

## Hutchison/MRC Research Centre

# Newsletter

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

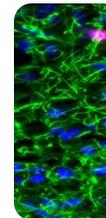
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Winter/Spring 2013

[www.hutchison-mrc.cam.ac.uk](http://www.hutchison-mrc.cam.ac.uk)

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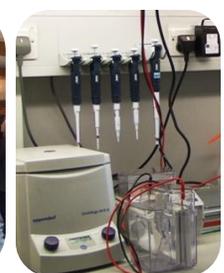
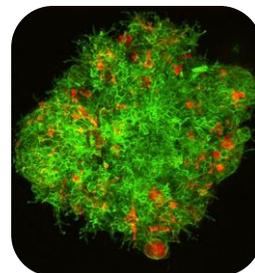
## MRC Centenary Celebrations Begin!



### Message from the Directors

Welcome to the new year issue of the Hutchison/MRC Research Centre newsletter. This edition puts a spotlight on the MRC Centenary, and the range of events and activities that are being planned around it. And as usual we have also highlighted some of the recent achievements of our research staff and students.

Professor Ashok Venkitaraman  
Professor Bruce Ponder  
Joint Directors, Hutchison/MRC  
Research Centre



This year marks the one hundredth anniversary of the foundation of the Medical Research Council (MRC) in the UK. Initially established as the Medical Research Committee in 1913, since then the MRC has funded 29 Nobel prize winners, and MRC scientists have been at the forefront of all areas of biomedical research, from regenerative medicine to cancer, and infectious disease to nutrition. A number of events and activities will be taking place over the course of this year to celebrate the MRC's achievements in medical research over the past one hundred years. And although the Research Centre and the MRC Cancer Cell Unit haven't been around for quite as long as the MRC as a whole (we only celebrated our tenth birthday last year!), plans are well under way for our own centenary-related events.



We'll be teaming up with our colleagues in the CRUK Cambridge Institute for the **Cambridge Science Festival**, to create a cancer research-focussed exhibit in the MRC-sponsored Biology Zone. The Biology Zone will be open on the 16<sup>th</sup> and 17<sup>th</sup>

March, so if you'd like to find out more about how cancer research has evolved and developed over the years, and the state of the art techniques we use today, do come and visit us! Full details can be found on the Cambridge Science Festival website: [www.cam.ac.uk/sciencefestival/](http://www.cam.ac.uk/sciencefestival/)

And along with other MRC Units and Institutes in the UK, the MRC Cancer Cell Unit will be holding an open day during the **MRC Science Open Doors week** (20-26<sup>th</sup> June). Keep an eye on both

the Research Centre and MRC CCU websites for more details.

As well as sharing our scientific achievements with the public, the MRC Centenary has also allowed further investment in biomedical research to occur. The MRC has created one off Centenary Awards, to enable the best of its early career stage researchers to explore new areas or build on existing research. We are delighted that our newest MRC CCU group leaders Dr Christian Frezza, Dr Carla Martins, and Dr Jacqui Shields were awarded £30,000 to investigate the effect of p53 mutations on the tumour micro-environment and develop a possible metabolic signature for lung cancer invasion. This collaborative project utilises their individual expertise in cellular biochemistry, mouse modelling, and stroma and lymphatic function, and hopes to produce insights which will improve our understanding of the disease progression process in lung cancer. Smaller funding awards for training and career development were made to Alessandro Esposito, Ferdinando Skoulidis, Siong-Seng Liao, Caryn Ross-Innes, and Marina Popliteeva.

MRC Centenary Awards have also been made to MRC-funded graduate students Kevin Cheng and Roberta Azzarelli, who are based in Dr Anna Philpott's group in the Department of Oncology. Roberta is currently located at the National Institute for Medical Research (NIMR), and this award will facilitate her joining the Philpott group in September to work on post-translational regulation of neuronal differentiation in embryonic stem cells.

For more information on the MRC Centenary visit the microsite: [www.centenary.mrc.ac.uk/](http://www.centenary.mrc.ac.uk/)

100 years of life-changing discoveries



## Rebecca Fitzgerald awarded NIHR Research Professorship



We are delighted to announce that MRC Cancer Cell Unit group leader, Rebecca Fitzgerald, has been awarded a National Institutes for Health Research (NIHR) Research Professorship. These highly competitive Professorships aim to strengthen research leadership in the UK and promote the effective translation of 'bench to bedside' research.

Rebecca's Professorship will support a research programme focussed on improving outcomes from oesophageal cancer through innovative screening and surveillance tests. Cancer of the oesophagus is a global problem with a high mortality due to late diagnosis, and Rebecca plans to extend her novel approach for detecting precancerous cells in Barrett's oesophagus to molecular tests for early detection of squamous cell cancer of the oesophagus. For higher risk cases, the Fitzgerald team are developing molecular imaging tools to define areas for biopsy and treatment.

Commenting on her appointment, Professor Fitzgerald said, "*I feel very honoured to have received this award which provides significant funding and support to help advance some of the laboratory work on early detection of oesophageal cancer into patients. This will dovetail with my MRC programme and I am excited about the new opportunities that this brings*".

**NHS**  
National Institute for  
Health Research

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## Professor Bruce Ponder returns to the Research Centre



On stepping down as Director of the CRUK Cambridge Institute, Professor Sir Bruce Ponder has moved his office back to the Hutchison/MRC Research Centre, together with his PA, Jean Miller, and secretary, Brenda Wright. They are based on the third floor of the Research Centre. Bruce's small lab group will remain for the time being in the Cambridge Institute, where they are working on the mechanisms of polygenic susceptibility to breast and lung cancer, and have close interactions with the computational biology groups in the Institute.

Bruce remains as Emeritus Professor, Head of the University Department of Oncology, and Director of the Cambridge Cancer Centre. He will continue in these roles until a successor (or successors) are identified. He has been reappointed as a Gibb Fellow of Cancer Research UK, which brings with it a programme grant to support his research. Bruce is looking forward to closer interactions with several of the groups in the Research Centre who share his interests around disease mechanisms

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## Fitzgerald group take research innovation to China



Last December saw Professor Rebecca Fitzgerald, and research group members Dr Pierre Lao-Sirieix and Dr Xinxue Liu, undertake a research visit to China. Part of their visit involved attending the UK-China Lung/Oesophageal Cancer Symposium, which was held in Beijing, and jointly organised by Cancer Research UK and the Chinese Academy of Medical Sciences. The symposium was aimed at fostering collaborations between British and Chinese laboratory and clinical scientists, and Rebecca was an invited speaker presenting on the subject of “*Early detection of oesophageal cancer and application of novel screening methods*”.

The group were also able to use their time in China to further a clinical research collaboration that has recently been established with the Cancer Institute and Hospital, Chinese Academy of Medical Sciences (CICAMS), one of the country's leading cancer research and clinical facilities. China has a significantly higher incidence of the squamous cell carcinoma form of oesophageal cancer, compared to the rest of the world, and it is the fourth most common cause of cancer death in the country. The Chinese government is investing heavily in early detection, and is currently funding an endoscopic screening programme that screens up to 70,000 patients a year. However this huge endeavour still barely scratches the surface of the problem. The NIHR-funded clinical study will aim to assess the feasibility and accuracy of administering the Cytosponge (the cell collection device developed by the Fitzgerald group) coupled with biomarkers as a screening tool for dysplasia and early cancer of the squamous oesophagus, compared with the "gold standard" of endoscopy combined with Lugol's iodine staining to highlight areas for biopsy and histopathological analysis. The Cytosponge can be used in a primary care setting, and Rebecca and her group hope to establish that it could be a cost effective alternative to endoscopy, which could be used for population-based screening for oesophageal squamous cell carcinoma. Commenting on their trip, Dr Pierre Lao-Sirieix said, "*This visit was very helpful to cement the collaboration and determine the practical details. Our biomarkers discovery work, funded by the Evelyn Trust and the NIH, is on-going in the laboratory. We are now submitting an ethics application and if all goes well we hope to perform a pilot study this spring, with a view to performing a full study in 2014*".

For more information on the Cytosponge device and its use in population-based screening, visit the Fitzgerald group pages on the MRC CCU website [mrc-ccu.cam.ac.uk/our\\_research/Rebecca\\_Fitzgerald/index.html](http://mrc-ccu.cam.ac.uk/our_research/Rebecca_Fitzgerald/index.html)

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## Arrivals and departures

We would like to welcome new graduate student Mateja Schorbia (Martins group) to the Research Centre, and welcome back Professor Sir Bruce Ponder, Jean Miller, and Brenda Wright.

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## Other news

### Research Centre Annual Retreat Poster Competition

The Hutchison/MRC Research Centre Annual Retreat took place on the 7<sup>th</sup> December last year, at the Imperial War Museum Duxford. As usual the day featured a wide range of scientific presentations and a poster competition. Congratulations to graduate student Jamie Weaver (Edwards/Fitzgerald groups), who won first prize in the competition with his poster on "*Characteristics of the oesophageal adenocarcinoma genome*". We hope that Jamie finds his prize of £750 for training and conference attendance, helpful for his future career.

Second prize in the competition was jointly awarded to Dr Mathew Lakins (Shields group) and Dr Massimiliano di Pietro (Fitzgerald group), while third prize went to Dr Emma Kerr (Martins group).

## Christian Frezza awarded new research grant

MRC Cancer Cell Unit group leader, Dr Christian Frezza, has been awarded a pump-priming grant by the Cambridge Cancer Centre. The award of £50,000 will be shared between Christian, and his collaborators Dr Eugenia Piddini (CRUK/WT Gurdon Institute) and Dr Pietro Cicuta (Cambridge University Department of Physics).

The grant will kick-start an ambitious cross-disciplinary collaboration aimed at elucidating the role of metabolism in modulating tumour-promoting cell interactions. This is a poorly characterised yet important area, that cannot be addressed without a multidisciplinary approach. The collaboration between the three groups will bring together a unique set of skills, which encompasses biochemistry, metabolomics, cell biology, state of the art time-lapse imaging, engineering for customised cell migration assays, and sophisticated image processing for cell shape analysis. This project is therefore well placed to tackle this fundamental aspect of cancer biology, and this award will provide the means of initiating it.




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## MRC CCU scientist short-listed for new MRC Award

The MRC launched its new CEO award scheme late last year to recognise contributions from employees for outstanding effort and commitment to both their work and the MRC. We were delighted that Dr Pierre Lao-Sirieix (Fitzgerald group) was shortlisted in the Outreach category, and was a runner-up in this section. We offer our congratulations to all the eventual winners.

# Hutch scientists in the media

**BBC NEWS HEALTH**  
13 January 2013 Last updated at 10:25

## Pill-sized scanner images gullet

Doctors have made a pill-sized device that can take detailed microscopic images of inside the gullet.

It is hoped the US technology could become an easier way of screening people for a condition called Barrett's oesophagus, which can lead to cancer.

Unlike current imaging techniques, the device can be used while the patient is conscious and takes only a few minutes.

The device has been tested in a small number of patients so far. **Nature Medicine reports**

Although researchers at Wellman Center for Photomedicine at Massachusetts General Hospital in Boston say the device has potentially wide application, it could be particularly useful for Barrett's oesophagus where many people do not realise they have it, but there is no easy way to screen for it.

In those with the condition, the cells in the lower gullet become abnormal due to chronic acid reflux, which puts them at a higher risk of developing cancer of the oesophagus.

Doctors can screen those at risk using an endoscope - a flexible tube containing a tiny video camera - but this is unpleasant and usually has to be done under sedation.

**Tiny capsule**

The new device is contained in a capsule about the size of a multivitamin pill connected by a thin wire.

Within the capsule is a rapidly rotating laser tip which emits infrared light that is then reflected back from the lining of the oesophagus.

The image doctors see on the screen is a 3D landscape showing far more microscopic detail than can be seen with endoscopy.

When the patient swallows the capsule it is carried down the oesophagus in the same way any piece of food would be then once it reaches the stomach, it can be pushed back out using the

**Top Stories**

- Bank warns inflation 'is way high'
- Blaze-accused father 'hit mistress'
- Pope thanks public for 'sympathy'
- Sars-like virus 'spreads in people'
- Kate bikini photos 'not scandalous'

**Features**

- Roses are red...  
But is romantic love really bad for people?
- I'm not Bent!  
The benefits and burdens of being called Barack
- Going rogue  
What makes an officer of the law turn criminal?
- Young, free... and careful  
How women around the world stay safe on a night out

**Most Popular**

Shared	Read	Video/Audio
Kate bikini photos 'not scandalous'	1	
Blaze-accused father 'hit mistress'	2	
Bank of England: 'Recovery in sight'	3	
Psyche 'bullied' into points swap	4	
How safe do women feel on a night out?	5	
See slug 'disposable penis' surrounds	6	

Prof Rebecca Fitzgerald was quoted in a [BBC News article](#) on the development of a new imaging device which may have a role to play in the detection of Barrett's oesophagus.

**1913 - 2013** 100 years of life-changing discoveries

MRC Medical Research Council CENTENARY 1913-2013

Home What's happening Latest news History MRC home page

**MRC Centenary Timeline**  
100 years of life-changing discoveries

Timeline navigation: 1913, 1914

Prof Rebecca Fitzgerald also features as part of the MRC centenary timeline on the new [MRC centenary microsite](#).

**1913 - 2013** 100 years of life-changing discoveries

MRC Medical Research Council CENTENARY 1913-2013

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**2010**

### Markers for early detection of cancer found.

MRC Cancer Cell Unit scientists have discovered that proteins in the body called mini-chromosome maintenance proteins (MCMs) can flag up early-stage cancers or precancerous cells at risk of developing into tumours. MCM testing is now being developed for the early detection of cervical, lung and colorectal cancers. In a related development, Dr Rebecca Fitzgerald is working on an inexpensive and simple cell-sampling device and antibody test for a precursor condition for oesophageal cancer. This could soon lead to a national screening programme to pick up cancer before it's too late to save patients' lives. Watch a video of Rebecca talking about the new test.

Timeline navigation: 2000, 2002, 2004, 2006, 2008, 2010, 2012, 2014, 2020

## Recent publications

*Structural analysis of the genome of breast cancer cell line ZR-75-30 identifies twelve expressed fusion genes.*  
Schulte I, Batty EM, Pole JC, Blood KA, Mo S, Cooke SL, Ng C, Howe KL, Chin SF, Brenton JD, Caldas C, Howarth KD, **Edwards** PA. BMC Genomics. 2012 Dec 22;13:719. doi: 10.1186/1471-2164-13-719.

*DNA Methylation as an Adjunct to Histopathology to Detect Prevalent, Inconspicuous Dysplasia and Early-Stage Neoplasia in Barrett's Esophagus.*

Alvi MA, Liu X, O'Donovan M, Newton R, Wernisch L, Shannon NB, Shariff K, di Pietro M, Bergman JJ, Ragunath K, **Fitzgerald** RC. Clin Cancer Res. 2013 Jan 22. [Epub ahead of print]

*Endoscopic TriModal imaging and biomarkers for neoplasia conjoined: a feasibility study in Barrett's esophagus.*

Boerwinkel DF, Di Pietro M, Liu X, Shariff MK, Lao-Sirieix P, Walker CE, Visser M, O' Donovan M, Kaye P, Bergman JJ, **Fitzgerald** RC. Dis Esophagus. 2012 Oct 15. doi: 10.1111/j.1442-2050.2012.01428.x. [Epub ahead of print]

*The role of treatment modality on the utility of predictive tissue biomarkers in clinical prostate cancer: a systematic review.*

Kachroo N, **Gnanapragasam** VJ. J Cancer Res Clin Oncol. 2013 Jan;139(1):1-24. doi: 10.1007/s00432-012-1351-7.

*Evidence for downregulation of the negative regulator SPRED2 in clinical prostate cancer.*

Kachroo N, Valencia T, Warren AY, **Gnanapragasam** VJ. Br J Cancer. 2012 Nov 20. doi: 10.1038/bjc.2012.507. [Epub ahead of print]

*Tracking cells in their native habitat: lineage tracing in epithelial neoplasia.*

Alcolea MP, **Jones** PH. Nat Rev Cancer. 2013 Feb 7. doi: 10.1038/nrc3460. [Epub ahead of print]

*From tumor prevention to therapy: empowering p53 to fight back.*

**Frezza** C, **Martins** CP. Drug Resist Updat. 2012 Oct;15(5-6):258-67. doi: 10.1016/j.drug.2012.10.001.

*HIF-independent role of prolyl hydroxylases in the cellular response to amino acids.*

Durán RV, Mackenzie ED, Boulahbel H, **Frezza** C, Heiserich L, Tardito S, Bussolati O, Rocha S, Hall MN, Gottlieb E. Oncogene. 2012 Oct 22. doi: 10.1038/onc.2012.465.

*Serine is a natural ligand and allosteric activator of pyruvate kinase M2.*

Chaneton B, Hillmann P, Zheng L, Martin AC, Maddocks OD, Chokkathukalam A, Coyle JE, Jankevics A, Holding FP, Vousden KH, **Frezza** C, O'Reilly M, Gottlieb E. Nature. 2012 Nov 15;491(7424):458-62. doi: 10.1038/nature11540.

*Complex regulation controls Neurogenin3 proteolysis.*

Roark R, Itzhaki L, **Philpott** A. Biol Open. 2012 Dec 15;1(12):1264-72. doi: 10.1242/bio.20121750.

*Using a fragment-based approach to target protein-protein interactions.*

Scott DE, Ehebauer MT, Pukala T, Marsh M, Blundell TL, **Venkitaraman** AR, Abell C, Hyvönen M. Chembiochem. 2013 Feb 11;14(3):332-42. doi: 10.1002/cbic.201200521.

*Expression of LY6D is induced at the surface of MCF10A cells by X-ray irradiation.*

Kurosawa M, Jeyasekharan AD, Surmann EM, Hashimoto N, Venkatraman V, Kurosawa G, Furukawa K, **Venkitaraman** AR, Kurosawa Y. FEBS J. 2012 Dec;279(24):4479-91. doi: 10.1111/febs.12034.

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