biomarkers. Being able to accurately predict a patient's response to treatment allows clinicians to match the appropriate treatment to a patient, thereby minimising exposure to negative side effects and preventing unnecessary treatments. One way of achieving this is by identifying and validating biomarkers.

Biomarkers act as signals that allow us to understand how cancer develops and progresses in the body. Their presence can be identified using various detection techniques. Here, researchers use circulating proteins and CTCs – circulating tumour cells – detected in the blood as markers of tumour malignancy and invasiveness. In parallel, they used an imaging biomarker with MRI to measure changes in tumour permeability and tumour volume.

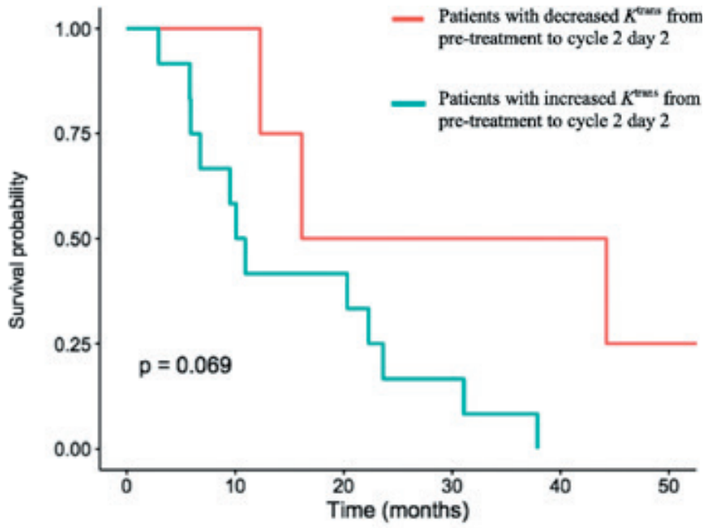
The team of researchers explored the utility of these biomarkers in colorectal patients with liver metastases undergoing first-line chemotherapy treatment. Their aim was to provide important information on how biomarkers in patients were affected by chemotherapy, and how these changes could inform the introduction of directly targeted treatments.

The researchers measured tumour permeability – represented by K^{trans}

– in patients pre-treatment and on the second day of their second chemotherapy cycle. They identified, on average an increase in K^{trans} between both time points. Interestingly, in a subset of patients with higher K^{trans} levels, a poorer overall outcome was identified when compared to patients without elevated K^{trans}.

This observed complexity in imaging biomarker changes with chemotherapy regimens led the researchers to offer several explanations for their findings. Patients with higher K^{trans} levels may have an increased blood vessel network surrounding their tumours, which enhances their resistance to chemotherapy and results in a poorer outcome. Another possibility is that higher K^{trans} levels identifies patients with greater permeable blood vessels where the chemotherapy drugs are cleared more efficiently from their body, thus unable to provide sufficient therapeutic benefits.

Overall, this prospective study revealed an important group of patients whose tumours do not respond well to traditional cytotoxic chemotherapy alone and suggests they may benefit from the early inclusion of targeted treatment to stop tumour cells from creating new blood vessels. These data can now act as a control group and underpin the results of future clinical trials.



Kaplan Meier Curve to show overall survival for patients with an increase in Ktrans from pre-treatment to cycle 2 day 2 compared with patients with a decrease in Ktrans from pretreatment to cycle 2 day 2.

Mahmood RD, Shaw D, Descamps T, Zhou C, Morgan RD, Mullamitha S, Saunders M, Mescallado N, Backen A, Morris K, Little RA, Cheung S, Watson Y, O'Connor JPB, Jackson A, Parker GJM, Dive C, Jayson GC. (2021)
Effect of oxaliplatin plus 5-fluorouracil or capecitabine on circulating and imaging biomarkers in patients with metastatic colorectal cancer: a prospective biomarker study.
BMC Cancer 21(1):354.

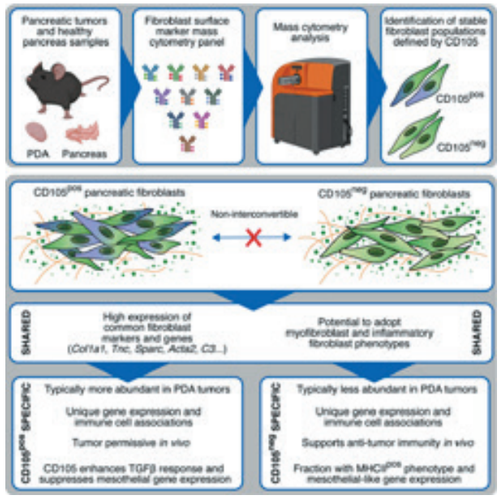
Fibroblast populations are found to suppress tumour growth in pancreatic cancer

By Aisling Minard
Senior Bioscientist, Drug Discovery Unit

In recent years a growing body of research shows that fibroblasts can influence tumour growth and are attractive therapeutic targets. Researchers here found contrasting fibroblast types that could influence tumour growth in pancreatic ductal adenocarcinoma (PDA).

PDA is one of the most lethal types of cancer. Patients generally have a five-year survival rate of less than 10%. PDA is typically diagnosed late because symptoms do not appear until the disease has progressed. This late detection means that traditional treatments such as chemotherapy do not really improve survival rate.

Disease progression and a patient's response to therapy are strongly influenced by non-mutant cells in the tumour microenvironment (TME). Fibroblasts are the most common cells of connective tissue, are a major component of the TME and play a prominent role in cancer progression.



Graphical abstract of the Hutton et al *Cancer Cell* paper. *Copyright © 2021 The Authors. Published by Elsevier Inc.*

The interaction between stromal cells and tumour cells is known to play a major role in cancer growth and progression. In this study, researchers from the Systems Oncology team used genetically manipulated mice to investigate the tumour stroma.

The researchers used single cell mass cytometry – a technique that analyses differences in protein amounts at the single cell level. They identified co-receptor CD105 for 'transforming growth factor β receptor' (TGF-βR) – a protein important in the inflammatory process – as a marker for two distinct but previously unidentified CAF populations.

The team found that one of these fibroblast populations dramatically restricts tumour growth and improves survival. This is the first evidence that a specific tumour-suppressive subgroup of fibroblasts exists.

The researchers show that these fibroblasts lose their tumour-restrictive properties when injected into immune-compromised mice. They found that tumour-suppressive fibroblasts elicit anti-tumour immune responses, suggesting these fibroblasts cause a reduction in tumour growth by establishing a 'tumour-suppressive inflammatory reaction'.

The findings outlined in this paper are ground-breaking for pancreatic cancer. For the first time, two contrasting subpopulations of fibroblasts are identified in the tumour microenvironment, defined by a single marker, with one showing promising tumour suppressive effects.

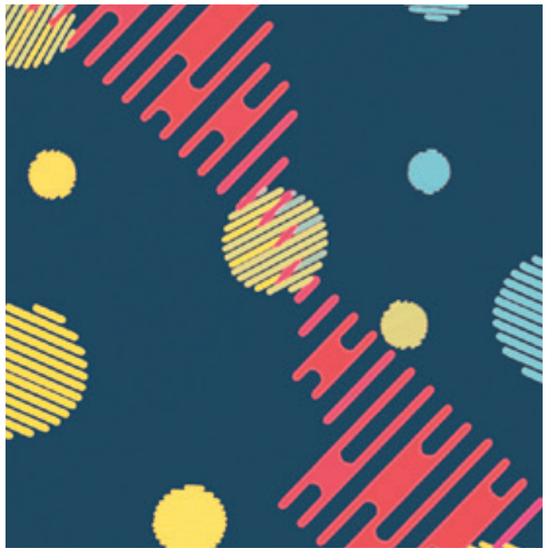
The next step is to target the anti-tumour properties of these fibroblasts for therapeutic exploitation to treat patients with pancreatic cancer.

Hutton C, Heider F, Blanco-Gomez A, Banyard A, Kononov A, Zhang X, Karim S, Paulus-Hock V, Watt D, Steele N, Kemp S, Hogg EKJ, Kelly J, Jackstadt RF, Lopes F, Menotti M, Chisholm L, Lamarca A, Valle J, Sansom OJ, Springer C, Malliri A, Marais R, Pasca di Magliano M, Zelenay S, Morton JP, Jørgensen C. (2021)
Single-cell analysis defines a pancreatic fibroblast lineage that supports anti-tumor immunity.
Cancer Cell 39(9):1227-1244.e20

Upcycling pain killers for cancer

By George Morrissey, Clinical Fellow, Cell Signalling

Exciting work from researchers at Manchester suggests that commonly used pain killers can boost response to immunotherapy in mouse models of cancer.



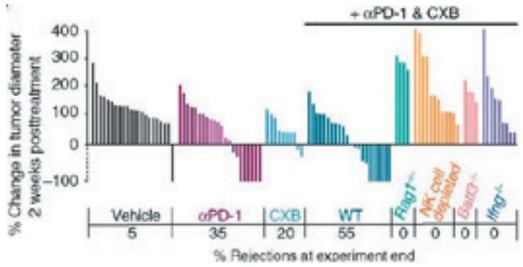
A combination of anti-inflammatory drugs targeting the COX2/PGE2/EP2-4 axis with immune checkpoint blockade reshapes the tumor immune microenvironment and increases infiltration of T cells with improved effector function. *Copyright © 2021, American Association for Cancer Research.*

Cancer is more complex than the single term suggests. It has many characteristics and the ability of a tumour to evade the immune system is one of the hallmarks of cancer. Immune checkpoint blockade – also known as immunotherapy – reduces the ability of cancer cells to hide from the immune system.

Some of the complexity of cancer is because tumours consist of different cell types: tumour cells, immune cells, blood vessels and fibroblasts, collectively referred to as the 'tumour microenvironment'. The tumour microenvironment differs between patients who respond to immunotherapy and those that do not. It is therefore believed that altering the tumour microenvironment will improve response to immunotherapies.

Immunotherapy has changed the treatment landscape for many cancers. In some cases, immunotherapy provides long term control of metastatic disease, but for many patients there are significant toxicities. Unfortunately, it is difficult to predict which patients respond favourably, and so many patients are exposed to significant toxicities with little chance of benefit. This study combines clinically approved medications with immunotherapy to try and increase the rate of response.

Victoria Pelly and colleagues show here that cancer cells secrete chemicals that reduce response to immunotherapy. The production of these chemicals is blocked by commonly



COX-2/PGE2 pathway inhibition acutely and transiently activates IFNγ signalling in the tumor microenvironment. Waterfall plot showing percent change in tumor diameter 2 weeks after treatment and percentage of tumor rejections at experimental endpoint.

used pain killers. In different models the scientists demonstrate that anti-inflammatory drugs improve response to immune checkpoint blockade.

Analysis of the tumour microenvironment revealed that treatment with anti-inflammatory drugs led to an increase in IFNγ – an important chemical linked to anti-tumour immunity – and an increase in immune cells associated with anti-tumour immunity.

The findings of this study have important implications for the treatment of cancer patients. This work raises the exciting prospect that a patient's response to immunotherapy can be improved with the addition of cheap, readily available, widely used drugs with known safety profiles.

Pelly VS, Moeini A, Roelofsen LM, Bonavita E, Bell CR, Hutton C, Gomez AB, Banyard A, Bromley CP, Flanagan E, Chiang SC, Jørgensen C, Schumacher TN, Thommen DS, Zelenay S. (2021)
Anti-inflammatory drugs remodel the tumor immune environment to enhance immune checkpoint blockade efficacy.
Cancer Discovery 11(10):2602-2619

New FOXC1 study suggests therapeutic targets against leukaemia

By Hannah Seberg, Postdoctoral Fellow, Leukaemia Biology

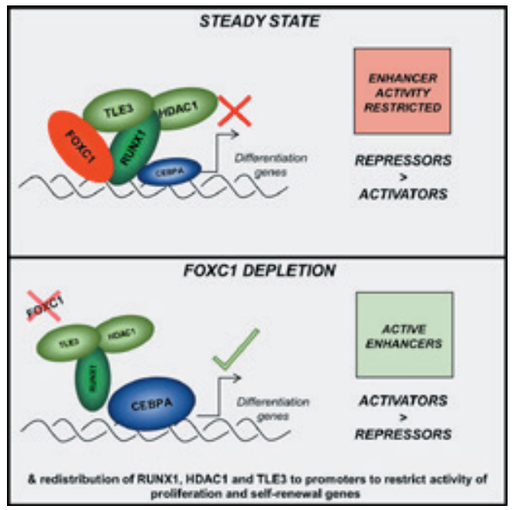
One of the main hallmarks of cancer is unregulated cell growth and division. This occurs in part by blocking 'cellular differentiation' – a process that normally specialises cells into the various mature tissue types.

In acute myeloid leukaemia (AML), mutations that occur in blood stem cells can prevent them from properly differentiating into mature red and white blood cells. This leads to the accumulation of immature leukaemic cells at the expense of healthy blood cells.

Researchers in the Leukaemia Biology group at Manchester are studying what causes the differentiation block in AML. Developing new therapies that can restore differentiation of leukaemic cells would be hugely beneficial in the treatment of this aggressive disease.

A previous study identified the transcription factor FOXC1 as being highly expressed in about 20% of AML cases. While FOXC1 is important for maintaining growth and stem cell function in various tissues, it is not normally expressed in healthy blood stem cells. Now the team has uncovered how FOXC1 acts as a transcriptional repressor to promote proliferation of leukaemia cells and contribute to the block in differentiation.

Transcription factors bind to DNA in multi-protein complexes that can either activate or repress the activity of nearby genes, depending on their composition. To understand the mechanism of action for FOXC1 in AML cells, the team started by identifying proteins that interact with it. Among the top candidates was another transcription factor called RUNX1, known to be important for blood development. They found that FOXC1 and RUNX1 physically interact through



Simeoni et al Graphical abstract. *Copyright © 1969, Elsevier*

their DNA binding domains and revealed shared binding sites across the genome. In addition to RUNX1, the team also identified other factors as part of the repressor complex, including co-repressor TLE3.

Notably, loss of FOXC1 caused the RUNX1 repressor complex to redistribute away from shared binding sites and led to higher expression of pro-differentiation genes. By contrast, an independent set of sites that gained RUNX1 after redistribution were associated with decreased expression of genes that help maintain stem cell characteristics. Together, these results support a model where inappropriate expression of FOXC1 recruits and stabilises binding of RUNX1 to repress differentiation in AML.

The FOXC1-mediated repressor mechanism identified in this study shows how the misexpression of one transcription factor can start to rearrange the gene expression program of leukaemic cells and promote growth instead of differentiation. In the future, new therapies may be designed to target interactions between FOXC1, RUNX1, and TLE3 and disrupt the oncogenic function of this repressor complex.

Simeoni F, Romero-Camarero I, Camera F, Amaral FMR, Sinclair OJ, Papachristou EK, Spencer GJ, Lie-A-Ling M, Lacaud G, Wiseman DH, Carroll JS, Somervaille TCP. (2021)
Enhancer recruitment of transcription repressors RUNX1 and TLE3 by mis-expressed FOXC1 blocks differentiation in acute myeloid leukemia.
Cell Reports 36(12):109725.

Loss of AMPK drives lung cancer growth

By Lucy Ginn, PhD Student, Cell Signalling

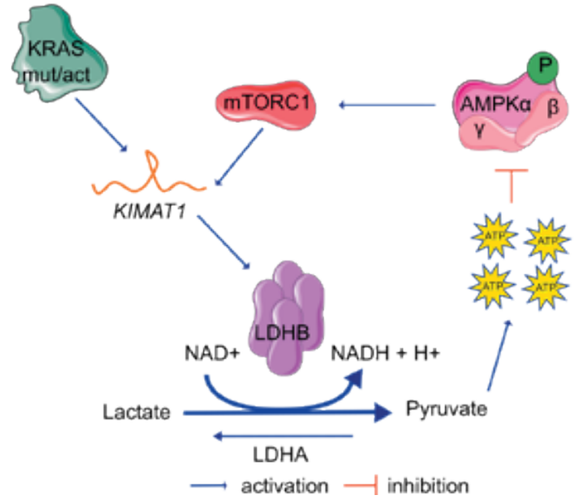
A team of researchers have identified a new regulatory mechanism that is important for the growth of lung cancer. A known hallmark of cancer is the uncontrolled growth of our cells. Therefore, cancer cells require even more energy than normal and need to adjust their metabolism accordingly.

Energy is extracted from nutrients and is stored in small molecules known as ATP. Important sensors notice when ATP levels drop in the cell and make changes to keep the energy levels constant. AMPK is an example of one of these energy sensors and is especially important in lung cancer.

The main subtype of lung cancer is non-small cell lung cancer (NSCLC). Patients are often diagnosed with advanced disease – where the cancer has spread – and have poor survival with limited treatment options.

KRAS is gene that is commonly mutated in NSCLC and has a key role in uncontrolled cell growth. Due to the high energetic needs of these KRAS mutant cancers, metabolic changes are common. However, the mechanisms responsible are largely unknown. Lead researcher in this study, Dr Manuela LaMontagna saw a gap in the field to determine the exact roles of KRAS and AMPK in NSCLC.

There is a high genetic similarity between mice and humans, so mice are used as model organisms to answer questions about cancer. The group used a mouse model to see the effect of AMPK on the growth of tumours, using mice that contained the mutant version of KRAS.



Schematic model of the human KRAS/KIMAT1/LDHB/AMPKα axis. KRAS activation and/or mutation activate KIMAT1. KIMAT1 binds and stabilizes LDHB, which by regulating lactate oxidation affects the ATP level and reduces AMPKα activation. AMPKα depletion, in turn, induces KIMAT1 through the mTOR pathway, establishing a negative feedback loop.

The team found that mice lacking AMPK developed more tumours and survived for less time than mice with AMPK.
In human cells, the researchers also showed that AMPK reduced growth by monitoring the number of cells over time. This key finding suggests that AMPK may act as a tumour suppressor in NSCLC, slowing the growth of the tumour.

To understand how AMPK affects tumour growth, the researchers carried out further experiments to determine what controls AMPK in cells. They found that the overall mechanism is a long non-coding RNA – a regulatory molecule that doesn't become a protein – named KIMAT1, previously shown by the group to be activated by mutant KRAS. The researchers show that KIMAT1 can increase ATP levels, which is detected by AMPK and in turn decreases its activation.

Overall, this study is important as it proposes new therapeutic angles for patients with lung cancer. Reported here, this newly discovered mechanism for AMPK in lung cancer growth can be used to design therapies that are more specific and cause fewer side effects in patients. Furthermore, these new findings may help to develop novel ways to target KRAS mutant NSCLC, which is becoming increasingly more difficult to treat.

LaMontagna M, Shi L, Magee P, Sahoo S, Fassan M, Garofalo M. (2021)
AMPKα loss promotes KRAS-mediated lung tumorigenesis.
Cell Death and Differentiation 28(9):2673-2689.

Face of the Institute retires

By Gillian Campbell, Editorial Team

We wish to congratulate our colleague Steve Morgan on his retirement. He was arguably the face of the Institute for many years as he sat on reception, often the first person staff and guests alike would see as they stepped into the building. It was always a pleasure to see his cheery smile and pass the time of day with chatting. So, it is with some sadness that we say goodbye.

Before his last day however, I managed to catch up with Steve on reception duty at the Oglesby Cancer Research Building – early one morning before people started arriving for the day – to ask him some pertinent questions about his time with us and pending retirement.

Set out here is my summary of our lovely chat.

It was over 12 years ago that Steve Morgan began working at the Institute as contract security with an external company. Steve must have made an impression, as four months later in December 2009, he was invited to work as in-house security, becoming an employee in January 2010.

His new role included not only providing security but also covering the reception desk. This brought more responsibility as Steve oversaw the stationery cupboard – he has plenty of funny memories about staff and their stationery antics – booked meeting rooms and registered visitors amongst many other tasks.

Being on reception meant he had to be prepared for anything. His biggest challenge though was using IT equipment. Steve had never used computers in a work setting before and was unfamiliar with programmes such as MS Word. So, he sought the training and developed his IT skills to enable him to carry out his role more effectively. Ever the professional, he also trained as a first aider and fire marshal.

What many of us may not know about Steve is that he had to get up every morning at 5:15am to start work on time. So, it is great to hear that he always loved coming into work, settling into his 'domain' and meeting people – from all walks of life, from all over the world. Steve was heartened to be recognised and appreciated by his colleagues and will miss so many people that he has known for many years, whom he enjoyed watching progress through the stages of their careers.

Steve enjoying a farewell lunch with colleagues

When asked what his greatest accomplishments have been, Steve said he was most proud of doing a professional job and maintaining high standards throughout the 12 years. It was important to Steve that staff felt they could talk to him and he would be supportive when listening about any problems that they faced. He always felt uplifted when people walked away with a smile on their faces.

Over the last 12 years, Steve has seen many changes, but the biggest must be the fire at the Paterson Building and losing the building that had been his workplace for so long. Steve is looking forward to his retirement but was at pains to make clear that he was going to miss everyone. He is hoping to see the new building when it opens and expects to be invited back for a tour!

Steve loves to travel and plans to start his retirement by visiting three places in the UK: Bamburgh in Northumberland, National Trust properties in the Cotswolds, and Cornwall. Happily, he and his wife intend to take three or four holidays per year. We are not at all jealous. With all those activities on the cards, Steve also wants to learn how to sleep in past 6:30am. We wish him luck!

Later that day, Steve was taken out to lunch by longstanding colleagues from Finance – Debbie, David and Denise were amongst the first people he met when he joined the Institute and made him feel welcome.

First day at work in the Armed Forces aged 17

"Hi Everyone,

Just a little note to say a heartfelt thank you.
To everyone who contributed to the fantastic presents, gifts, cards and kind comments that I've received, I'm overwhelmed by your generosity. I'll miss everyone and even though I'm looking forward to retirement, I'll be sad to not see you again.

Last day of work aged 66. Steve is pleased with his retirement gift.

I also thought I would share a couple of photos. The first from when I started work and joined the Armed Forces aged 17 and the other when I finally finished work aged 66! Scary isn't it? 😊

Once again, thank you so much."

Memories from colleagues:

Denise Owen

"I will always remember Steve fondly. We developed a friendship pretty much as soon as he arrived. He was always there to listen, and I was also there for him when he needed to talk, offering advice where I could. He was always funny and everyone liked him. We were also lucky enough to share his wedding day with him and that was a really good day as he had found happiness and we were all really happy for him. 😊

Obviously since the fire we were not in touch as much as we should have been, but we were not going to let him retire without taking him for lunch or celebrating in some way.

The Institute will not be the same without him and we will miss him being around."

Andy Lloyd

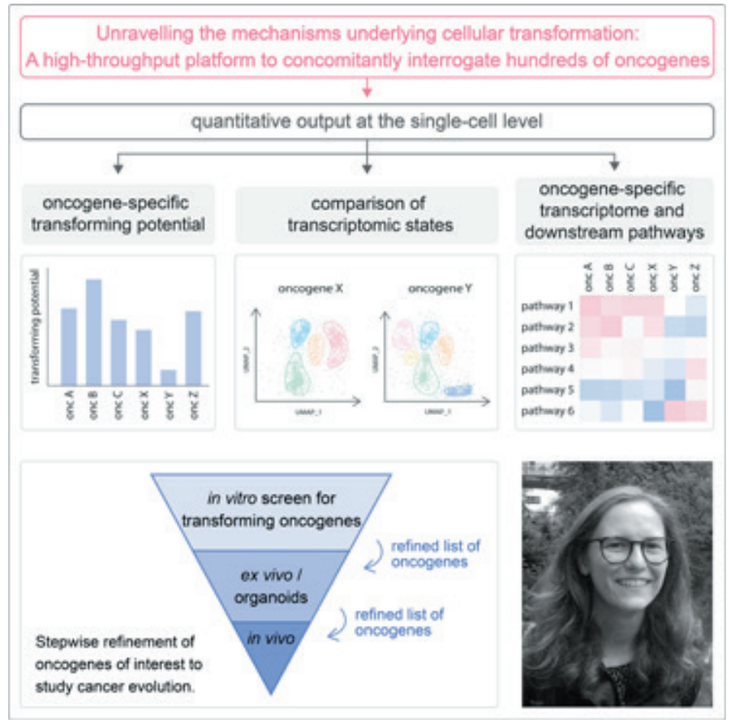
"Steve is a massive character and will be greatly missed. For me, he was from an 'old school' era where he wouldn't take life too seriously and always made everyone laugh. Our common ground was football, and we would often discuss the result after a weekend game. I particularly enjoyed going out with him and the old estates teams at Christmas – pre-Paterson fire. More often than not, the night would turn into a cheerful debate between Steve and (former colleague) Steve Alcock, and end with me leaving with an aching jaw from all the laughter."

3Rs poster prize event

In September, we jointly held our annual 3Rs poster prize event with scientists from AstraZeneca and Agenda Life Sciences. Speakers presented virtual posters to an online audience highlighting how their work has supported the Replacement, Reduction or Refinement of animal experiments.

The poster prize was won by PhD student Bianca Blöchl from our Cell Plasticity & Epigenetics group. She impressed the judges with her systematic approach and by demonstrating technology that will help reduce the number of animals used in certain experiments. Bianca is now looking to expand the application of her experiments to many different cancer cell lines.

Huge CONGRATULATIONS to Bianca Blöchl for winning the joint CRUK MI, AstraZeneca and Agenda Life Sciences 3Rs poster event!



Animal research developments and the 3RS

Humans share around 90% of their genes with all other mammals, and because of this animal research has been used to discover how the basic processes of the body work and how these can go wrong when the body is affected by disease.

Most of the research at our Institute does not involve animals but some animal research is essential if we are to understand, prevent and cure cancer.

Our collaboration with clinicians, such as those in The Christie NHS Foundation Trust, enables us to quickly translate our discoveries in laboratory mice into effective treatments for cancer patients.

As part of our commitment to animal welfare, we regularly review our use of animals and share best practice. Set out here are a few recent examples of how we do this at the Institute.

How to move forward after COVID19

Natalia Moncaut, who runs our Genome Editing and Mouse Models facility, has recently co-authored an article with Sarah Hart-Johnson from the Colony Management Services at The Francis Crick Institute in London.

During the first COVID-19 lockdowns, many mouse breeding facilities significantly reduced the size of their animal colonies. However, this can speed up genetic drift – a natural process which introduces random DNA mutations that can affect the reproducibility of mouse experiments.

Here, they outline three approaches to combatting genetic drift: refreshing colonies by crossing with wild-type animals, replacing animals from cryopreserved stocks, or by changing breeding strategies.

This publication also highlights the significant work that Natalia and her team did during the pandemic to cryopreserve many lines at the Institute, providing a fantastic resource for reproducible science for decades to come.

SCAN ME

Moncaut N, Hart-Johnson S. (2021)
The impact of COVID-19 lockdowns on the genetic integrity of your mouse colonies.
Lab Animal (NY) 50(11):301-302.
Scan the QR code to download

Training

Across the Institute we continue to share developments in animal experimentation and reporting.

Andrew Porter, Research Integrity and Training Adviser, hosted a webinar in November on the updated ARRIVE Guidelines – Animal Research: Reporting of In Vivo Experiments – a checklist of recommendations to improve the reporting of research involving animals. Andrew discussed with our researchers across the Institute how they can meet these new reporting guidelines when writing their research papers.

Caroline Wilkinson, our Establishment License Holder, recently updated the Institute on changes to the regulatory delivery model of the Home Office's Animals in Science Regulation Unit (ASRU).

Caroline is a member of the Home Office's Regulated Community Change Team who are advising ASRU as they continue to develop their new strategy.

A key objective of the Regulated Community Change Team is to provide input and guidance to the ASRU Change Programme on the impact and deliverability of proposed changes on the regulated community.

Related news on animals in research also features in these pages

- ➜ See how animal research in cancer is explained at the Cancer Revolution: Science, innovation and hope' exhibition at the Science and Industry Museum, Manchester (page 6)
- ➜ Find out how new Institute Fellow Carlos Lopez-Garcia is replacing animals with a novel human model of lung cancer (page 16)
- ➜ Discover more about animal technician Rose Storey (page 32)

Choosing the right technology

Important in scientific research is producing data that can be reproduced by other researchers. Another way to enhance data reproducibility is by reducing observer bias.

When planning an experiment and faced with multiple options, researchers in our Tumour Suppressors group asked, which machine should I use? With no published data available, they carried out their own in-house test of three different animal imaging machines. They used this data to produce a new software-based approach to measure tumour size more consistently.

This was the first study of its kind to rigorously compare the performance of three similar imaging machines.

By sharing their study – which was chiefly to determine the best machine for their own experiments – the group were able to provide valuable insights for other researchers looking to refine their experiments.

Their findings have significant implications for animal welfare – they show that choosing the right machine can reduce variability in data, meaning the number of animals used in an experiment can be reduced.

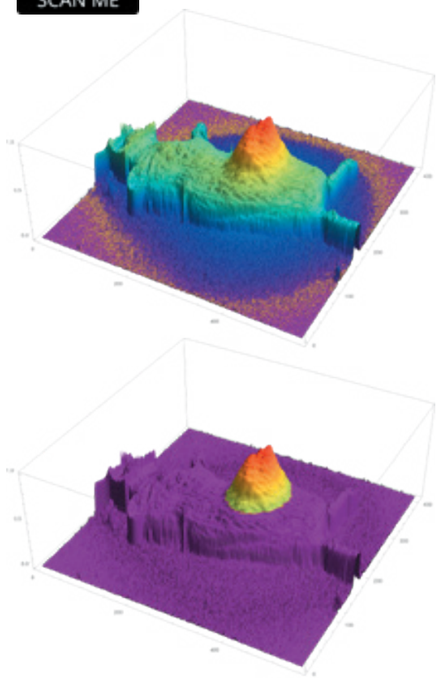
SCAN ME

Scan the QR code to download

iRFP (near-infrared fluorescent protein) imaging of subcutaneous and deep tissue tumours in mice highlights differences between imaging platforms. (2021)
Hall C, von Grabowiecki Y, Pearce SP, Dive C, Bagley S, Muller PAJ.
Cancer Cell International 21(1):247.

SCAN ME

Scan to watch first-author Callum Hall and study lead Patricia Muller discuss their work.



MouseTensity – quantifies fluorescent images of subcutaneous tumours in mice. By displaying the intensity of the whole mouse in 3D (top), one can clearly see the overall intensity (flat and homogenous over the whole mouse) compared to the intensity of the tumour (appearing as a mountain). Using a sliding scale, the 'gate' can be set and the intensity of the mountain calculated (bottom). *Simon Pearce and Callum Hall*

Archiving and sharing resources

SCAN ME

Archiving and sharing genetically altered mouse strains can refine colony management and reduce animal use.

Natalia Moncaut also contributed to new guidance published by the NC3Rs – an organisation that supports development of new technologies and approaches to replace, reduce and refine the use of animals for scientific purposes. This document summarises current best practice and includes a checklist for facilities on cryopreservation.

Scan the QR code to download

Translational Lung Cancer Biology

We are delighted to welcome Carlos Lopez-Garcia as a new Institute Fellow. Up until recently, he was a Senior Research Associate in the CRUK Manchester Institute Cancer Biomarker Centre, led by Caroline Dive.

Carlos completed his PhD at the University of Murcia, Spain in 2007 and later joined the laboratory of Doug Winton at the CRUK Cambridge Institute to study stem cell dynamics in the intestinal epithelium. There, he showed for the first time a new model of adult stem cell self-renewal in the intestinal epithelium by studying the evolution of clonal size in vivo.

In 2011, he joined Charles Swanton's group at the London Research Institute (now The Francis Crick Institute) where he made the significant discovery that loss-of-function alterations in BCL9L were frequent in aneuploid colorectal tumours, where it regulates aneuploidy tolerance by p53-dependent and independent mechanisms. It was during his time there that led Carlos to identify lung squamous cell carcinoma as a problem in cancer medicine and the lack of adequate models to investigate it. Motivated to explore this research niche further, he joined Ian Adcock at Imperial College London, where he learned to culture and genetically manipulate human bronchial epithelial cells.

Equipped with a comprehensive perspective on stem cell biology, cancer genomics, models of cancer and genomic instability, Carlos arrived at the Manchester Institute in 2019 to develop his research ideas in lung squamous cell carcinoma.

Lung cancer is a cancer type characterised by multiple histological subtypes – such as small cell and non-small cell lung cancer – that can also be subdivided into molecular subtypes with different prognoses, driver genes and dysregulated pathways. This heterogeneity is especially prominent in lung squamous cell carcinoma (LUSC), the second most frequent type of non-small lung cancer after lung adenocarcinoma, and one of the most aggressive forms of lung cancer that accounts for approximately 5% of all cancer mortality in the UK and notably lacks targeted therapies.

Developing a novel human model of lung squamous cell carcinoma progression is therefore an urgent need in basic and preclinical LUSC research and would replace mouse models in a wide range of applications.

Earlier this year, Carlos secured a project grant from the NC3Rs – an organisation that funds new technologies and approaches to replace, reduce and refine the use of animals for scientific purposes – to develop preclinical and tractable human models of lung squamous cell carcinoma.

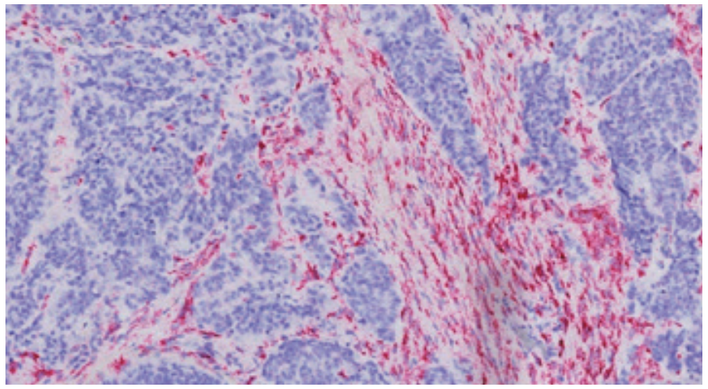
With this funding, he was able to establish his own independent group, Translational Lung Cancer Biology. Also a member of the Lung Cancer Centre of Excellence, Carlos is joined by PhD student Julia Ogden and newly recruited Scientific Officer, Anthony Oojagger.

The Translational Lung Cancer Biology group aims to unravel the biological meaning of lung squamous cell carcinoma heterogeneity. LUSC arises from the accumulation of genomic alterations in basal cells, the resident stem cells in the bronchial epithelium. Exploiting LUSC genetics, the group will build more accurate in vitro LUSC models that better reflect patient heterogeneity and the developmental stages of the disease as well as replacing large cohorts of mouse models in a wide range of basic and translational research areas.

Understanding the biological meaning of this LUSC evolution and inter-patient heterogeneity is necessary to design new personalised therapeutic strategies and to gain a better knowledge about the mechanisms that drive LUSC progression.

We congratulate Carlos on his success and wish him all the best in building his independent research programme over the coming years. Well done!

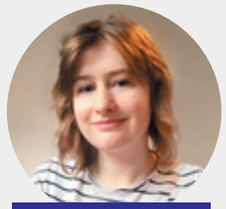
NC3Rs National Centre for the Replacement Refinement & Reduction of Animals in Research



Human lung squamous cell carcinoma stained with chromogenic in-situ hybridisation targeting mRNA from the gene lumican (red), which accumulates in the cellular component of the tumours' interstitial matrix. Counterstained with haematoxylin. *Image supplied by Andre Koper (Signalling Networks in Cancer – former group at CRUK MI).*

Meet the new students

We welcomed 7 new PhD students, one MB-PhD student and one clinical research fellow to the Institute in September 2021, and although their inauguration to the CRUK MI took place virtually during the Colloquium, they still enjoyed a comprehensive and interesting introduction to their new peers and colleagues.



Holly Greenaway

Hi, I'm Holly and I'm from Cambridge. I'm a new PhD student in the Cell Division group led by Iain Hagan. I've spent the last five years in Sheffield studying Biomedical Science. I became interested in cancer, and specifically cell cycle control, after taking a Cancer Biology module in my third year. My final year project was investigating a novel protein involved in the G2/M checkpoint and this pushed me to find a PhD related to the cell cycle. My PhD project will be investigating the role of specific centrosome components, kinetics of mitotic commitment and roles in cell cycle control and hopefully translating some of the lab's work on the role of the spindle pole body in yeast to the role of the centrosome in mammalian cells.

Outside of the lab I spend most of my time crocheting or indoor bouldering. I also love walking and I've explored many of the peaks on the Sheffield side, so I'm hoping to do some more walking on the Manchester side and maybe try some outdoor climbing too.

Seung Hyun Lee

I'm Lee and I am a first year clinical PhD student based in the Systems Oncology group at the Cancer Research UK Manchester Institute. I am originally from Seoul, South Korea. After spending some time in Toronto, Canada I studied medicine in St Andrews and Edinburgh. Later, I decided to pursue histopathology, as I am interested in combining science and its application to clinical medicine (and vice versa). During my histopathology training, I undertook postgraduate certificate degrees in surgical sciences and molecular pathology. Studying these subjects helped me to think more about the molecular underpinnings of cancers. After careful consideration, I undertook a molecular pathology fellowship offered by the NIHR BRC Royal Marsden and Institute of Cancer Research, before arriving here.

My research interests are in upper gastrointestinal cancers, especially HPB malignancies. I have been particularly drawn to pancreatic cancers since there has been little improvement in survivorship or effective therapies over last 50 years. Fortunately, I found an awesome team – Claus Jorgensen and the Systems Oncology group – in which to undertake my project on the tumour ecosystem of pancreatic neoplasms. I am very much looking forward to embarking on this new adventure.

Outside of work, I enjoy travelling, going to nice coffee and tea shops, and visiting art museums.

Michael Jones

Hey, I'm Michael and I'm from South-East London. I completed my Master's degree in Biomedical Sciences at the University of Southampton. My fourth-year project gave me my first glimpse into the world of cancer research and involved looking at oncogenic KRAS signalling in lung adenocarcinoma. I then made the journey north of the M25 when I was lucky enough to be given the opportunity to study a PhD at the CRUK Manchester Institute.

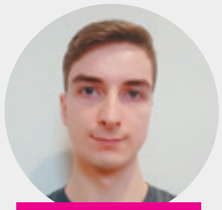
I am now based in the Leukaemia Biology group led by in Tim Somervaille, where my project is centred around dissecting the role of Groucho proteins in acute myeloid leukaemia (AML). Groucho proteins – or TLE proteins in humans – are transcriptional corepressors that enforce a differentiation block to haematopoiesis; ultimately encouraging leukaemic onset. By studying the effects of Groucho/TLE proteins and their binding partners on AML, we can build a better picture of the critical role these corepressors have to play. Ultimately, the hope is to identify potential druggable targets for AML treatment in the future.

Outside the lab, I love to run, play the guitar, and watch the Formula 1 – although not usually at the same time.

Sophie Richardson

Hi, my name is Sophie. I'm currently living in my hometown of Nantwich, Cheshire but looking forward to moving to Manchester before we return to the new Paterson Building. I completed a four-year BSc Genetics at The University of Manchester, with an industrial placement year at QIAGEN in my third year. After graduating in 2019, I went back to QIAGEN's Next Generation Sequencing assay development department for 6 months before starting as a Scientific Officer in the Nucleic Acid Biomarker team in the Cancer Research UK Manchester Institute Cancer Biomarker Centre in January 2020. It was with the Nucleic Acid Biomarker team that I gained an interest in liquid biopsies by contributing to the development of cell free DNA analysis techniques for mutation and methylation profiling. I'm now continuing with the Nucleic Acid Biomarker team as a PhD student, looking at the use of liquid biopsies to support the management of Ewing Sarcoma, which is a rare childhood and young adult cancer of bone and soft tissue.

When I'm not in the lab, I enjoy baking (and eating the results!), watching Formula 1 races and playing video games. I also volunteer with a Girlguiding group in my local area.



Louis Roussel

Hi, my name is Louis and I'm from Lyon in France. I recently started my PhD within the Systems Oncology group. Although I have a degree in Chemical Engineering from École Supérieure de Chimie Physique Électronique de Lyon (or CPE Lyon), I studied Life Sciences and Biotechnologies for my Master's specialisation before completing a 6-month end-of-study internship at the French National Centre for Scientific Research. There, I started a novel research project investigating the remodelling of the calcium-signalling toolkit in uveal melanoma cancer cells which, through a GNAQ/GNA11 mutation, have a deregulated amount of IP3. Then, two years ago I found my way to the UK, working at the Wellcome Sanger Institute near Cambridge. During these two years, I looked to characterise hits from a CRISPR screen to uncover cancer cell vulnerabilities to Natural Killer cell mediated death. I am very excited to start my PhD project which, under the guidance of Claus Jorgensen, aims to determine how pancreatic cancer early tumourigenesis bypasses restrictive signals from the microenvironment. Outside of work, I enjoy watching movies and spending time with my friends.

Alexia Strickson

Hi, I'm Alexia and I started an MB-PhD in Cancer Sciences in October. I have completed the first 3 years of my MBChB at Manchester and will return to do the final 2 years after completing this PhD.

Projects within the medicine course allowed me insight into blood cancers, specifically looking at myelodysplastic syndrome and AML. I am now lucky enough to be working in the Leukaemia Biology lab, which is led by Tim Somervaille. I have moved from myelodysplastic syndrome to myelofibrosis to discover interactions within the bone marrow microenvironment which can hopefully lead to potential therapeutic targets. I am very new to lab work and will be spending the first few months of the PhD settling into the environment before setting off on my own work for my project.

Outside of university, I enjoy hiking, football (watching not playing) and spending time with friends.

Kirsty Tinsley

Hello! I'm Kirsty and I've just begun my PhD within the Cell Signalling group under Angeliki Malliri. My project will focus on the Rac activator STEF and its contribution to tumour initiation, as well as cell migration and metastasis in KRAS- mutant non-small cell lung cancer. Before coming to Manchester, I studied an integrated Master's in Biomedical Science at the University of Sheffield, where I investigated phosphoinositide dynamics during macropinocytosis in KRAS mutant cells. It was during my A levels after completing an extra-curricular project on apoptosis that my interest in cancer research began, and after completing the last year and a half of my degree without setting foot in the lab I'm super excited to start planning some experiments. I am originally from a small, sleepy town in Oxfordshire best known for its power station and being statistically the UK's most 'normal' town.

I am very excited to have only moved across the Pennines as the Peak District is what I will miss most about Sheffield, but I am eager to start exploring walks nearer to Manchester, as well as in the Lakes. In my spare time, I love reading, climbing, and playing the flute – if anyone is interested in starting an Institute orchestra let me know!

Jingru Xu

Hi, my name is Jingru. I was born in Jinan, a city from the north of China halfway between Beijing and Shanghai. I obtained my undergraduate degree in Biological Sciences at Imperial College London in 2020, after completing a research placement at the National Institute Biological Sciences, Beijing in 2018, where I studied CRISPR-Cas9 gene-editing strategy. Before joining the CRUK Manchester Institute, I completed my MPhil studies at the University of Cambridge, working on investigating the function of a GTPase activator in the activation and differentiation of CD8+ T cells at the Department of Pathology. Bringing together my interests in cancer biology, immunology and stem cells, I am very excited to join the Stem Cell Biology group led by Georges Lacaud. My project will study the role and requirement of transcription factor SIX1 in acute leukaemia cells.

In my free time, I enjoy cooking, playing the piano and practising calligraphy. I am also taking a tennis course at a local club and want to expand my interest in sports in general.

Jessica Young

Hi, my name is Jessica and I have just started my PhD in the Tumour Immunology and Inflammation Monitoring laboratory in the Cancer Biomarker Centre. I am doing a joint PhD with The University of Manchester and the University of Melbourne, looking at whether differences in the tumour microenvironment and immune response can predict relapse in melanoma patients. As part of this programme, I will spend a year in Australia, which is very exciting!

I am originally from Manchester but have spent several years away from the city, doing my undergraduate degree in York – with a year in France – then completing my Master's in Newcastle.

Outside of the lab, I enjoy going to the theatre, seeing drag shows and during lockdown last year I took up crocheting.

The Rosetrees Trust funds lung cancer research

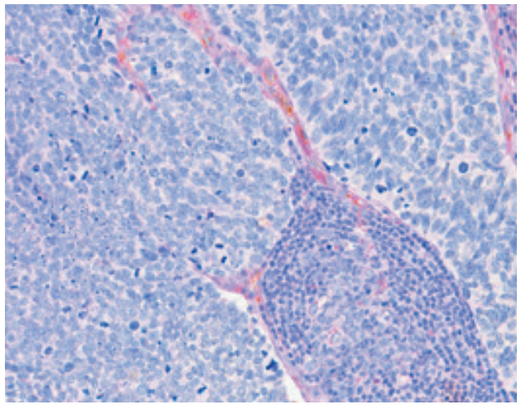
Congratulations to Caroline Dive and Kathryn Simpson from the CRUK Manchester Institute Cancer Biomarker Centre, who have been awarded a 3-year project grant from the Rosetrees Trust. This funding will be used to study mechanisms that promote the early spread of small cell lung cancer and reveal new treatment strategies and improve patient outcomes.

Small cell lung cancer (SCLC) is an aggressive, incurable neuroendocrine cancer that quickly spreads through the bloodstream to form metastases in the liver and brain. Improved treatment is required but often the paucity of tissue biopsies to study the disease obstructs progress.

Kathryn, Team Lead of Preclinical Pharmacology in CBC, will lead the study. They plan to use mouse models made using circulating tumour cells from patients' blood samples – mouse models that were pioneered by the group – to investigate metastasis, especially to the brain, a common cause of patient death. SCLC cells make their own blood vessels via a process called vasculogenic mimicry, and the team will study how these vessels connect with endothelial vessel networks to facilitate metastasis.

They also aim to identify and characterise the first tumour cells to reach the brain and study how they grow in that environment.

Overall, the goal is to seek strategies to suppress metastasis and improve patient outcomes.



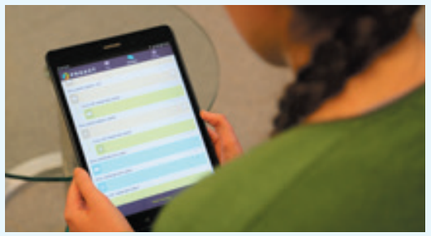
Vasculogenic mimicry shown in small cell lung cancer. *Image supplied by Francesca Trapani, former colleague, Cancer Biomarker Centre.*

Encouraging inclusivity in technology clinical trials

Congratulations to the digital Experimental Cancer Medicine Team, who were awarded funding through the MAHSC Cancer Domain Project Competition earlier this year.

The aim of this competition is to invest in projects that support transformational change in cancer related life sciences for the benefit of Greater Manchester patients and citizens.

The dECMT – part of the CRUK Manchester Institute Cancer Biomarker Centre – brings together researchers, clinicians, technology and patients to transform decision-making in early clinical trials.



The team will use the award to address health disparities associated with the use of digital technologies and ensure that technologically enabled healthcare pathways are inclusive to all.

Digital technology, such as mobile applications (apps) and devices, is becoming a greater part of healthcare, with the potential to make health and care delivery more equitable. However, for those with limited access to or understanding of technology, there is a risk of inadvertently excluding certain groups.

Through this project, the dECMT will collaborate with diverse community groups across Manchester in virtual workshops to get a clear understanding of the different needs and challenges of using technology in healthcare.

Together, they aim to develop guidance for researchers to ensure that research involving new healthcare technology is designed to include all patients, regardless of access and skill with technology.

Annotating the Tumor Microenvironment in Mouse Models Using Mass Cytometry

Claus Jørgensen is Fluidigm Scientist in the Spotlight

Our own Claus Jørgensen was invited by Fuidigm to be their 'Scientist in the Spotlight' for October.

Fluidigm is a biotech company that works with researchers worldwide to provide technology solutions in mass cytometry, tissue imaging, and single-cell genomics to improve health and accelerate the development of more effective therapies for disease. They focus on the most pressing needs in translational and clinical research, including cancer.

Claus, who leads the Systems Oncology group, focused on the work published in his recent Cancer Cell paper, "Single-cell analysis defines a pancreatic fibroblast lineage that supports anti-tumor immunity" – a review of this publication can be read on pages 8-9 in the newsletter.

During the virtual seminar, Claus discussed in-depth CyTOF – an application of mass cytometry used to quantify labelled targets on the surface and interior of single cells – and how its use in the stromal composition of healthy tissue in mice and spontaneous tumour models can identify new relationships between mesenchymal and immune cell subsets in pancreatic ductal adenocarcinoma.

Claus' instructive presentation was well received by the scientific community.

Institute Scientists to attend Global Young Scientist Summit 2022

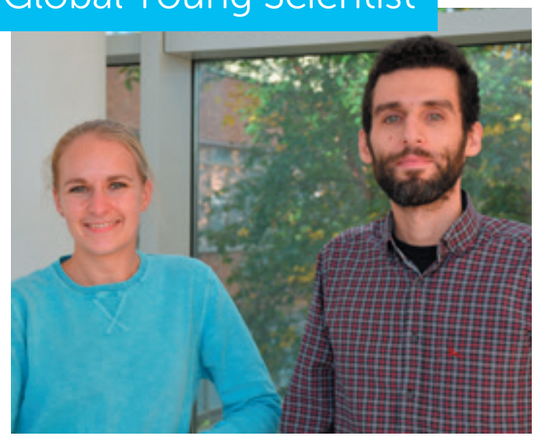
Congratulations to Institute postdoctoral scientists Lisa Shlyakhtina and Efthymios-Spyridon Gavriil, who have been selected to attend the Global Young Scientist Summit next year.

Each year, around 280 international young scientists are invited to engage with peers and invited eminent speakers to discuss key areas of science and research, technology innovation and society, and potential solutions to global challenges.

The summit is multidisciplinary, covering topics relevant to chemistry, physics, medicine, mathematics, computer science and engineering. Invited speakers are globally recognised scientific leaders, including recipients of the Nobel Prize, Fields Medal, Millennium Technology Prize, and the Turing Award.

Participants will be able to take part in live plenary lectures, panel discussions and Q&A sessions, engage with their pre-selected speaker and interact with other attendees during the networking sessions.

Participation is through nominated selection and The University of Manchester was invited to submit 10 participants and 10 viewers. Lisa from Cell Plasticity & Epigenetics has been selected as a participant and Efthymios from the Drug Discovery Unit has been selected as a viewer. Lisa will take part and contribute to break out sessions.



Lisa and Efthymios will attend the virtual Global Young Scientist Summit 2022.

The Global Young Scientist Summit will be celebrating its 10th anniversary in 2022 and takes place virtually from 17 to 21 January. We look forward to hearing all about their experience in the next edition of the newsletter.

The Institute gathered virtually for Colloquium 2021

The annual CRUK Manchester Institute Colloquium has regularly taken place at Lancaster University. However, since the COVID19 pandemic struck, we have held the event virtually.

Institute Group Leader shares his latest research.

The purpose of this assembly is to share current research with talks from our Group Leaders and second year PhD students, as well as poster presentations from a range of scientists across the Institute, covering all aspects of cancer research.

Last September, we triumphed over the challenge of translating a retreat-based event onto a virtual platform and successfully held the Colloquium via Zoom.

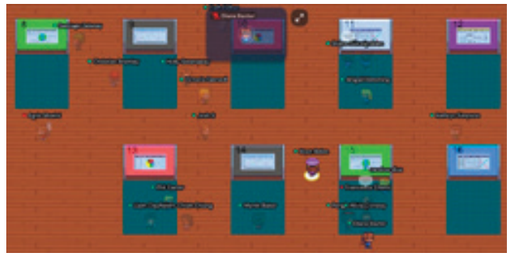
This year, we wanted to enhance the experience and use an alternative digital platform. We chose Gather Town, which replicated the feel of a real-life event by enabling our colleagues to move around a virtual conference centre – with a lecture theatre, poster rooms and breakout areas. The result was a huge success and provided an enjoyable way for everyone to interact with each other over the three days, including with our new intake of students.

Opening the Colloquium, Institute Director Caroline Dive gave a warm welcome to everyone and set the scene for the science-packed event. There were a variety of interesting talks on both fundamental and translational research from several of our Group Leaders and Institute Fellows. We heard excellent presentations from our second year PhD students, given in person in front of the Education Committee, who were greatly impressed with their professionalism and enthusiasm. We also welcomed to the event Jamie Honeychurch, from the Division of Cancer Sciences at the University of Manchester, who gave an interesting overview of his research on radiotherapy and natural killer cell cytotoxicity of cancer.

When it came to our poster sessions, the platform Gather Town really made a difference in how we interacted. Being able to build our own virtual spaces and use personalised avatars that could move around the space allowed us to virtually meet up and spend time with our colleagues more easily.

Elevator pitches preceded the poster sessions, featuring selected posters where the authors each gave a 90-second pitch on their research.

Poster sessions were hosted in 'Poster Rooms', where each presenter could display their poster and be seen by visiting colleagues. They could then talk about their poster with a virtual audience that was more akin to real life conferences.



Virtual poster session in action.

As always, the quality of the posters was outstanding, and it made hard work for the panel of judges to choose the winners of the two prizes. The Lizzy Hitchman Prize for the best poster was awarded to two PhD students this year, Charlotte Bell from the Cancer Inflammation and Immunity group for her work on chemotherapy induced COX2, and Francesco Camera from Leukaemia Biology for his studies on transcription factor IRX3 and acute myeloid leukaemia. The Best Poster Prize to a postdoc went jointly to Ellyn Hughes of the Cancer Biomarker Centre and Rob Sellers from Computational Biology. Prizes for the best elevator pitch were also awarded this year, going to Felix Heider and Francesca Chemi.

As with last year's event, the virtual platform enabled us to diversify the programme and invite external guests.

We were privileged to hear from Professor Doug Lauffenburger, esteemed Ford Professor of Biological Engineering, Chemical Engineering, and Biology at the Massachusetts Institute of Technology, Boston. He gave a fascinating talk on how systems biology approaches can help us understand the immune cell effects in tissue microenvironments. He then spent time chatting with early career researchers.

The Lizzy Hitchman Prize for Best Poster goes to Charlotte and Francesco; Best Poster Prize goes to Ellyn Hughes and Rob Sellers

The alumni session last year was so enjoyable, we decided to hold another one. This wonderful occasion enabled us to reconnect with former colleagues and discover where a PhD or postdoctoral position at the CRUK MI can lead, from university lecturer to industry, and see how to balance an academic career with family life. We would like to thank for their time and frank discussions, Natalie Mack, now a Teaching Associate at the University of Nottingham; Avinash Patel, Senior Director at Dewpoint Therapeutics in Germany; and Alba Maiques-Diaz, a postdoctoral researcher based in Spain.

Alumni session was enjoyed by all.

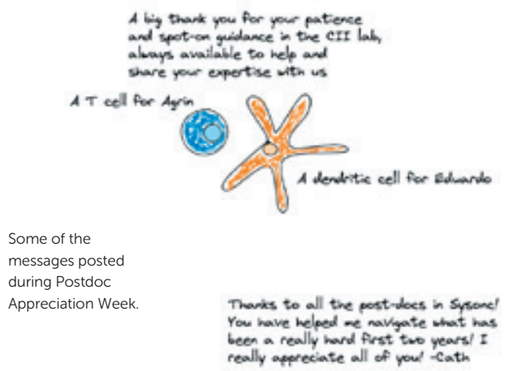
This year's Colloquium coincided with Postdoc Appreciation Week. So, we used our occasion to celebrate our postdocs and invited staff to post messages in the Gather Town platform.

Best elevator pitch goes to Francesca and Felix

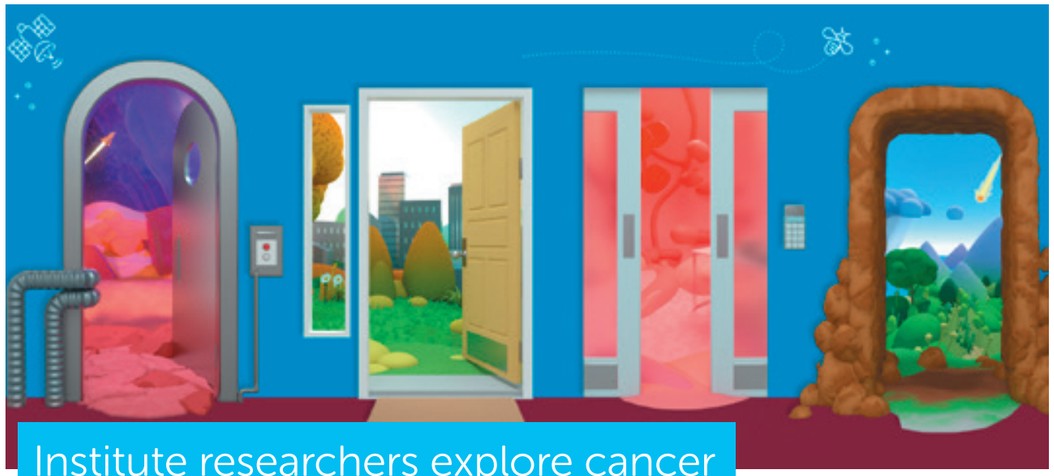
In addition, we invited a panel of experts from Cancer Research UK to talk about communicating our science in an accessible and engaging way for a variety of audiences and the channels available.

And finally, it would not be a colloquium without the socialising element. During breaks, we made the most of the virtual space and chose to spend time together in the park or at the beach. The evening's social events took place in the lounge, where we could sit at tables together and play several different card games. Some of us even battled it out in Tetris. It was great fun and really gave the feeling of bringing everyone together.

In September next year we hope to hold the event in real life and return to Lancaster.



Some of the messages posted during Postdoc Appreciation Week.



Institute researchers explore cancer landscapes with the Royal Society

Explore the world of Summer Science

This summer, scientists at the Institute were delighted to showcase their research at the prestigious Royal Society Summer Science Exhibition.

The exhibition is the Royal Society's flagship annual public engagement event. It is normally held at their headquarters in London and features more than 20 exhibits of cutting-edge science from research institutions across the UK, with visitors meeting scientists and getting hands-on with interactive displays unpacking the latest technological and scientific developments.

Our Institute successfully applied to host an exhibit at the 2020 event to highlight work from multiple labs on research exploring the cancer microenvironment. We wanted to explain that tumours are not simply balls of cancer cells but are in fact complex 'landscapes' that contain healthy cells, immune cells and connective tissue.

Within that complex microenvironment, 'messages' whiz around between cancer cells and the other components. Cancer cells can even make healthy cells behave in unusual ways, such as feeding the cancer cells or protecting them from cancer treatments.

For their central exhibit, the team planned a large interactive tumour wall into which visitors could insert different kinds of cells and watch the cancer grow, all supported by live microscope demonstrations, and other games and activities.

However, the in-person event was cancelled due to the COVID19 pandemic. At the start of 2021 we learned the Royal Society were going to run their first ever online exhibition. So, from January our team of researchers had to work hard to translate their physical ideas into content that was accessible online. The Royal Society offered several training sessions to assist our team in hosting engaging workshops over Zoom and delivering online lectures.

With help from Institute members Yannick von Grabowiecki and Belen Conti Vyas, they produced an outstanding introductory video featuring researchers at work in their labs, as well as animations showing the complexity of tumours.

PhD student Chris Bromley developed the centrepiece of our online experience, a brilliant interactive 3D tumour model. Here users learn about the different kinds of cells that make up a complex tumour landscape – a virtual recreation of our original tumour wall concept – and use this knowledge to understand why patients might respond differently to cancer therapies.

Marek Dynowski and his team in Scientific Computing, along with external companies StoryThings and Peak Digital, supported the complex development and online hosting of this content. The whole Institute also played a vital role in beta-testing the tumour model during an online Director's update.

Learning about tumour microenvironment with interactive 3D tumour model game . *Designed by Chris Bromley*

The Summer Science Exhibition ran from 8-11th July, during which the Royal Society hosted 'lightning lectures' on their YouTube channel, giving more insight into the research behind the exhibition. Our lightning lecture was presented by postdoctoral researcher Joanna Kelly, where she compared her research to a walk in the countryside – connecting the two themes with a map of the landscape. After her talk we ran a live audience Q&A, and Jo's video has now been watched over an amazing 13,000 times on YouTube.

Scan the QR code to watch

One of the main aims of this Royal Society exhibition is to enthuse the next generation of researchers about science, and to give them a taste of real science in action.

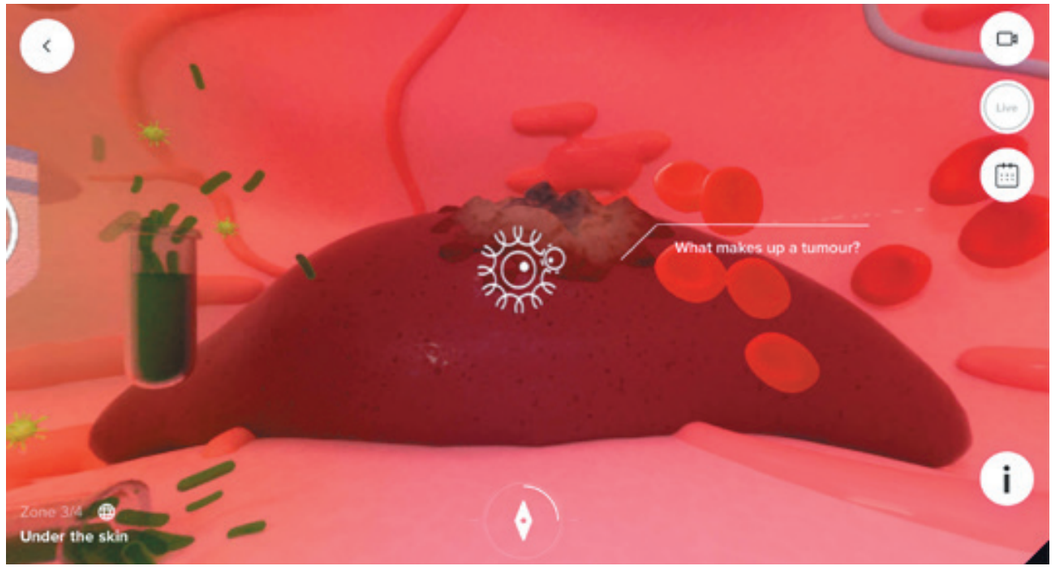
An important part of the event is therefore engaging with schools. Members of our team interacted with students online, answering their questions and stimulating instructive discussions about research and career choices.

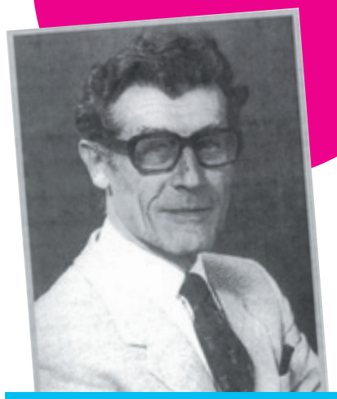
The team also had the opportunity to engage children in science with family friendly activities. PhD student Charlotte Bell repurposed a mock-up of one of her original activities – inspired by the well-known children's game KerPlunk – into an ingenious online craft workshop. Here 30 children and their parents had fun building a 3D model of a tumour from cereal boxes. Making slits in the sides of the boxes, they inserted different kinds of 'cells' cut out from card, then dropped down paper balls that represented immune cells. The aim of the game was to insert the right combination of cells to enable the immune cells to enter the tumour and attack the tumour cells. This workshop was a great success and a clear demonstration of why we need more research to improve the efficacy of immunotherapies to help the body's own immune cells defeat cancer.

Links to all these activities and more – including instructions for making your own cardboard tumour – can be found by scanning the QR code (produced with help from our web developer Chris McCauley). Here you can also find links to our content hosted at the Royal Society, which features a virtual world in which you can explore all the other exhibits.

SCAN ME

Over 15,000 users accessed our content during the main period of the event, far more than could normally attend in person. While the team missed the hands-on exhibition space, it is great to know that participation has been widened through this move online.





Laszlo Lajtha
(1920 – 1995)

A celebration of the life of Professor Laszlo Lajtha

On 8 October, we celebrated the life and scientific contributions of Professor Laszlo Lajtha, who was the first full-time director (1962-83) of the research laboratories that later became the Paterson Institute, and now the Cancer Research UK Manchester Institute. In fact, it was Laszlo who named the building after Ralston and Edith Paterson, who had started research on this site into radiation and its use for treating cancer in the 1930s.

Laszlo Lajtha was born in Hungary and moved to England in 1947. He would have celebrated his 100th birthday last year and this event was originally planned to coincide with the centenary of his birth in May 2020. The celebration of the fascinating life of Laszlo was arranged in collaboration with the Consul General of Hungary in Manchester.

Laszlo was the son of one of Hungary's most distinguished musicians, who bore the same name. He completed his medical degree in Budapest in 1942, after which he began a research career in the use of radioisotopes in medical research.

Moving to England on a British Council scholarship, he first worked at the Radcliffe Hospital in Oxford, before setting up his own research team at the Churchill Hospital, Oxford. Recognised for his research prowess in experimental haematology, he was invited in 1962 to become the first Director of Research at the Christie Hospital.

This event also marked the first time members of the Institute got together to talk about science since before the pandemic, so it was an especially poignant occasion. Happily, we were able to invite a limited number of guests to attend in person, while also live streaming the event.

The aim of the day was to bring together Mancunian and Hungarian research through the celebration of Professor Lajtha, who was a pioneer in the research of cell proliferation, stem cell biology and haematology. We heard about current research in that field being carried out by our researchers here in Manchester and those in Hungary.

Blood cancer research is a key area of interest at the CRUK Manchester Institute, and we heard from three of our researchers on the subject – Tim Somervaille, Kiran Batta and Dan Wiseman – and from two Hungarian guest speakers in the field, Dr István Peták of Encompass Medicine and Dr Csaba Bödör from Semmelweis University, Budapest.

We were also delighted to have join us eminent guest speaker Dr Péter Nagy, Scientific Director at the National Institute of Oncology, Hungary whose scientific interest lies within the reprograming of metabolic and cellular signalling pathways in cancer. He opened the scientific talks with an overview of his own research on redox regulation of protein functions, antioxidant defence mechanisms and alterations of transulfuration pathways in breast cancer.

Tim Somervaille, from the Leukemia Biology group, shared how his team identified FOXC1 as a major factor in acute myeloid leukaemia, trapping cells in a less-differentiated state. Next, Dan Wiseman and Kiran Batta, both Oglesby Research Fellows, took us from bench to bedside discussing research from across Manchester into chronic myelomonocytic leukaemia (CMML), a rare type of blood cancer.

Livestreaming from Hungary, István Peták joined us virtually to describe an exciting computational method that can select the most effective targeted therapies for cancer patients based on the individual molecular profile of their tumour. Continuing the blood cancer theme Csaba Bödör

Commemorative plaque

Consul General of Hungary and guests unveil commemorative plaque in honour of Laszlo Lajtha

Agnes Grallert

– an expert in molecular pathogenesis of haematological malignancies – travelled from Hungary to talk about B-cell lymphomas and novel biomarkers.

The day felt like a real-life scientific event as we enjoyed a small poster event during lunch, which showcased the research of some of our early career researchers on leukaemia and stem cell biology. We would like to thank Ewan Selkirk, Liam Clayfield, Joanna Storer and Kristian Gurashi for their contributions.

In the afternoon, we heard about the work of one of our most successful Associate Scientists Agnes Grallert, a researcher from Hungary who was based in the laboratory of Iain Hagan and who sadly died last year. Iain shared some of the remarkable body of work she left behind as her legacy.

We were thrilled that one of our former colleagues, Professor Terry Allen, was able to join us along with another colleague Dr Nydia Testa, who both knew Laszlo well. Terry was recruited by Laszlo in 1970 and worked closely with him for several years. He is a well-known expert in electron microscopy and has amassed an impressive library of publications.

Terry shared his fond memories of the formidable Director and gave us an interesting, warm and often entertaining

Going back to 1977 with Terry Allen and colleagues

Terry Allen entertains with his stories about Laszlo Lajtha

account of life working alongside Laszlo – a nice personal addition to the programme.

Moving to the present day, we heard about how we lost the Paterson Building to fire and the impact that has had on us all. Chief Operating Officer, Caroline Wilkinson and Chief Laboratory Officer, Stuart Pepper also talked about the amazing resilience displayed by our scientists and operational staff throughout the long period of recovery.

Looking to the future, Prof Nic Jones – former Institute Director and now Director of Strategic Initiatives at the University of Manchester – shared the vision, plans and development to date of the exciting new building that is being erected on the site of the old Paterson Building. Caroline Dive also talked about the exciting new lab space – a whole floor – for the Cancer Biomarker Centre.

Finally, the day closed with the unveiling of a commemorative plaque in honour of Prof Laszlo Lajtha, which will eventually be displayed in the new building. There was also an opportunity to get together and sample some delicious Hungarian wine, kindly provided by the Consul General of Hungary. The small reception was enjoyed by all and reminded us how important it is to share our science and collaborate. Hearing about the remarkable life of our former Director brought us together and has inspired us to continue his legacy of cancer research in Manchester.

Institute postdoc presents at Hot Topic Meeting: Small Cell Lung Cancer

By Francesca Chemi, Postdoctoral Fellow, Cancer Biomarker Centre

It was my great honour to be invited to participate as a Speaker for the *IASLC 2021 Hot Topic: Small Cell Lung Cancer Meeting.*

It was a worldwide event, usually held in person every two years, but because of the current pandemic, the 2021 edition took place virtually from October 29-30, 2021. The focus of the meeting is to provide an update on recent progress in small cell lung cancer research, including both basic research and highlights of ongoing clinical translation.

I was asked to give a presentation within the early career session which involved other Postdocs and PhD students from several different countries. I presented the results of my project which focused on the analysis of DNA methylation in both pre-clinical and circulating cell-free DNA samples and its utility as a biomarker for detection and subtyping of small cell lung cancer. A live QA session followed with all the speakers invited for the early career session.

Francesca presents at the IASLC 2021 Hot Topic: Small Cell Lung Cancer Meeting

STAy update

The STAy group of early career researchers have been working hard to help people across the Institute stay connected throughout lockdown and during the ongoing restrictions of COVID19. We have taken advantage of having more people back on site to create opportunities for some face-to-face contact.

Once small groups could meet outdoors, we organised a treasure hunt around the Radnor Mere at Alderley Park. Teams had to solve clues to find a series of words which – when inputted into the What3Words app – gave the locations of flags hidden around the lake. Finding all the flags revealed the final answers, with a small prize for the winning team.

We have been hosting fortnightly 'STAy for Lunch' sessions, where anyone from the Institute can bring their packed lunch to the Radnor Atrium at AP (a rather cavernous open-plan space, perfect for social distancing!) to meet other Institute members, and we plan to run some similar events at the OCRB.

To make people who have joined the Institute during lockdown feel welcome and part of our community, we have hosted two small evening meetups for our new PhD students who have just arrived in Manchester, and STAy committee members have enjoyed catching up with other members in person for the first time.

The STAy team also helped run a virtual quiz night at the Colloquium, following the success of our 'ColloQuizium' at last year's virtual event. This year the competition included some added extras thanks to the GatherTown platform, such as a race to find objects hidden around the virtual conference venue.

Our committee continues to meet online via Teams to plan events and support the ECR community. Membership of the committee is open to anyone, and we are always glad to receive suggestions for events or training.

CGI render of the reception and entrance.
Picture credit: Arcadis

Paterson Building Redevelopment updates

In December 2022, construction will be completed on our new £150m world-leading facility.

Work is continuing at pace and we are on track to be operational by spring 2023.

This new comprehensive facility will be twice the size of the Paterson building that it replaces. Whilst the fire back in 2017 was devastating and disrupted much of our research, it led to these ambitious plans to create a brand new, globally leading cancer research facility here in Manchester. As you can see in these pages, our ambitions are now finally being visualised.

Bringing together on one site the largest concentration of researchers, clinicians and allied healthcare professionals in Europe will foster more powerful collaboration between these specialists and accelerate progress for cancer patients in Manchester and across the world.

In November, we celebrated an impressive construction milestone – the building has now reached its highest point. Director Caroline Dive and Nic Jones, Director of Strategic Initiatives at the Manchester Cancer Research Centre, marked the occasion on top of the building in a 'topping out' ceremony.

Caroline and Nic celebrate topping out on top of the new building

Construction has continued to complete the first eight floors of the building and supports have been laid for the 9th floor. The concrete frame of the building is almost finished – the aim is to complete this phase by early December. Work on the internal walls, electrical and heating systems from the basement to third floor continues and the walls on levels 4 to 6 will be completed in the coming months.

In further building updates, anyone walking or cycling past the building will have noticed the new external glass panels being installed. Over the next few months, the installation of these specially designed glass panels and rainscreens will be completed, transforming the look of the building.

Installation of glass panels transforms the look of the building

"It was awful, but our institute is far more than bricks and mortar. We pulled together. Our staff were incredibly resilient and, miraculously, no patient samples were lost."

Professor Caroline Dive
CRUK Manchester Institute Director

"This building is a great testimony to the way that all of our partners see the future of cancer research in Manchester. They are all fully committed to this development and what it means for improving patient outcomes."

"It's the people that will be located within this building that will fulfil its ambition and bring this vision to life to improve cancer outcomes for all and re-write the future of cancer."

Professor Nic Jones
Director of Strategic Initiatives

Re-write the future of cancer

In December 2019, Cancer Research UK launched the 'Re-write Cancer' campaign to deliver the final £20m needed to build our new cancer research facility in Manchester. The campaign was kick-started with the first donation of an incredible £1m from the Garfield Weston Foundation.

Over the past two years, donations are still being received from a wide range of generous supporters, including the Warburton family. So far – by the end of November – an amazing 339 donors have given to Re-write Cancer, Manchester raising a further £29,220.

To mark the topping out milestone of the building, Caroline Dive was invited to join a virtual ceremony with major donors for the project alongside Rob Bristow (MCRC Director), Michelle Mitchell (CEO of CRUK), Nancy Rothwell (President of UoM) and Roger Spencer (Chief Executive, Christie). Here they showed this film featuring Nic Jones and Caroline, thanking our donors for their support.

We are incredibly grateful for the continuing generosity of the public that will enable our new research facility will be filled with state-of-the-art equipment, attracting and retaining the best talent from around the world, which will help deliver solutions to cancer more quickly.

Through innovative advances in prevention, early detection and treatment, this world-leading cancer campus will change – and even save – people's lives.

Reaching the £20m target is a priority for all three partners - CRUK, The Christie and The University of Manchester - but currently the University is leading the final fundraising drive.

We urgently need to raise the final funds to complete the building, and get it ready for our scientists to move in.

Scan the QR code to make a donation

SCAN ME

Staff news

Belen Conti Vyas, Executive Assistant to the Senior Management Team and her husband Cian Vyas welcomed their first child Thiago Conti Vyas on 25th October 2021. He weighed 3.48kg / 7lb 10oz and mother and baby are both very well.

Cancer Biomarker Centre Travelling Postdoc wins prize

Congratulations to Kate Bloch, a Cancer Biomarker Centre Travelling Postdoc, working in Avrum Spira and Marc Lenburg's labs in Boston, who won first prize for a Clinical Poster Presentation at the recent Boston University Department of Medicine Evans Days.

The event showcases the research activity of the whole of Boston University Medicine Department. The title of Kate's poster was "Predicting Malignancy in Indeterminate Pulmonary Nodules Using Models Integrating Quantitative CT Imaging and Nasal Gene Expression".

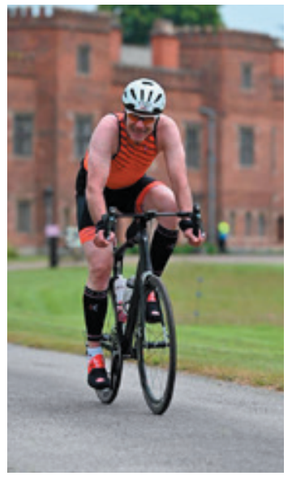


Image credit: www.outlawtriathlon.com

Richard Marais, former Institute Director and Senior Group Leader of the Molecular Oncology group has been a fantastic fundraiser for CRUK in the past with his epic cycle rides.

This year he undertook the challenge of a 70.3 distance triathlon, which comprises a 1.2 mile swim, a 56 mile bike ride followed by a half marathon (13.1 miles). He completed the race on 20th June 2021 in 6h14m and raised over £400 for Cancer Research UK.

Francesca Chemi, a Postdoctoral Scientist in the Cancer Biomarker Centre and Eduardo Bonavita a Postdoctoral Scientist in the Cancer Inflammation and Immunity group celebrated their wedding on 19th June 2021 in Italy. The location was the beautiful small town of Scalea, Francesca's hometown in the Calabria region of southern Italy.

Georges Lacaud, Senior Group Leader of the Stem Cell Biology group shared this great photo of his dog Teddy enjoying a walk in the sunnier months.

CORONET: COVID-19 Risk in Oncology Evaluation Tool

CORONET – a COVID-19 Risk in Oncology Evaluation Tool – was highlighted in NIHR Clinical Research Network Greater Manchester's Evening of Excellence 2021, in the category of 'Trailblazers in COVID-19 research response' which recognises the significant and important impact in response to the pandemic made by an individual or team.

The analysis for the project is performed by CRUK MI Cancer Biomarker Centre Bioinformatics and Biostatistics team member Cong Zhou and digital Experimental Cancer Medicine Team members Andre Freitas and Oskar Wysocki. The clinical side of the project is led by Dr Rebecca Lee and Dr Anne Armstrong from The Christie NHS Foundation Trust. The IT side is led by Louise Lever in Research IT at The University of Manchester.

The award ceremony was held online on 18th November 2021. You can catch up on the other winners of the night by using the hashtag #GMEOE on Twitter.

CORONET

Rose Storey

Rose is a scientific officer in the Transgenic Breeding Team within the Biomedical Resource Unit here at the CRUK Manchester Institute. The BRU provides support to all scientists who conduct laboratory animal work as part of their research at the Institute.

Rose has worked with us for over ten years in the Transgenic Breeding Team, which is responsible for breeding genetically modified mice for our researchers as required. They provide a high standard of care for a variety of immune compromised and immune competent lines.

Rose is part of a team of professional animal technicians that provide day-to-day care for several breeding lines of mice. She offers expert advice in the areas of transgenic mouse breeding and maintenance and works closely with our researchers to support their individual research requirements.

You can find out more about how mice are used in cancer research at the 'Cancer Revolution: Science, Innovation and Hope' exhibition, currently at the Science and Industry Museum, Manchester until March 2022.

1. **What is your favourite part of the UK?**
The North East, where my family are from. The beach at South Shields is my happy place.

2. **What was your best ever holiday and why?**
The ice hotel in Swedish Lapland. A truly amazing experience with snowmobiles and Huskies and the spectacle of the Northern lights.

3. **Which website do you always check, and why?**
Ryanair, I'm desperate to see my sister in France. I have not seen her since the start of the pandemic, nearly 2 years ago now.

4. **What is your favourite film?**
Pulp Fiction.

5. **What is your favourite band/singer?**
That's tricky, I love music. I'd have to say Bob Marley.

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

7. **What is the most important lesson that you have learnt from life?**
Life's not fair! (Thank you to the late Tom McAlpine OBE for this. The founder of MoodSwings mental health charity and to whom I shall be forever grateful).

8. **Name three things you would take with you to a desert island?**
Eyebrow tweezer (my friends over 50 will appreciate this one 😊), sunscreen and fizzy water.

9. **What is your greatest fear?**
Losing my memory.

10. **How would you like to be remembered?**
As a generation X woman. It's been one incredible ride so far.

11. **If you could change one thing in your past what would it be?**
Not to have dropped out of university – I disappointed my parents.

12. **What is your signature dish to cook?**
Lemon cream pie, 3 ingredients whipped up on a biscuit base, ta dah! I'm no Nigella.

13. **You've just won the lottery and have £5 million pounds to spend. What do you buy first?**
1st class tickets to New York at Christmas. We got upgraded to business class on a trip there once, it was marvellous.

14. **What is your idea of perfect happiness?**
Time with my family somewhere snowy, drinking hot Columbian coffee.

15. **What keeps you awake at night?**
Kingston, my very vocal and mardy old cat – but he's allowed.

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