As the march of time continues and as we head into a new decade, the MRC Cancer Unit has had its own rite-of-passage moment in its history.

After more than a decade of leading the Unit, Professor Ashok Venkitaraman has handed over the baton to Professor Rebecca Fitzgerald who has taken over as Interim Director of the Unit from December 2019.

Rebecca and Ashok, who have both been at the Unit since its very inception when the first Director, Professor Ron Laskey, started the place from literally a hole in the ground, have been witness to the many changes that have taken place in an around a campus that has morphed beyond recognition over the past decade.

Ashok's contributions, in shaping the ethos of the place, nurturing its vibrant and collegiate ambience and championing a credo of robust science, have been immense, and who better than Rebecca to carry forward that legacy and continue to make it flourish. We wish Ashok the very best in his onward journey as a key figure shaping the cancer research landscape of Singapore and congratulate Rebecca on her new role as Interim Director of the CU!
To pastures new

Autumn 2019 was all about the changing of guards! The Hutch suddenly found itself shorn of two of its most loved and popular sentinels, Jordi Gomez Alberti and Archie Nepomuceno, who looked after our countless IT needs and steered the good ship through many an IT storm alongside their captain Steve, moved on to new jobs in different University quarters - the Whittle labs and the Clinical School IT team, respectively. We will miss them both dearly but wish them well in their new exciting roles.

Other recent arrivals & departures

We welcome, Abigail Kerridge (Research Governance coordinator), Veronica Caraffini, Dylan Ryan (Research Associates), Nastazja Pilonis, Apostolos Pappas (Clinical Research Fellows), Clare Atherton (Research nurse), Gene Koh, Niklas Müller-Bötticher, Elsita Jungkurth, Colver Ne-Ken-Howe (visiting/projects student), Dylan McClurg (MPhil student) and Charlotte Cassie, Leonor Nunes Rodrigues, Aishat Yusuf, Shawn Zamani, Suraj Pavagada, Komal Gupta, Anna Dyas, (new PhD students). We would like to wish Caitriona Hughes, Amber Grantham, Irene Debiram, Anne-Marie Lydon, Ganesh Kumar, Houda Abla the very best in their future careers.

The first Hutch Post-Doc Retreat

The Hutch Post-doc Soc and Grad-Soc have been amazing over the last year. One highlight of the many innovative and enthusiastic ventures was the first ever (PI free!) post-doc Retreat they organised in October. The event, comprising of short talks, coaching sessions with professional trainers and lots of opportunities for team building was very well received by both Graduates and Post Docs and an excellent example of how the CU is committed to supporting mentoring opportunities tailored to the needs of its communities.
Annual Retreat, 2019

At the start of November, the Hutch got together at the Møller Centre in Churchill College, for its Annual Science Retreat. What was Ashok’s last Retreat as Director, kicked off with a poignant address from him recounting his days in and around the Unit, the contributions of the MRC as a whole and the contributions of the Unit in particular to research and ended with a reminder of a moral obligation we have towards excellence in science and above all else, excellence in humanity. We also had Professor Ron Laskey, the founding Director of the MRC Cancer Unit and Dr Katie Ridd, senior editor from Nature Communications, attending the event. Throughout the 2 days of scientific talks, posters and vibrant discussions, students and post-docs from across research groups presented their research. The winner of the poster competition was Christina Schmidt, PhD student from the Frezza Group with the Runners-up poster prize going jointly to PhD students Shoko Hirosue and Will Moody (Samarajiwa-Vanharanta and Shields groups). The award for best oral presentation was won jointly by Karol Nowicki Osuch (Fitzgerald group), Michele Petruzzelli and Estrella Guarino Almeida (Venkitaraman Group) and the Runners-up talk prize went to Marco Sciacovelli (post-doc, Frezza group). A full-on day was brought to a close by yet another brilliant Bryn Hardwick quiz with a special surprise round thrown in for Jordi, on his last working day at the Hutch.

Overall, the two-day event was an enjoyable and informative experience and provided a great opportunity for all, especially newcomers, to get a glimpse of the varied and stimulating research that is ongoing at the Centre.

Congratulations to all the poster and oral prize-winners and a big thank you to all who were involved in the organisation of the event!
MRC Cancer Unit: Research successes

The potential of whole genome sequencing to enable personalised cancer treatment

A recent collaborative study with Lund University, Sweden involving Serena Nik Zainal’s group published in *Nature Medicine* in September highlights how whole genome sequencing of tumour cells could help predict the prognosis of a patient’s cancer and offer clues to identify the most effective treatment.

To understand whether WGS might be useful in a clinical setting, Serena’s group teamed up with colleagues in Sweden running a population-wide project called SCAN-B, which has been recruiting all women diagnosed with breast cancer in the South of Sweden since 2010 and thereby with access to a huge amount of clinical data from these patients. WGS was used to analyse tumours from these patients who had been diagnosed as having triple negative breast cancers. (cancers that account for around 9% of breast cancers and are associated with poorer outcomes, mostly amongst women with African and Asian ancestry).

The researchers then applied their machine learning algorithm called HRDetect, which they had previously developed, to identify tumours with signatures caused by mutations in the BRCA1 or BRCA2 genes. Taking the scores, the team categorised each patient as either high, intermediate or low scoring. Patients who scored highly were those that had the best outcomes using current treatments for triple negative breast cancers – they were also most likely to respond to PARP inhibitors. Those patients with low scores also had poor outcomes, though not as badly as those in the intermediate group. The WGS profile in some of these tumours suggested biological abnormalities that could potentially be targeted by existing drugs or drugs currently going through clinical trials, such as the checkpoint inhibitors or AKT inhibitors.

Current triple negative breast cancer treatments have limited effectiveness, suggesting that new approaches would be necessary to tackle these cancers. The genetic changes and signatures revealed through WGS analysis of these tumours thus gives clues to the mechanisms driving these tumours, which in turn may help inform the development of new drugs. The study powerfully showcases the importance and role of WGS in better informing about more personalised treatment options for those affected with cancer.

The study by Staaf, J. et al. entitled *Whole-genome-sequencing of triple negative breast cancers in a population-based clinical study* was published in *Nature Medicine*; 30 Sept 2019. It has since received widespread attention across several, mainly science related, portals (Science Daily, Genomeweb, Medical Express, UCAM main website, ecancer, Hospital Healthcare, etc) and on Twitter.
A new model for metastases in Esophageal adenocarcinoma

Cancer of the oesophagus has very poor outcomes with less than 13% surviving beyond 5 years. Most patients present with what appears to be a similar extent of disease on their scans (CT and PET) but yet the outcomes can be highly variable and unpredictable between patients. A recent study by Noorani et al from Rebecca Fitzgerald’s group, published in Nature Genetics takes an in depth look at how this cancer spreads at a molecular level using samples collected from multiple time points and from multiple tissue sites. This was possible through the very generous tissue donation from patients and their families and through a huge team effort. The study uncovers new pattern of spread in which multiple cell population in metastatic sites are directly linked to the primary tumour. This is seen as a stellate pattern on a phylogenetic tree. There is very little tropism observed - meaning that metastases do not seed other metastases. Furthermore, metastases in solid organs can bypass the lymph nodes. This is quite different from the traditional concept of linear evolution in which spread occurs gradually from neighbouring areas of the body. The authors call this new pattern “diaspora” - analogous to diaspora crossing national boundaries. Looking back in time the researchers can observe evidence for molecular events in the blood before they are evident as metastases. These findings give clues about how to detect harbingers of metastases early on in the patient’s clinical pathway. More work is required to understand the triggers for the widespread metastases in oesophageal cancer and whether it pertains to other cancer types.

The study by Noorani. A, et al. entitled Genomic evidence supports a clonal diaspora model for metastases of esophageal adenocarcinoma was published in Nature Genetics; 06 Jan 2020.

Widely discussed on Twitter, an overview of the study and a tribute to the patients and families who took part in the study, written by Dr Noorani, was also published in the Nature Community website: https://cancercommunity.nature.com/channels/465-behind-the-paper/posts/57963-the-legacy-of-a-cancer-gone-rogue-the-evolutionary-trajectory-of-metastatic-oesophageal-adenocarcinoma
Other News
That long overdue lick of paint and the rest...

2019 has been the year that finally brought about a lot of infrastructure renewal for the Hutch: new chillers, new temperature controls, TC gas and freezer monitoring systems, but perhaps more noticeably the new bike racks, and redecorated passageways with new staircase flooring – all to help brighten up the place and to improve the general ambience and ease of working.

Christmas giving at the Hutch The tradition of generous giving continued in the Festive season at the Hutch. This year our chosen charities were Maggie’s and the Arthur Rank Hospice - both local charities that have directly benefitted our staff or their families. Through the Christmas Raffle and Christmas Jumper Day donations we raised a total of £750! Thank you all.

Workshops and Engagements

Dr Ben Hall and colleagues presented a demonstration for A-level students at the Royal Society Summer Exhibition as part of the new schools hub. Working with materials developed in collaboration with OCR https://www.ocr.org.uk/blog/getting-started-with-computational-biology-in-cancer-research/ Ben and his team gave practical demonstrations of cancer modelling using the BioModelAnalyzer to teachers and student visitors.

Dr Sakari Vanharanta and colleagues organized the 2019 edition of Frontiers in Metastasis Biology, a two-day intensive workshop that took place in the Hutch in September. The programme, following on from similar events in Basel and Vienna, featured several local and international experts who discussed various topics of metastasis biology, covering clinical medicine and surgery, tumour immunology, genetics, experimental metastasis biology and drug development. The trainees represented PhD students and postdocs from several institutes around Europe and the US.

Once again, our researchers (David, Izzy, Marko, Carlo and Laura) were there to support the efforts of Hills Road 6th Form at Big Biology Day 2019 – a great opportunity for kids and local youth to engage with the local research community. Thanks to the CU team!

Upcoming events
Dr Serena Nik Zainal was awarded the prestigious Josef Steiner Cancer Research Prize for 2019. Endowed with one million Swiss francs and originally also known as the "Nobel Prize for Cancer Research", it is the award of a private foundation with the biggest cash prize of its kind in the world. Serena was selected for the award for her research on mutations in cancer and the application of new bioinformatic methods that enable new approaches to targeted therapies.

The award was presented to her by Dr Stephan Rohr, Co-Director of the Institute for Physiology and president of the foundation's board, in October in a ceremony at Berne.

Our heartiest congratulations to Serena!
Recent publications


8: Genomic landscape of metastatic breast cancer and its clinical implications. Lindsay Angus, Marcel Smid, Saskia M. Wilting, Job van Riet, Arne van Hoeck, Luan Nguyen, Serena Nik-Zainal, Tessa G. Steenbruggen, Vivianne
