Welcome to the first of the MRC CU newsletters in 2019. The first quarter of the year has been a busy one already, full of fulfilling Public Engagement endeavours such as at the Science Festival and a rejuvenation of the Hutch Graduate and Post-doc societies. As always, there is news of all the exciting research, scientific and other related achievements of our students and staff.

To keep up to date with our news, till the next edition, please visit our Website, Facebook and Twitter pages.

With Best Wishes,

Professor Ashok Venkitaraman.

**Director, MRC Cancer Unit**

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**The spring tides at the Hutch**

Of a time to take back control and future declarations …

At a time when these words have come to epitomise confusion and chaos, a young bunch of graduate students and Post-docs at the Hutch have been doing just that - and brilliantly so - taking control of how they would engage with their communities and beyond, and making a fantastic declaration of well thought out plans for events and activities throughout the year ahead!

For the Graduates this has meant both the opportunity to relax after a hard day’s work and a way to meet colleagues and new starters from the institute. Their events have included themed happy hours such as the Valentine’s Day and Easter Happy hours, (the latter even promises a building wide Easter egg hunt!) as well as more creative ventures over a drink and a nibble, no doubt creating an avenue of stress relief for many, but also serving as an inspiration for their upcoming ‘The Art of Science’ competition. Last but not least, jointly with the Post-doc society they will be brightening up our summers with the Hutch Barbecue! Future-plans include a grad symposium- so let’s watch this space.
The Post-doc society, representing a more diverse tribe of researchers in terms of career stages and needs, has chosen to draw the Units attention to talks/workshops and events organised and advertised by wider Post-doc societies such as the PdOC/OPdA/EPOC alongside organising their own hugely popular Bring-a-Dish parties, Pizza Nights and Happy Hours, coupled to interesting talks.

Going Nuclear!

The ‘Hutch Hoppers’ (Archie, Jordi, Francois, Oana, Luisa P., Alberto, David S. and Steve) are gearing up for the gruelling Nuclear Races scheduled for the 19 May. The event is a 12 km obstacle race to the accompaniment of lots of mud, live music and entertainment. Inspired to “Be Active” and to “Give to Others”, two of the five recommended steps to improving mental wellbeing, these brave-heart amateurs are preparing in earnest and having lots of fun along the way. All of this of course comes with fundraising for The Teenage Cancer Trust (a charity that facilitates care for young people with cancer) and The Moor House School & College (provides specialist education for children and young people with severe and complex speech and language impairments).

To sponsor the Hutch Hoppers, please visit: https://www.sponsorme.co.uk/stephenjones/hutch-hoppers-nuclear-race-rush-event.aspx

Recent arrivals & departures

We welcome Alvin Ng (Bioinformatician), Laura Tronci, Apostolos Pappas (Research Associate), Lorea Valcarcel, Nikkitha Umesh, Ganesh Kadamur Bhavani, Andreas Hadjinicolau, Lars Anderson, Chetan Poudel (Visiting Researcher), Suraj Pavadga (MPhil Student), Conor Flint (Apprentice technician) and Adam Austwick (Finance Administrator, maternity cover). We would like to wish Naseer Pasha, Daniel Loureda, Alicja Malinowska, Wladylaw Januszewicz, Sabarinath Peruvemba Subramanian, Sofia Henriques da Costa, Ben Bowers, Anchal Chandra, Alex Frankell, Nazhif Zaini and Saiful Syafuddin all the best in their future careers.
Cambridge Science Festival 2019

24 March once again found team Hutch galvanised into action, at the Cambridge Science Festival. Hosted at the CAST building on campus and featuring most departments and local Pharma/Biotech companies under the same roof, the day provided a fabulous opportunity to experience a range of research themes and ultimately recorded a foot-fall of more than 3000 people. Sharing the ‘cancer corner’ with the CRUK CI - CCC team the Hutch activities, diverse and each brilliant in its own way, were as always themed around the importance of ‘Early’ in Cancer.

We had a record number of volunteers this year, several new activities and refreshed ever-greens, back by popular demand. So the ducks with QR codes and Raspberry Pis tagged onto them were out on display, accompanied by the lego Robots that stall on mutant DNA strands to the tune of fruit pianos that are jarry when they encounter the wrong base pair. Then there were the railway tracks of metabolic pathways and the normal/mutant proteins, aka remote control cars, whizzing down cancer or normal signalling tracks, next door to the cancer invasion maze. Ever-youthful ‘Norman’ with his gurgling guts captivated audiences as he swallowed the pill-on-string -to reveal the potential power of simple detection devices coupled to powerful biomarker research in saving lives. Last but not the least we had nifty demos of separation techniques and fishing experiments ranging from western blots to ChIP seq and mass-spec. This year 3 MRC CU group-leaders, Ashok, Alessandro and Shamith all gave talks at the Festival – all to packed audiences. Between them they covered the wide
swathe of topics such as, what is determined by our genes and what isn’t in Cancer, to the decision making power of cell and what goes awry in Cancer, to how AI and Big Data have an increasingly powerful role in helping us detect and fix things when they go wrong.

And at the end, depending on your audience’s age, when the smiley stickers, yellow stickies with comments, and thank you emails trickled in, months of hard work and meticulous planning were all well worth it. Here’s looking forward to CSF 2020!

MRC Cancer Unit: Research successes

New ways of looking at Kidney Cancers

Clear cell renal cell carcinoma (ccRCC), the most common subtype of kidney cancer, is characterised by biallelic inactivation of von Hippel Lindau tumour suppressor gene (VHL), mTORC1 signalling pathway activation and accumulation of cytoplasmic lipid. Inhibitors against receptor tyrosine kinases (e.g. VEGFR and PDGFR) and the mTORC1 complex are the current clinically approved therapies for ccRCC. Nevertheless, the overall objective response rates especially for advanced ccRCC remain low, with 5-year survival at less than 10%. A recent study by Syafruddin et al. from the Vanharanta group, published in Nature Communications, elucidates previously uncharacterised molecular mechanisms underlying ccRCC pathogenesis. The new results show that a cellular signalling network centred around Kruppel-like factor 6 (KLF6), a super enhancer-associated zinc finger transcription factor, promotes ccRCC growth by supporting lipid metabolism and mTORC1 activity. KLF6 activates mTORC1 through the expression of the secreted factor PDGFB, a ligand for the PDGFR receptor. Thus, these results reveal a molecular link between two approved kidney cancer therapeutic targets, PDGFR and mTORC1. The new results also highlight the links between super enhancer-driven transcriptional networks and the activity of essential metabolic pathways. Detailed understanding of such links could pave the way for novel therapeutic intervention strategies.

In quest of new genomic biomarkers for the clinic in Esophageal Cancer

Only around 12% of patients survive oesophageal cancer for 10 years or more. This is partly due to late diagnosis, as symptoms often do not present until the cancer is advanced, and partly due to limited treatment options. Oesophageal Adenocarcinoma (EAC) is the main subtype of oesophageal cancer in the UK and is on the rise in western countries – mainly because of lifestyle factors.
A recent study by Frankell et al. from the Fitzgerald group, published in Nature Genetics, scans 551 EAC samples alongside matched RNA sequencing data from 116 samples of this cohort to provide an exhaustive catalogue of mutations and copy number alterations that are selected for in EAC and could have clinically relevant impact on the prognosis of the disease.

Importantly, the study reveals driver mutations for EAC in 99% of patients and that more than half of the mutations (mainly related to Receptor Tyrosine kinases and or Cell Cycle proteins) could be targeted by drugs currently in trials for other cancer types, such as the CDK4/6 inhibitors already approved for breast cancer. This research could help stratify oesophageal cancer patients to give them more personalised therapies. This in turn could provide options not currently available to patients beyond standard chemotherapy, radiotherapy or surgery. This also means phase II/III clinical trials to treat oesophageal cancer could be feasible in one to two years.

Interestingly, women were found to have more KRAS mutations than men. These mutations are often seen in other cancer types but are rarely found in oesophageal cancer. This could indicate a different sub-type of the disease in women and suggest they might have a different prognosis or need alternative treatment.

Getting started with computational biology in school curricula

As part of his efforts in spreading awareness and embedding training about the use of computational modelling in research, Dr Ben Hall working with the OCR examination board has been involved in the development of material and distributing a set of worksheets on cancer and computational biology to schools for testing. These activities, developed jointly between Ben and the A-level examiners from the board, show how network modelling can be used to understand drug specificity for different cancers. As part of the exercise, they have released a new blog post introducing the activity and some of the research behind the activity. Future steps will include formal incorporation of these worksheets into OCR’s national A level Biology curriculum.
Other News

The Bury-Padova-Eton story

A reason why the CU has been a steadfast champion of Work Experience placements is the sheer opportunity to spark young minds. Harry Dunne, who won a state scholarship to go to Eton (from a comprehensive school in Bury St Edmunds) was a shy lad who came for a little stint of work experience in the Frezza laboratory. He was truly inspired by the research and the Unit’s ambience and decided to follow up, not just by applying to Cambridge (from where he now has a conditional offer to study medicine) but by inviting Christian to the famous Eton College to speak to other year 13s about cancer and metabolism. Christian admits to being (slightly) overwhelmed not just by the grandiose portals of what is after all just a school, but by the grilling and depth of questions from these budding scientists. Ranging from why naked mole rats don’t get cancer, to the Peto’s paradox, he was hostage for half a day to a captivated audience hungry to learn more about cancer, metabolism and research.

Awards & Conferences

Dr Saif Ahmad, former student and current associate of the Venkitaraman lab, was runner-up at a Post Doc Business Plan Competition where he won £10K of investment from Cambridge Enterprise towards his business idea for a medical device to detect neutropenia in chemotherapy recipients. Saif feels that this was a great opportunity to learn about how to pitch an idea, write a business plan and to acquire useful transferable skills. Well done Saif!

Dr Christian Frezza and colleagues from the Cambridge Metabolomics Network organised a 2 day meeting in January that focussed on “Advances on the interface of epigenetics and metabolism”. Bridging two distinct disciplines, the meeting featured eminent scientists like Paolo Sassone-Corsi, provided a platform for early career researchers and highlighted innovation linked careers options as an alternative to academia.

Upcoming events

MRC CU Open Day – 19 June. As part of the annual MRC Festival of Medical Research, the Unit will once again host 60 high school students for its Open Day, including a hands-on tour of the CU labs.

Dr Sakari Vanharanta from the Unit is one of the lead organisers of an international PhD course on metastasis biology in Basel (11-13 September). More details and registration links can be found on: https://www.baselbc.org/events/frontiers-in-metastasis-biology-2019

Drs Shamith Samarajiwa, Jacqui Shields and Christian Frezza from the MRC CU and Dr Charlie Massie (from the ED programme at the Hutch) will all be speaking at the ‘Pint of Science’ meetings in Cambridge between 20-22 May 2019.
Our scientists in the limelight

In April 2019 Professor Ashok Venkitaraman was awarded a Distinguished Visiting Professorship in the Department of Medicine at the National University of Singapore (NUS). Ashok also delivered a plenary talk at the 25th anniversary of the National Medical Research Council of Singapore on “Shaping the future of cancer research from the end of the beginning”.

Dr Serena Nik Zainal, along with Dr Nitzan Rosenfeld and Dr Sam Janes, was part of the scientific panel that was invited to interact with donors and benefactors at an event organised by the CRUK on 14 March. The event, attended by more than 200 people, called ‘Behind-The-Scenes, 2019’ was designed to give donors a flavour of the science that they were helping to fund.
Recent publications


