

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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MRC Cancer Cell Unit welcomes new group leaders

The MRC Cancer Cell Unit is delighted to announce the appointment of two new group leaders, who have joined the Unit this month. Dr Jacqui Shields joins the Unit from the EPFL in Lausanne, Switzerland, and Dr Carla Martins moves over from the CRUK Cambridge Research Institute.

Message from the Directors

Welcome to the new issue of the Hutchison/MRC Research Centre. This edition introduces the two new research group leaders who have joined the MRC Cancer Cell Unit. As they settle in within the Research Centre, we hope that their time here is both enjoyable and productive. We have also highlighted some of our other successes and achievements over the past few months.

Professor Ashok Venkitaraman
Professor Bruce Ponder

Joint Directors, Hutchison/MRC
Research Centre



Dr Carla Martins (left), and Dr Jacqui Shields at the Research Centre.

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Carla Martins will lead a programme on *in vivo* modelling of tumour development and targeted cancer therapies. Throughout her research career Carla has been interested in understanding how the well regulated pathways that ensure accurate proliferation in normal cells are reprogrammed to enable tumour growth. She completed her PhD with Professor Anton Berns at the Netherlands Cancer Institute where she used *in vivo* forward genetic screens to identify mutations that are both necessary and sufficient to drive tumorigenesis. She demonstrated that p27^{Kip1} deficiency collaborates with *Myc*-overexpression during lymphomagenesis, and mapped twenty-one potential new oncogenes. Carla then carried out post-doctoral research in the group of Professor Gerard Evan at the University of California San Francisco where she aimed to identify potential tumour-specific targets for therapeutic intervention. Using novel regulate-able mouse models she established the therapeutic potential of p53 restoration in lymphoma and lung cancer, and defined the mechanisms involved in p53 activation during tumour evolution and those responsible for p53-resistance. More recently she has worked within the group of Dr Dave Tuveson as an Associate Scientist at the CRUK Cambridge Research Institute where she focused on translational research in lung cancer. At the MRC CCU Carla's group will continue this work by employing a multi-disciplinary approach involving mouse modelling, *in vivo* imaging, molecular biology, and genomics, to define the mechanism required for lung tumour evolution and maintenance. Ultimately, the goal of the group is to contribute to the development of improved cancer diagnostics and therapeutic tools.

Jacqui Shields studied for a PhD at the University of Bristol, where her interest in tumour-associated lymphatic vessels began. She then joined the lab of Professor Melody Swartz at the EPFL in Switzerland as a post-doctoral researcher to explore more functional based investigations of tumour lymphatics. This work identified that tumours hijack aspects of the immune system and exploit lymphatic function. Specifically, they secrete lymphatic and lymph node-associated factors such as CCL21, using these factors to find functional lymphatic vessels, and to recruit immune cells and support changes towards a pro-tumour microenvironment. These findings led her to become interested in the specialised tumour stroma that shares features of the stroma found in lymphoid tissues, where it helps to direct our immune responses. In the tumour however, these responses are dampened. Jacqui's work at the MRC CCU will investigate the mechanisms underlying the formation and maintenance of the specialised lymphoid-like tumour stroma that fosters tumour development, and how lymphatic vessel function contributes to this.

Commenting on her arrival at the Unit, Jacqui said, "*Coming to the CCU is personally and professionally exciting for me. It provides the perfect combination of scientific excellence, coupled with an environment rich in collaborative endeavours extending both building and also Cambridge-wide, all with the ultimate aim to improve diagnosis and therapeutics*".



MRC Cancer Cell Unit Director, Professor Ashok Venkitaraman, added, "*I am delighted that Carla and Jacqui have chosen to join the Unit. As we complete almost a decade of research since our formation, I am sure that they will both make valuable contributions to the Unit which will enable us to continue to deliver new insights into the pathogenesis and treatment of cancer*".

Other news

Award for Venkitaraman group researcher

Dr Ferdinandos Skoulidis, from the Venkitaraman group, has won the Medical Research Society's Young Investigator Award at its Meeting for Clinical Scientists in Training which was held in February. The prize was awarded for Ferdinandos' presentation on '*Germline Brca2 heterozygosity promotes Kras^{G12D}-driven carcinogenesis in a murine model of familial pancreatic cancer*', and was presented by MRS chairman Professor Steven O'Rahilly.

CCU Scientists at AACR Special Conference

Researchers from the both the Jones and Fitzgerald groups presented a poster on the '*Validation of epithelial stem cells in human squamous esophagus and generation of a 3D organotypic model*' at the American Association for Cancer Research Special Conference on Stem Cells, Development and Cancer held in Canada, in March.

Rebecca Fitzgerald wins NHS Innovation Challenge prize



Congratulations to Rebecca Fitzgerald and her team, who were awarded an NHS Innovation Challenge Prize this month. These prizes have been created

to recognize and reward ideas that tackle some of the most challenging areas of healthcare, and are judged by an expert panel of medical scientists, industry professionals, and innovators. Rebecca's work on developing the new 'Cytosponge' test for the diagnosis and monitoring of the pre-cancerous condition Barrett's oesophagus was recognised by the panel. As well as providing clinical benefits, the Cytosponge should also deliver cost savings for the NHS by reducing the number of endoscopies required by patients and allowing the diagnostic process to take place in a primary care setting such as a GP's surgery.

Health Minister, Lord Howe, added his congratulations saying, "*We need to support innovation in the NHS, not suffocate it. In every hospital, GP practice and clinic we need to ensure innovation can flourish by supporting clinicians to develop new ways of thinking and delivering care to benefit patients and the NHS. Innovation is essential to help the NHS modernise by delivering more for less – improving the quality of care for patients whilst at the same time saving money.*"

Rebecca was been awarded £50,000 in prize money which will go towards developing the Cytosponge further, and accelerating its use in general practice.



Cytosponge shown in both capsule and sponge form

Success for the Gnanapragasam group



The Translational Prostate Cancer research group led by Dr Vincent Gnanapragasam has celebrated a number of scientific achievements recently. Firstly an abstract submitted by Clinical Research Fellow Naveen Kachroo to the British

Association of Urological Surgeons Annual Meeting has been selected to be presented in the Best Academic Paper session. Naveen has also been awarded a Fellowship from The Urology Foundation, and in April took the runner's up spot

in the Royal Society of Medicine Urology Section meeting prize for his short paper presentation "*Systematic review identifies 3 key predictive biomarkers in prostate cancer*". He was also recently awarded the BASO-ACS (British Association of Surgical Oncology - Association for Cancer Surgery) prize for his presentation at the Association of Surgeons in Training conference on "*Prognostic value of the number of positive core biopsies in prostate cancer*".

Congratulations are also due to group member Dr Satoshi Hori who has been awarded an MRC Clinical Training Fellowship.

CCU at Cambridge Biomedical Campus event

May saw the Cambridge Biomedical Campus development hold its first public event. A number of Research Centre staff were able to attend an evening of presentations and networking, and hear about the plans for transforming the Addenbrooke's Hospital site into a world-leading centre for healthcare-related research, education, and patient care. Among the speakers at the event held at the CRUK Cambridge Research Institute were Professor Sir Bruce Ponder (Cambridge University), Dr Gareth Goodier (Cambridge University Hospitals NHS Foundation Trust), and MRC CCU's Dr Rebecca Fitzgerald.

Also speaking at the event, Biomedical Campus Project Director Jeanette Walker highlighted the importance of research institutions such as the

Hutchison/MRC Research Centre, CRUK CRI and MRC LMB which had the potential to attract commercial organisations to the wider site in order to co-locate with them, and the opportunities for collaboration which this would create.

Further information about the plans for the Biomedical Campus can be found on the website: www.cambridge-biomedical.co.uk



*Plans for the Cambridge Biomedical Campus
(Image credit CPPLC&LPT)*

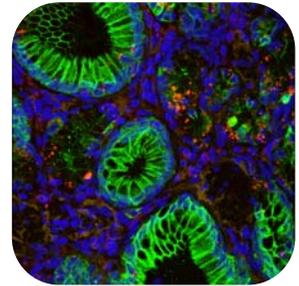
Hutch at Cambridge Science Festival



including numerous schools groups. Visitors were also able to about to find out about the variety of life sciences research taking place in Cambridge through numerous posters, as well as examine many of the Zoology Museum's weird and wonderful exhibits.

The Cambridge Science Festival took place this March, and as part of this the Research Centre was able to participate in the Graduate School of Life Sciences Poster and Image Exhibition.

The event was held in the Zoology Museum in Cambridge, and the Research Centre was represented by Dr Pierre Lao-Sirieix from the Fitzgerald group. His image of the oesophagus (a previous winner of our own photography competition, and shown to the right) was viewed by hundreds of visitors



Arrivals and departures

We are delighted to welcome Pooja Sharma and Alex Crooks, who join the Venkitaraman group as a Research Associate and Research Assistant respectively.

We also wish Ami Cull, David Sorrell, and members of the Itzhaki, Coleman, Laskey and de la Cueva Mendez research groups every success in their careers since leaving the Research Centre.

Hutch scientists in the media



Collaborative research into the behaviour of stem cells by Professor Ben Simons and CCU group leader **Dr Phil Jones** is profiled in the current issue of Cambridge University's Research Horizons magazine. A pdf version of the full article can be found [here](#).

Research on tumour drug-resistance from a recent publication by **Dr Paul Edwards**, and colleagues from the Babraham Institute, was reported in various local press outlets, including the Cambridge News.



Research work undertaken by the Cambridge Molecular Therapeutics Programme (part of the **Venkitaraman** group), in collaboration with the biotech company Phylogica has resulted in the formation of a new company. The creation of the new drug discovery venture Phenomica was widely reported in the business press including Business Weekly.

Recent publications

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Single-molecule analysis of genome rearrangements in cancer. Pole JC, McCaughan F, Newman S, Howarth KD, Dear PH, Edwards PA. *Nucleic Acids Res.* 2011 Apr 27. [Epub ahead of print]

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Integrative analysis of array-comparative genomic hybridisation and matched gene expression profiling data reveals novel genes with prognostic significance in oesophageal adenocarcinoma. Goh XY, Rees JR, Paterson AL, Chin SF, Marioni JC, Save V, O'Donovan M, Eijk PP, Alderson D, Ylstra B, Caldas C, Fitzgerald RC. *Gut.* 2011 Apr 12. [Epub ahead of print]

Hes6 is required for actin cytoskeletal organization in differentiating C2C12 myoblasts. Malone CM, Domaschenz R, Amagase Y, Dunham I, Murai K, Jones PH. *Exp Cell Res.* 2011 Jul 1;317(11):1590-602.

Acute sensitivity of the oral mucosa to oncogenic K-ras. van der Weyden L, Alcolea MP, Jones PH, Rust AG, Arends MJ, Adams DJ. *J Pathol.* 2011 Jan 5. doi: 10.1002/path.2853. [Epub ahead of print]

Geminin escapes degradation in G1 of mouse pluripotent cells and mediates the expression of oct4, sox2, and nanog. Yang VS, Carter SA, Hyland SJ, Tachibana-Konwalski K, Laskey RA, Gonzalez MA. *Curr Biol.* 2011 Apr 26;21(8):692-9.

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Does metabolite deficiency mark oncogenic cell cycles? Venkitaraman AR. Cell. 2011 Apr 29;145(3):337-8.

From crystal-packing to molecular recognition: prediction and discovery of a binding site on the surface of Polo-Like Kinase 1. Sledz P, Stubbs CJ, Lang S, Yang YQ, McKenzie GJ, Venkitaraman AR, Hyvönen M, Abell C. Angew Chem Int Ed Engl. 2011 Mar 29. doi: 10.1002/anie.201008019. [Epub ahead of print]

A vertebrate N-end rule degron reveals that Orc6 is required in mitosis for daughter cell abscission. Bernal JA, Venkitaraman AR. J Cell Biol. 2011 Mar 21;192(6):969-78.

A mitotic function for the high-mobility group protein HMG20b regulated by its interaction with the BRC repeats of the BRCA2 tumor suppressor. Lee M, Daniels MJ, Garnett MJ, Venkitaraman AR. Oncogene. 2011 Mar 14. [Epub ahead of print]

Design and application of a confocal microscope for spectrally resolved anisotropy imaging. Esposito A, Bader AN, Schlachter SC, van den Heuvel DJ, Schierle GS, Venkitaraman AR, Kaminski CF, Gerritsen HC. Opt Express. 2011 Jan 31;19(3):2546-55. doi: 10.1364/OE.19.002546.

G-quadruplex-binding benzo[a]phenoxazines down-regulate c-KIT expression in human gastric carcinoma cells. McLuckie KI, Waller ZA, Sanders DA, Alves D, Rodriguez R, Dash J, McKenzie GJ, Venkitaraman AR, Balasubramanian S. J Am Chem Soc. 2011 Mar 2;133(8):2658-63.

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