

Hutchison/MRC Research Centre

Newsletter

To undertake world leading research into cancer cell biology that can be translated into clinical practice

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Message from the Directors

Welcome to the second edition of the Hutchison/MRC Research Centre newsletter. A major focus of this issue is the public outreach work that many of our staff and students have been involved in. We are very pleased about the continued enthusiasm for the Cambridge Science Festival, and the community work undertaken by the Fitzgerald group. Other recent achievements include the establishment of the Hutch post-doc society, and the highly successful MRC Cancer Cell Unit Annual Lecture.

Professor Ashok Venkitaraman
Professor Ron Laskey
Professor Bruce Ponder

Joint Directors, Hutchison/MRC
Research Centre

Hutchison/MRC Research Centre reveals magic and marvels at the Cambridge Science Festival

March saw National Science Week celebrated in Cambridge in the form of the annual Science Festival. As regular participants, members of the Hutch provided a number of creative activities for visitors to the festival's Biology Zone.



With the theme of this year's event being 'Centuries of Science', the Hutch team decided to look into the past, present and future of cancer research with a display entitled Mysterious Magic to Modern Marvels. Posters showed how our knowledge and understanding of cell biology and cancer has developed and progressed rapidly over the past hundred years, and provided a useful starting point for those with questions about the work that we do.

Of course, one of the main aims of the Cambridge Science Festival is get younger children enjoying science. And some inventive thinking from members of the Jones group meant that all the fun of the (cancer research) fair was brought to our stand.

Our hook-a-cancer duck game drew some enthusiastic crowds, who attempted to find the hidden cancer duck in one pond or hook the more obvious cancer duck that was identified by its devil pirate biomarker. Visitors also got to target lung cancer using dart-o-therapy. Successful players used magnetic darts to hit only the tumour whilst avoiding other areas of the lungs and other organs, as an ideal drug would do.



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Another big attraction to the Hutch stand was Norman, our fibreglass colleague with unique, removable organs. Norman was used for several demonstrations of the capsule/sponge technology developed by the Fitzgerald group, as well as helping to explain what endoscopy involves. Microscopes, with slides displaying MCM protein stained cancer cells and unstained, healthy cells made up the final part of the activities. Everyone from toddlers to grandparents seemed very keen to take a look and see if they could make a diagnosis! As usual the Biology Zone drew several thousand visitors during the day, and other attractions included the MRC Epidemiology Unit's X(ercise) Factor, the MRC LMB's nematode worm lab and MRC HNR's Saturday Kitchen.

A huge thank you to all the members of the Hutch who helped out in preparing for this event, as well as on the day. The Directors are delighted that so many staff and students from all our different research groups were prepared to give up their spare time in order to promote some of the work that the Hutch undertakes. Here's looking forward to next year!



Fitzgerald group take outreach out on the road



Schools road shows are also organised every year to coincide with the Cambridge Science Festival. MRC Cancer Cell Unit group leader Rebecca Fitzgerald, and members of her research group Chris Peters and Pierre Lao-Sirieix, took to the road to put on events across Cambridgeshire, including a stop at Burrough Green Primary School. Our stalwart of public outreach, Norman, completed the team.

The 'Gurgling Guts' show they've developed is aimed at children at Keystage 2 (between 7-11 years old) and shows them the journey that our food takes after we eat it. Thanks to Norman's removable insides the children were able to see how long our intestines actually are, and what happens inside the stomach once we've eaten something. Videos of the inside of the oesophagus and the intestine were greeted with a variety of

exclamations ranging from "awesome" to "disgusting"! A lively Q&A session with the children after the show produced some interesting questions, including ones on acid reflux and what the biggest muscle in the body might be! The team has received some excellent feedback from all the schools they have visited including comments on how helpful the session had been for children preparing for exams.



Chris, Rebecca and Pierre with Norman



MRC Cancer Cell Unit Annual Lecture draws the crowds

The MRC Cancer Cell Unit Annual Lecture took place on the 24th March. We were privileged to host Nobel Prize winner, Phillip A Sharp from the Koch Institute of Integrative Cancer Research at MIT. Professor Sharp's work on the discovery of RNA splicing won him the Nobel Prize in 1993, and laid the foundation for research into the complexities of gene expression and regulation in both normal and disease states.



During his talk, Professor Sharp described the role of microRNAs (miRNAs) in a number of cancers, outlining how their role in the regulation

of the cell cycle might impact on the development of these diseases.

For instance, the let-7 family of miRNAs has been implicated in non-small cell lung cancer, with high

levels of expression associated with tumour progression and lower survival rates. In contrast, down regulation of miRNAs 15 and 16 have been



associated with prostate cancer. Professor Sharp also discussed the cooperative nature of miRNA regulation, for example in B cell development, and the use of T cell activation as a model system to study miRNA regulatory functions.

This incisive and informative lecture from one of the world's leading RNA researcher's drew a large crowd with the auditorium packed to capacity. Questions continued over tea and biscuits, and concluded one of the MRC CCU's most successful annual lecture events.

Hutch PhD student enters the dragons den



Anna Paterson, an MRC Cancer Cell Unit PhD student from the Fitzgerald group, successfully took on the MRC Technology dragons den recently.

In an event held last month in Cambridge, MRC Technology challenged MRC students and post-docs to come up with a translational research project with the potential to address a currently unmet need. The entrants into the innovation competition were narrowed down to just four successful candidates who had the opportunity to pitch their proposals to the MRC dragons. In this instance the panel of commercial experts consisted of Martin Drysdale (Head of Drug Discovery

Programme, Beatson Institute for Cancer Research), Regina Hodits (partner in the life sciences investment group Atlas Venture), Ian Tomlinson (Vice-President, GSK-Domantis Group), and Michael Dalrymple (Director of Intellectual Property and Business Development Division, MRC Technology). Anna's proposal for "A Molecular Assay to Allow Targeted Cancer Chemotherapy" won favour with the dragons and secured the top spot. She won both an individual prize of £500, together with £5000 for her group. Commenting on her success Anna said, "Taking part in the MRC Technology innovation competition was a really good experience and involved thinking about my research with a different commercial slant".

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As well as the competition the event also showcased some of the work that MRC Technology undertakes in the areas of drug discovery and commercialisation, and the opportunities for collaborative working with MRC scientists.

For more information on MRC Technology visit- www.mrc technology.org/

For more information on the work of the Fitzgerald group visit- www.hutchison-mrc.cam.ac.uk/Research/Rebecca_Fitzgerald/index.html

Women in Science



Over fifty post-graduate students and researchers took up the opportunity to hear from a range of female scientists at various points in their careers, at the Women in Science meeting on the 23rd February. The event was organised by Department of Oncology group leader Anna Philpott, and featured informal presentations from active researchers as well as those who had followed different post-PhD paths. Rebecca Fitzgerald and Laura Itzhaki, (MRC Cancer Cell Unit group leaders), spoke about establishing research careers while also bringing up families. A number of themes emerged from their talks, including the importance of mentors, the need for flexibility and even the role of luck! Professor Christine Holt from the Department of Physiology, Development and Neuroscience, spoke about the need for resilience when undertaking a research career and at a senior level being able to balance administrative work with lab-based activities. Anna's presentation highlighted how the time she spent as a post-doctoral researcher at Harvard was crucial in the development of her career.

All these scientists acknowledged that building a career in this field could be tough but didn't feel that gender had had a significant impact on this. They also agreed that academic research provides one of the most flexible career choices for women, with the ability to work your own hours and not be excessively constrained by fixed schedules.

Participants also heard from Ireena Dutta and Anne Forde. After completing her PhD, Ireena worked in bioinformatics and project management before finding her niche in scientific communication at the MRC Cancer Cell Unit. Anne spent several years as a post-doctoral

Other news

Grants Awarded

The de la Cueva Mendez group have received an award from the MRC Technology Development Gap Fund for their project on "Nanocell delivery for Kid/Kis technology".

The Itzhaki group, in collaboration with Professors Ernest Laue (Dept of Biochemistry) and David Spring (Dept of Chemistry) have been awarded a one year grant from the Cambridge Cancer Centre to establish a project on "The use of structure stabilising small molecules to reactivate missense mutants of the tumour suppressor p16INKa".

Talks

Rebecca Fitzgerald gave an open lecture in February for the Cambridge branch of the Society of Chemical Industry (SCI). Entitled, "Improving outcomes for cancer patients", the talk stimulated some interesting debate about the reasons for the increasing incidences of oesophageal cancer in the UK and the processes involved in medical device development.

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researcher before branching out into scientific journalism, and is now a careers advisor for the University of Cambridge. Both these speakers emphasised that although they no longer conducted research, their PhD backgrounds were essential in getting them into the roles they currently occupy, and that the skills they learnt as researchers were still being utilised.

The meeting was followed by some informal networking and delivered an important message that with the right support in place a successful academic career could be combined with a family and that scientific research was not the only career option after a PhD.

Hutch Post-doc Society takes off

*The newly formed Hutch Post-doc Society is rapidly moving from strength to strength. Here, **Pam Rowling** describes how things have developed since its inception.*



Post-doc Society meeting with Phillip Sharp

The idea of creating a society for post-docs in the building was first mooted in February's newsletter, and now in June things have really moved forward. We have a group of key people willing to organise and co-ordinate events; Chuks Agu (de la Cueva Mendez group), Mari Barbera (Fitzgerald group), Barbara Nikolaidou (Coleman Group) and myself (Itzhaki group). We now also have our own intranet page www1.hutchison-mrc.cam.ac.uk/Postdocs/postdocs.html so you can have a look at past events, and find information on future plans and key contacts.

Our first event in March was to host a tea for Professor Philip Sharp, as part of his visit to the MRC CCU, where animated discussions were had. Our second event, which was purely social, was a 'bring-a-dish' lunch. And having discovered that so many people are great cooks it was decided that this event would definitely be repeated! Over 50% of the post-docs in the building attended each event, which we are very pleased about.

A date for your diary- our next event is a barbeque on Darwin Island on Friday 5th June which will be held jointly with the Graduate Student Society. Visit our intranet page for more details.

And finally, look out for the questionnaire that we'll be circulating to determine what events the post-doc community in the Hutch would like to see in the future.



Post-doc Society bring-a-dish lunch

Hutch scientists in the media

Phil Jones features in the March/April edition of the MRC Network magazine, in an article about his multi-disciplinary work with **Ben Simons**. Visit the MRC site to [download a PDF](#) version of the article.



A webstory on **Anna Philpott's** Women in Science event featured on the Cambridge University website in February.



Upcoming events

5th June: Joint Hutch post-doc and graduate student societies barbeque at Darwin College. More details [here](#).

19th June: Wolfson College June Event. David Gaboriau from the Itzhaki group is the drummer in the band 20Story, and they'll be playing at this event. To listen to the band in action have a look at their [MySpace page](#).

26th June: Cambridge Cancer Centre Symposium. More details and registration information [here](#).

Focus on.....the Gnanapragasam group



Vincent Gnanapragasam from the Department of Oncology and his Translational Prostate Cancer group (TPCG) have recently moved into the Hutch. Vincent is a University Lecturer in uro-oncology and an honorary consultant urological surgeon. His group is a part of the larger uro-oncology grouping headed by Professor David Neal in the University of Cambridge. Vincent was formerly a specialist registrar and clinical lecturer in urology at the University of Newcastle, and he currently holds a CRUK Clinician Scientist Fellowship. His background is in basic science and translational research with an interest in fibroblast growth factor biology in prostate cancer. His remit in Cambridge is to develop clinical and translational research in prostate cancer. He has a clinical practice in urology with a specific interest in the surgical management of localised prostate cancer in men with advanced castration resistant disease. Here Vincent describes some of his research group's aims and

what they hope to achieve in the coming years.

Prostate cancer has attracted a huge amount of investment in research, and knowledge about this disease is growing exponentially. There is however, comparatively little translational research undertaken directly into the clinical disease. The aim of the TPCG is to develop the clinical to laboratory models that will allow more "relevant in man" investigations of prostate cancer in terms of biomarkers, disease progression, response to therapy and novel targets; in essence to use the clinical disease as a model for investigator-led, hypothesis driven studies. This model can then be used to more rapidly and directly evaluate new markers or drugs. Our group works closely with the uro-oncology group in the CRI and is also actively seeking collaboration with interested groups in the Hutchison and wider Cambridge scientific community.

Our lab is currently focused on two main areas; the role of signalling regulators in prostate cancer growth factor biology, and molecular profiling to determine treatment specific outcomes. Growth factors are known to be important mediators to tumour growth and progression. In recent years endogenous regulators of growth factor pathways have emerged as potential targets for manipulation. We are investigating the expression and function of key regulators including Sef and Spred. The goal is to test if these regulators can have clinical application as prognostic biomarkers and therapy targets. Prostate cancer can be effectively treated by different modalities including surgery and radiotherapy. In each modality however there will be those who have a durable good response and those who will not. The ability to predict how a tumour will respond to a particular treatment type would therefore be a powerful tool in clinical decision making. It is currently unknown however if prognostic markers identified in one therapy context are also applicable to other treatments. In this work we are using molecular profiling using mRNA to identify prognostic markers that can predict clinical outcomes for specific treatments for prostate cancer. A further aim is to develop the clinical interface for recruiting patients to investigator led clinical trials in prostate cancer. This is being undertaken in close collaboration with the clinical and academic expertise in oncology, pathology and radiology readily available in Cambridge.

For more information on the Gnanapragasam group and its work please visit their new webpages on the Hutch website www.hutchison-mrc.cam.ac.uk/Research/Vincent_Gnanapragasam/index.html

Arrivals and departures

We welcome post-doctoral researchers Camino Bermejo Rodriguez and Irena Hreljac to the de la Cueva Mendez group, Farhad Ali to the Philpott group, and David Sorrell who joins the Venkitaraman group as part of the CMTP.

We also welcome visiting researchers Ina Schulte (Edwards group), Keith McLuckie (Venkitaraman group) Marianna Mela and Aloysious Aravinthan (Coleman group). In addition, Sharon Richards joins the MRC CCU as part of the administration team.

Vignesh Venkatraman has left his role within the MRC CCU admin team, but will be staying at the Hutch for a little longer as he joins the Venkitaraman group over the summer as a vacation student.

Recent publications

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Linking the cellular functions of BRCA genes to cancer pathogenesis and treatment. **Venkitaraman AR.** *Annu Rev Pathol.* 2009;4:461-87.

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Paving the way for H2AX phosphorylation: Chromatin changes in the DNA damage response. Ayoub N, Jeyasekharan AD, Bernal JA, **Venkitaraman AR.** *Cell Cycle.* 2009 May 20;8(10).

The BRC repeats of BRCA2 modulate the DNA-binding selectivity of RAD51. Carreira A, Hilario J, Amitani I, Baskin RJ, Shivji MK, **Venkitaraman AR**, Kowalczykowski SC. *Cell.* 2009 Mar 20;136(6):1032-43.

c-ABL tyrosine kinase stabilizes RAD51 chromatin association. Shimizu H, Popova M, Fleury F, Kobayashi M, Hayashi N, Sakane I, Kurumizaka H, **Venkitaraman AR**, Takahashi M, Yamamoto K. *Biochem Biophys Res Commun.* 2009 May 1;382(2):286-91.

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