A time to give something back

A chronicle of Public Engagements over the summer…

The MRC CU, and indeed the Hutch community as a whole, has always strongly believed in a duty of collegiate support for other organisations, big and small, that help fight cancer and other disabling conditions, especially in young people. Spurred on by this mantra, a bunch of hardcore fitness enthusiasts embarked on what at the start frankly seemed a little crazy. The Hutch Hoppers (that’s what they christened themselves) comprising of Jordi, Alberto, David, Luisa, Oana, Francois, and Steve trained tirelessly over months for The Nuclear Races - an obstacle course spread across 90 hurdles, 12 km of running and lots of mud! Drawing on support from the generous Hutch community and helped along by yet another gourmet Cake Sale at the end of it all, they managed to raise more than £1,000 pounds for the Teenage Cancer Trust and the MoorHouse School – both wonderful organisations that support young adults (coping with cancer and speech and language difficulties, respectively). Hats off to the Hoppers and for sure this has ushered in a new wave of enthusiasm for running, fitness and community work. For soon after, we had the inception of the cleverly acronymed (M)olecular (R)unning (C)lub at the Hutch whose first adventure was at the CRUK Race for Life event in July, through which they raised more than £600.0 for cancer research. Long may this legacy of giving back last amongst us.
On a different note ‘giving back’ was also what spurred on our researchers who visited the Sawston Village College Junior STEM club in June to enthuse young children and give them a flavour of the excitement of research - as one kid put it: “I enjoyed it because I was so amazed by all the tech and it was really fun. Thanks”. A big thank you to Rebecca, Jamie and their team members for so generously devoting their time for this. Last but not least, we had our students and Pls (Jake, Jacqui, Christian and Charlie) speaking on the theme of “Combating Cancer” at the annual ‘Pint of Science’ Festival in May which provides a worldwide platform to ‘quench one’s thirst for knowledge’ in the comfort of one’s local pub or café. Thank you to Jake for being lead organiser!

Goodbye Jennifer!

The MRC CU will dearly miss Jennifer Furman - the Hutch Research Governance and Integrity co-ordinator, undoubtedly not just the world’s most generous RG expert cum gourmet baker, but someone who won hearts with her seemingly endless capacity for helping people, her passion for her job, and her can-do spirit in all things at the Hutch. As Jennifer moves to other challenges within the School we all thank her for her support and extraordinary generosity of spirit and wish her every success and happiness in her new job. HTA has never been so delicious before - thank you!

Other recent arrivals & departures

We welcome Joao Lopes Dias (Bioinformatician), Hannah Coles, Tim Young (Research Assistants) and Rob O’Neill (Visiting Clinician). We would like to wish Rachel de la Rue, Houda Abla, Erika Vojtasova, Pauline Bourigault and all our work experience/summer visiting students the very best in their future careers.

The new chillers are here

After years of air-conditioning woes, courtesy ageing infrastructure, the building finally had brand new chillers commissioned by the University. After extensive building works over the past 3 months, the new rooftop chillers have been installed (on time!) and have so far functioned seamlessly. Hopefully a reason to celebrate with the return of the ice-cream van soon.
The MRC Festival of Research, 2019

Alongside promoting world class research, the MRC CU considers it a cardinal responsibility to support the education and training of the next generation of cancer researchers and provide opportunities to high school students to engage in and gain exposure to the latest cancer research and be inspired to pursue a career in research. Therefore, as in previous years, as part of the MRC Festival of Medical Research in June, we chose to focus on school students and organised the Schools Open Day. As part of this on the 19th June, sixth form students from several 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. Suffices to say an afternoon of thrilling discoveries followed for the young visitors - perhaps aptly summed up in one of the feedback comments: “Working in a lab seems much more exciting and fun than (I) previously thought!” A big thank you to all who volunteered to make this event possible.

For Festival week, our local MP, Heidi Allen was invited back to the Unit. Heidi met with a panel comprising of support staff, students, post-docs, group leaders and the Director. Frank and compelling discussions about the future of British R&D in the current political climate, the case for continued funding of niche research organisations such as the CU within the wider landscape of cancer research across the country and a general update on the progress of the Unit’s Research over the past year were the highlights of the visit. Refreshingly, following up on her promise last year to visit our labs, Heidi went on a tour of the building, discovering for herself cutting edge research and equipment and stopped to engage with students and members of staff along the way.
'Fingerprint database' could help to identify new cancer culprits

Somatic mutations in cancer cells, arising through cell-intrinsic and exogenous processes, mark the genome with distinctive patterns termed mutational signatures. In a collaboration with David Phillips, King’s College London, Serena Nik Zainal’s group systematically explored mutational signatures associated with environmental agents that are either known or suspected to be linked to cancer. In all, 79 agents from 13 families were used to treat human induced pluripotent stem cells (IPSCs), including agents found in everyday exposures like exhaust fumes, tobacco smoke, chemical dyes and things we ingest. A highly standardised set-up was used to ensure that all results were comparable to one another. Cell viability was aimed for 40-60%, functional DNA damage response assays were obtained, and metabolic activation was taken into consideration. Single-cell subclones were derived from recovered cells. In all, 324 iPSC subclones were whole genome sequenced to seek genome-wide mutation patterns. Computational analysis highlighted pathognomonic “fingerprints” of 41 environmental agents including 41 substitution patterns, 6 double-substitution and 8 indel signatures. New mechanistic insights were gained into mutagenesis and learned about contributions of DNA repair pathways to the final mutational outcome. Critically, these results will serve as a reference set of mutational signatures with public health and surveillance implications. In the future, when all tumours are sequenced, these reference catalogues of mutational signatures can be used to understand whether environmental mutagens are culprits in the development of a patient’s tumour.

The study entitled A Compendium of Mutational Signatures of Environmental Agents has been published in Cell.

It has received wide press coverage including in newspapers like the Guardian and the Telegraph and has also been widely discussed across social media channels and highlighted on various scientific and University websites. A video summary of the article released by Cell Press is available here: https://www.youtube.com/watch?v=kzorkO2rsm8
Improved nanoparticles for lymph node mapping are non-disruptive to immune function

The Shields lab is involved in a long-term collaboration with Cambridge-based company Endomag, towards the development of Carboxydextran-coated superparamagnetic iron oxide particle (SPIO)-based technologies for use in the clinic as an alternative to radioisotopes for intraoperative lymph node (LN) mapping - an important part of staging cancers, particularly breast cancer and malignant melanoma. Whilst this approach has proven to be a safe and effective alternative to radio-labeled tracers in both European and the US clinics, the mechanisms of transport to lymph nodes, and longer-term impact of SPIO accumulation in tissues remained unclear. A recent study in collaboration with the Shields Lab, led by Luisa Pedro, identified that rapid transport to lymph nodes was governed by mechanical (lymph flow) rather than cell-mediated (transport within immune cells) means. Particles were detected in draining lymph nodes within 10 minutes of administration and localized predominantly with lymphatic structures. In contrast, cell-driven trafficking to lymph nodes required 24 hours. Longer-term, SPIO could be observed in association with macrophages, raising the question whether this could change their behaviour, impairing their ability to mount an appropriate immune response when needed. Consistent with previous reports, the study demonstrates that although alterations in macrophage behavior could be observed immediately after exposure, the changes were transient, resolving to baseline levels by day 7. Moreover, macrophages retained the capacity to proteolytically process antigens and respond to an inflammatory stimulus following exposure to particles. Thus, while particles persist at injection sites and LNs where they may be sampled by perturbation, carboxydextran-coated SPIO nanoparticles within macrophages conferred no long-term disruption to macrophage phenotype or functional capacity.

The study entitled Impact of Locally Administered Carboxydextran-Coated Super-Paramagnetic Iron Nanoparticles on Cellular Immune Function has been published in Small.

Antioxidants prevent mutation harbouring cells in the oesophagus from progressing after Low Dose Radiation exposure

Low doses of radiation, such as from medical imaging, are considered safe as they cause little DNA damage and apparently minimal effect on long-term health. However, a recent study involving Phil Jones’ group in collaboration with Christian Frezza finds that exposure to low doses of radiation, equivalent to three CT scans, may promote the spread of cancer-capable cells in healthy tissue. The team found that such radiation exposure increases the population of cells with mutations in p53. However, giving the mice an antioxidant before radiation promoted the growth of healthy cells, which outcompeted and replaced the p53 mutant cells. Researchers from the Jones group have previously shown how normal tissues, like skin, are battlefields where mutant cells compete for space against healthy cells. Using mouse oesophageal tissue as a model system, this new study shows that low doses of radiation weigh the odds in favour of cancer-capable mutant cells in the oesophagus.
Exposure to a 50 milligray dose of radiation, equivalent to three or four CT scans, would result in the p53 mutant cells spreading and outcompeting healthy cells. However, giving these mice an over-the-counter antioxidant – N-Acetyl Cysteine (NAC) before exposure to the same level of radiation gave normal cells the boost needed to outcompete and eradicate the p53 mutant cells. Interestingly, the antioxidant alone without exposure to radiation did not help normal cells outnumber the mutant clones. The study highlights the effects of low doses of radiation and the risks it may carry and also offers the possibility of developing safer preventative measures to lower the risk of developing cancer by boosting healthy cells to outcompete and eliminate cancer-capable cells.

The study entitled *Outcompeting p53-Mutant Cells in the Normal Esophagus by Redox Manipulation* has been published in *Cell Stem Cell*. 
**Awards & Conferences**

In June, **Karol Nowicki-Osuch**, post-doc in the Fitzgerald group, was awarded a Canada-UK Postdoctoral Fellowships for Innovation and Entrepreneurship. The exchange fellowship will enable Karol to work on the Global Challenges together with the Centre for Global Equality whilst developing entrepreneurial and leadership skills in an international context. Well done Karol!

**Saif Ahmad**, former student and current associate of the Venkitaraman lab, was also a recipient of the same fellowship last year. As part of this award, working in tandem with the Borysiewicz Biomedical Sciences Fellowship (which also started last year), Saif was part of a team of post-docs from diverse backgrounds whose mission was to contribute to a United Nations Sustainable Development Goal. The main part of the project involves travelling to Argentina this summer and working with Argentinian Universities and Government to provide an outreach programme on air pollution. Saif and his team members organised interactive events and training for volunteers and University students whilst out there to introduce low-cost air pollution sensors and then use these sensors on bikes around Buenos Aires. The sensor was created by students at the University of Cambridge.

**Upcoming events**

- Big Biology Day – 5 October
- Postdoc Retreat and welcome event for new starters – October (date tbc)
- Hutch Annual Retreat – 15 Nov.

**Other News**

The **BEST3 Trials come to an end**

In one of the most successful examples of tax payer funded basic research from the Unit dovetailing onto charity funded translational efforts to benefit patients, the BEST3 clinical trials, to assess the efficacy of the Cytosponge™ test in comparison to traditional endoscopies for the detection of Barrett’s Oesophagus, carried out in GP surgeries across the country, has come to an end this summer. 110 GP sites, 15+ hospitals and 13000 patients on, the collection of data - a Herculean team effort - is now complete; the findings from the Trial are expected in early 2020. We wish the team the very BEST in their efforts to promote cost effective, convenient, early detection of a condition that predisposes to a potentially deadly cancer.

**Royal Soc. Summer Science Exhibition**

Ben Hall’s lab was invited to this huge annual event where they highlighted the role of computational modelling in cancer.
Our scientists in the limelight

The Unit featured in a couple of recent special editions of the local newspaper - The Cambridge Independent – first, in May, in a supplement showcasing outstanding schools outreach efforts at the Biomedical Campus and more recently in its latest August edition focussing on clinicians who bridge the world of laboratory research, featuring Dr Serena Nik Zainal.
Recent publications


---

MRC Cancer Unit
University of Cambridge
Hutchison/MRC Research Centre
Box 197, Cambridge Biomedical Campus, Cambridge CB2 0XZ

Tel: 01223 763240
Email: contact@mrc-cu.cam.ac.uk

[facebook.com/MRC.Cancer.Unit](https://www.facebook.com/MRC.Cancer.Unit)  [@MRC_CU](https://twitter.com/MRC_CU)