We had joy, we had fun…
Looking back at a summer of many visitors

It wasn’t just the beast from the east and a string of glorious bright days that visited us this summer. From celebrities to ice-cream, we had it all!

Professor Stephen Toope, the new Vice Chancellor of the University, as part of his tour of the Biomedical Campus, visited the Unit on the 29th May and had discussions with the Director and senior group leaders about the Cancer Unit’s mission, its science, and its direction of travel.

Speaking of travel and the fortuitous friendships it kindles, Dr Christian Frezza had a chance encounter with the snooker superstar Ronnie O’Sullivan on a plane to China. Over a pint, in mid-air, Ronnie was curious to find out all about metabolomics and cancer. True to his word though, when on firmer ground, he arranged to visit the Cancer Unit on the 31st May. It was a privilege to host the legendary sportsman, who mingled with staff and students, peered over microscopes and listened attentively to all the talks that the Frezza group had laid out for him. A great example of how to communicate our science, its societal relevance and impact to the world outside of academia.
May was followed by some glorious sunny days when it was time to celebrate the ‘chiller anniversary’ - to commemorate a year of the rooftop chillers (the workhorses behind the building’s air-conditioning) not repeating their catastrophic breakdown the year before, bang in the middle of the hottest week of that year.

A welcome diversion to the humdrum of daily Hutch business came from the jingle of the ice-cream van, that the Centre Manager had arranged for that afternoon in June - soon we had onlookers and visitors from nearby buildings along with all the happy faces of our own.

As summer paves way to autumn and the start of a new term, the chillers trudge on, sometimes perilously close to another meltdown, come sunny days, even as we patiently wait for our turn on the University estates repair list. Perhaps a quiet testimonial to the unfailing infrastructure and backend service that the building provides to the research community it houses. Long may it last!

The newest additions to the CU family!

In August, Dr Serena Nik-Zainal joined the Cancer Unit as a faculty member, an affiliation to be held in conjunction with her current appointment at the Department of Medical Genetics (ADMG). A very warm welcome to Serena, Andrea Degasperi, Jan Czarmecki, Scott Shooter, Xueqing Zou, Tauanne Dias Amarante, Scott Nanda, Yasin Memari and Helen Davies from the Nik-Zainal Group! Hope you enjoy your time at the Hutch.

Other recent arrivals & departures

We welcome Jianfeng Ge, Tanmoy Mukherjee (Research Associates) and Aisling Redmond (Fitzgerald Group Research Manager). We would like to wish Shona MacRae, Sine MacDonald, Gianmarco Contino, Callum Campbell, Garrett Beeghly, Melissa van-Velthoven, Clément Bodineau, and all our summer and work experience students the very best in their future careers.
The MRC Festival of Research, 2018

For a fortnight in June, all MRC organisations across the country, indeed even in other countries across continents, gear up to host a range of events that highlight the MRC’s mission in medical research and commitment to public engagement. As part of this, the ever popular Schools Open Day was back at the CU. On the 19th June, sixth form students from local schools were given a hands-on tour of the CU labs, followed by a careers session with scientists at various stages of their research journeys.

In the labs, the young people scraped petri dishes and poured over cells under microscopes, learnt about assay development, not to mention the importance of accurate pipetting, discovered what computational modelling and metabolism had to do with cancer, and marvelled at the exquisite regulation of the cell cycle, what goes wrong with it in cancer and how scientists are targeting these Achilles heels. Their questions were engaging, their feedback later gratifying! A big thank you to all staff and students from the CU who volunteered to make this event possible. More photos of the day are on our Facebook page.

For Festival week, we also chose to highlight our work, its needs and its impacts to our local MP, Heidi Allen. Over an engaging conversation with the MRC CU’s group leaders and PhD students, the MP was given a whistle-stop tour of our science, a feel (quite literally!) of what it is to develop a tool through years of research that potentially improve patient outcome and a chance to hear about experiences and views from staff and students relating to recent developments in British politics and its potential impact on collaborative research.
Not all schools have the culture or resources to engage at events such as ours, much that we would have liked to provide the same experience to all students/children. With this in mind, our staff and students take every opportunity, despite their busy schedules, to fit in public engagement with schools. Professor Ashok Venkitaraman gave one such talk in June at the Castle Manor Academy in Haverhill, after which a clearly moved head teacher thanked Ashok for coming along to talk to his students to inspire them to think that research was well within their grasp and that everything was possible!

MRC Cancer Unit: Research successes

Cellular identity theft leads to cancer metastasis

The spread of cancers to distant organs, or metastasis, is responsible for the majority of cancer-related deaths. How cancers develop the capability to spread has remained mostly unclear, however. New research led by Dr. Sakari Vanharanta at the Unit, has now identified molecular mechanisms that allow cancer cells to acquire characteristics from other cell types, such as white blood cells, in order to spread and form metastasis.

Each cell in our body carries the same genes. Yet, due to differences in the way cells read their DNA, and consequently express their genes, tissues behave differently. Gene expression is orchestrated by tissue-specific networks of gene regulatory elements called transcriptional enhancers, i.e. DNA sequences that control when and where specific genes should be expressed. Enhancers are therefore critical determinants of cellular identity. The new work, published in Cancer Discovery, sheds light on how cancer cells read DNA in unique ways, leading to vastly different behaviours, such as variability in metastatic potential. The work demonstrates how some cancer cells are able to co-opt tissue-specific enhancers from unrelated cell types in order to activate genes that support metastatic progression. Through inappropriate enhancer activation, cancer cells thus ‘steal’ features from normal cells, consequently facilitating metastatic spread.

The new observations provide fundamental insight into a long-standing biological and clinical problem of metastasis, and they suggest that therapeutic approaches that would limit the capability of cancer cells to aberrantly activate enhancers could inhibit metastasis in patients.

The study entitled ‘NF-κB–Dependent Lymphoid Enhancer Co-option Promotes Renal Carcinoma Metastasis’ by Rodrigues et al. has been published in Cancer Discovery in June 2018.

The article has also been covered as a feature by New Scientist, referenced by the Daily Mail and highlighted on the MRC website.
Establishing organoid cultures as a new tool to study evolution and precision therapeutics for a deadly solid tumour with very poor prognosis

Models of cancer are needed to test drugs and understand how they develop. Few models exist for cancer of the gullet (oesophagus). This month Nature Communications Editors’ Highlight on Stem cell and Disease as well as Genomes and Epigenomes has selected a collaborative study between the Sanger Institute (Mathew Garnet) and the MRC Cancer Unit (Rebecca Fitzgerald), which established a panel of organoid cultures derived from Oesophageal Adenocarcinoma. These 3D cultures which were established from patients undergoing extensive molecular characterisation as part of the International Cancer Genome Consortium. The authors were able to show that these organoids faithfully recapitulated the morphological, functional and genetic features of tumours and the cultures yielded interesting data on tumour evolution and susceptibility to chemotherapy and molecularly targeted agents. This provides the community with a powerful translational tool for this very poor prognosis disease.

The study entitled ‘Organoid cultures recapitulate esophageal adenocarcinoma heterogeneity providing a model for clonality studies and precision therapeutics’ by Li et al. was published in Nature Communications in July 2018.

Novel Uses of Computational Modelling to understand the role of Membrane Transport in Cancer

Membrane transporters are proteins used to maintain the concentration gradients of various chemicals between the exterior and interior of a cell. The gradients of these chemicals are then generally used for processes like maintaining cell size (osmotic regulation), and are also signalling molecules for processes like cell migration and division.

In their new publication in Nature Communications, researchers from Dr Ben Hall’s group at the MRC Cancer Unit show for the first time that alterations in the expression of these membrane transporters consistently occurs in all cancers. Going further, the researchers were able to construct a computational model of the key chemical gradients and transporters within a cell, and show precisely how changes in the expression of them can alter cancer cell behaviour. The research is a start at understanding how these proteins can be used as potential markers or drug targets in the future. The study entitled ‘Exploring the role of stromal osmoregulation in cancer and disease using executable modelling’ by Shorthouse et al. was published in Nature Communications in August 2018.
Conferences from the CU

In June Dr Christian Frezza and his team hosted the first workshop on Metabolomics sponsored by the “TRANSMIT” PhD programme funded by the Marie Curie Innovative Training Network. The event, attended by several students, included presentation on the principles of metabolomics, hands-on experience of liquid chromatography and mass-spectrometry as well as analyses of small molecule metabolites. Dr Frezza was also a lead organiser of the 4th Abcam “Cancer and Metabolism” conference (25-27 June). The congenial meeting had a great line-up of speakers who dwelt on the impact of metabolic factors on tumour growth and metastasis, and other hot topics in the field, such as the analysis of metabolism in vivo and at subcellular level. Saiful Effendi Syafruddin from the CU was one of the poster prize winners at the meeting. Well done Fendi!

Dr Ben Hall and colleagues organised the first “Discrete models and formal verification in biology” meeting in August. Attended by 40 academic and industrial scientists from 8 countries the conference created a great platform for the specialist community to come together to foster new collaborations and discuss how to highlight developments in the field.

Upcoming events
Hutchison MRC Annual Retreat – 30 November 2018.
Our scientists in the limelight

**Professor Ashok Venkitaraman** received his Basser Global Prize at an award ceremony held at UPenn, Philadelphia in May. Congratulations to Ashok!

**Dr Sakari Vanharanta** spoke at a recent event to celebrate confluence across various disciplines and cultures. The public event themed “Arts Meet Science” held at the quirky Beaconsfield Gallery, Vauxhall, London (with trains crisscrossing overhead) was organised by the Finnish Institute. In addition to Sakari’s talk ‘Open Questions in Cancer Biology’ the event featured The Trace, a multidisciplinary performance developed by Hannaleena Heiska, a visual artist and also featured Minna Tervamäki, a dancer/choreographer and the prima ballerina at the Finnish National Ballet.
Recent publications


