Cancer research at Bristol is a vibrant cross-disciplinary community which focuses on core strengths in cancer cell biology, genetic and lifecourse epidemiology and health services research. In partnership with Bristol NHS Trusts and the University of West of England, we aim to accelerate the identification and translation of research into clinical practice for the early detection and treatment of cancer.

Cancer is a leading cause of death and morbidity worldwide, and with the ageing of the population and changes in lifestyle such as increasing obesity, its incidence is likely to continue to rise. Research in Bristol, lead by internationally recognised experts in the field, is looking to enhance early diagnostics, screening and prevention of a variety of cancers.
THIS MONTH’S SHOWCASED ARTICLE

The ‘dnet’ approach promotes emerging research on cancer patient survival

Schematic workflow of dnet in discovering and interpreting the patient-survival gene network:

Julian Gough is Professor of Bioinformatics in the Department of Computer Science. This paper from his lab based in the new Life Sciences Building offers completely model insights and, to any cancer aficionado, some of the highlighted genes leap as key players. Others may indeed offer new drugs and targets as the authors propose. - Paul Martin, Theme Lead

We propose that patient survivalness can be addressed at cross-tumour levels. Like the cancer hallmarks, there might exist common molecular programs (likely acting as gene networks) controlling cancer patient survivalness, irrespective of tumour type, age and gender. Patient survivalness is probably not merely a statistical product of correlation with survival time, but also is a cumulative outcome of mutated genes that are rooted in their evolutionary history. Any attempts to address these questions will reshape our clinical practice in cancer prognosis, diagnostics and even therapy.

To promote hypothesis-driven research on survivalness, we present an integrative approach called ‘dnet’. This method supervises both mutation and survival data, in the context of prior knowledge of the network, to search for a core gene network controlling cross-tumour cancer patient survival. This survival network is robust to data removal and is statistically significant as estimated under data randomisation. On evaluating performance on survival gene identifications, our method is superior to existing network-based methods (although most of them are not designed for this purpose). Via integrating with ontology and evolution knowledge, dnet is also able to clarify the survival network
with relevance to: prognostic and druggable power, tumour heterogeneity and commonality, and evolutionary origins. The ‘dnet’ approach thus represents a significant advance in emerging research on cancer patient survivalness, especially in an ever-maturing era of personalised medical genomics.

Applying dnet to analyse all of the ‘TCGA’ mutation and clinical data of >3,000 patients covering multiple tumour types, we uncovered a network of genes (see figure above) for which most mutations are significantly correlated with patient survival. This survival network has community structure responsible for distinct aspects of tumour hallmarks. It is insensitive to the removal of single tumour types, is not an artifact of data characteristics, can be used for characterising relationships between tumour types and is generally informative for characterising survivalness for individual tumour types as well. The kind of survival network would not be identified via other commonly used methods or indeed attempted. Genes in this core network seem to be far more informative for prognosis when used in combination than when used individually, and are potentially druggable in the clinic; we also show this druggability is universal for cancer-specific survival networks even though their gene members differ greatly.

**EVENTS**

**RED Medical lunchtime surgery series - How best to respond to reviewers comments**
26 March 2015, 13:00, Medical Sciences Building, room C4

**Abigail Smith: Resolving conflicts between replication and transcription / Asha Bayliss: Trafficking of Vascular Endothelial Growth Factor Receptor 2**
27 March 2015, 13:00, Medical Sciences Building C42
**BioDynamics Workshop**  
15 April 2015, John McIntyre Conference Centre, The University of Edinburgh

**One Health Bristol Conference**  
25 April 2105, Langford

**Prof. Sherif El-Khamisy, University of Sheffield**  
29 April 2015

**Festival of Postgraduate Research**  
30 April, 14:30, Anson Rooms, Richmond Building

**David Church: title tbc**  
Project title: *Mechanistic and biomarker evaluation of POLE proofreading mutations in cancers.*  
19 May 2015, 13:00 (Clinical Science Fellow, Health Foundation, University of Oxford)

**Show and Tell**  
To note: the next Show and Tell session being organised by Population Health will take place in May / June time. Details will be confirmed closer to the time.

**Mr Ramsey Cutress, Faculty of Medicine, University of Southampton**  
2 June 2015

**MRC Integrative Epidemiology Unit: Mendelian Randomization Conference**  
22 June 2015, 9:00, Victoria Rooms, Bristol

**Dr Peter Campbell (Head of Cancer Genetics and Genomics, Wellcome Trust Sanger Institute): title tbc**  
3 December 2015, 16:00, The Seminar Room, Second Floor, Oakfield House

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**NEWS**

- Heartfelt congratulations to [Richard Martin](#) and [Caroline Relton](#) who are in receipt of a major CRUK programme grant entitled *Reducing the burden of cancer: causal risk factors, mechanistic targets and predictive biomarkers*. Along with several co-investigators across the School of Social and Community Medicine, researchers from Manchester University and the International Agency for Research in Cancer in Lyon will be involved. Expected to start June 2015 for a period of 5 years, the programme seeks to strengthen causal inference in cancer epidemiology through the application of Mendelian randomization approaches and the exploration of epigenomic and metabolomic intermediates in 6 types of cancer (lung, prostate, renal, breast, ovarian, and head and neck). The CRUK have awarded £4.1 million and recognised this as ‘an ambitious programme with potential for high impact’. The team leading the programme was also recognised by the CRUK as ‘being at the cutting edge of developing and deploying Mendelian randomization methodology’. The programme will be affiliated to the [MRC Integrative Epidemiology Unit](#).
The incidence of prostate cancer among men of Afro-Caribbean origin is higher than in white men, they are more likely to be diagnosed as emergencies and their mortality rates are higher. Until now, it has been unclear why these disappointing outcomes exist. Researchers at the Universities of Exeter, Bristol and College London studied the preferences and choice of more than 500 men who were presented with a realistic hypothetical prostate cancer investigation scenario while attending general practices in Bristol. Each man was presented with a description of a prostate cancer symptom and estimated risk of the disease. The team found that preference for investigation was lower in black men irrespective of the risk presented in the scenario. This difference was strongest in relation to the scenarios associated with the lowest risk level, with just 44 per cent of black males opting for investigation compared with 91 per cent of white males. In both groups, the most common reason for declining investigation was low risk, but significantly more black men stated that they simply did not want to know if they had cancer. The study, published on 2 March in the British Journal of General Practice (BJGP), was supported by the NIHR Collaboration for Leadership in Applied Health Research and Care South West Peninsula (PenCLAHRC). Dr Jonathan Banks, one of the study’s co-authors from the Centre for Academic Primary Care, said: “The findings help us understand some of the reasons why black males have a lower preference for investigation in prostate cancer. We hope these findings may lead to new ways to help educate the black community and health professionals about symptoms and the importance of early investigation.”


Brain tumour tissue is removed every day by surgeons but very few patients know they can donate brain tumour tissue to research. A new national campaign launched on 24 February seeks to raise awareness for patients and healthcare professionals about donating brain tumour tissue and helping researchers find a cure for this disease. The campaign is led by leading medical researchers and the charity, brainstrust. A recent survey indicated that only 30 per cent of brain tumour patients are offered the opportunity to consent for their brain tumour tissue to be used in research. Yet a recent poll by brainstrust suggested that over 90 per cent of patients would be keen for their tissue to be used. Researchers will be able to use the donated brain tumour tissue for research into better treatments and to help find a cure for brain cancer.

MINI MD

The UoB Mini MD programme is a new initiative to give early career basic scientist researcher with an interest in cancer an opportunity to learn about clinical issues, treatments and pathways. PhD students beginning basic science programmes related to cancer will spend several half day sessions over a two week period visiting outpatient clinics, surgical theatre sessions and teaching sessions on clinical issues to gain a better understanding of the potential relevance to patients of their current research, help them shape the science questions to be better aligned with clinical issues, and build the relationships with clinicians to drive forward translational research. The programme will be run as a pilot beginning in October 2015, with limited places but with a view to expanding it in the coming years. There are no costs associated with this programme.
Current PhD students are invited to send an application by email to Dr Axel Walther, Prof Ann Williams, or Prof Paul Martin outlining their research aims and how participation in the programme would help their research. A brief statement of support from the supervisor is required, including an indication that the PhD student will be able to spend the time in the clinic.

**FUNDING OPPORTUNITIES**

A calendar of potential funding opportunities for Cancer has been set up via Research Professional which details the funding opportunity according to submission deadline for the whole year. This calendar is accessible via their website and will be updated automatically according to the search criteria for Cancer Studies and Oncology. Other areas can be added by request- please email the theme with suggestions and/or comments.

**British Medical Association Research Grants**

Aim to encourage and further medical research in a variety of subject areas, ranging from rheumatism and arthritis to cardiovascular disease, cancer and neurological disorders. The following awards are available: TP Gunton grant (£40,000) for proposals on public health relating to cancer; Strutt and Harper grant (£40,000) on improving the uptake of preventative measures.

Award Amount: £40,000               Deadline: 09-Mar-15
Department of Health

Programme Development Grants for Applied Research: Mesothelioma Themed Call
Aim to increase the rate and number of successful applications for a full programme grant by supporting the completion of the necessary preparatory work involved in a competitive stage-2 grant application. Development grants can support activities such as: evidence synthesis that might include modelling; selection or development of interventions or measures of outcome; pilot or feasibility studies to determine recruitment and participant retention rates, inform sample sizes calculations or optimise delivery of the intervention; demonstration of practical ability to undertake elements of the future programme, such as when complex data linkage is required; strengthening of existing collaborations with methodological experts necessary to deliver the proposed research programme.

Award Amount: £100,000                      Deadline: 10-Mar-15

Society for Pediatric Radiology Research and Education Foundation

Pilot Award
Aims to provide a higher level of support for pediatric radiology-related projects can be used to fund protected time. Applications should endeavor to focus on unique aspects of imaging expertise in improving health care in children, embrace broader cross boundary impact, including public policy or translational medicine, cultivate multidisciplinary cooperation, and provide opportunities for additional funding.

Award Amount: US$50,000                      Deadline: 15-Mar-15

Cancer Research UK

Multidisciplinary Project Award
Supports collaborations between cancer researchers and scientists from engineering or physical science disciplines. The research themes within remit for this award include: the direct application of physics, engineering, chemical or mathematical concepts to address the underlying physical processes of cancer, including tumour initiation, growth and metastasis; the development and translation of technologies for direct applications in, or a clear path to, a direct application in the prevention, diagnosis or treatment of cancer.

Award Amount: £500,000                      Deadline: 25-Mar-15

Cancer Research UK

Prospective Sample Collections Project Grants
Support prospective collections of samples associated with clinical trials as well as strategy enabling sample collections.

Award Amount: not specified                  Deadline: 25-Mar-15
**Cancer Research UK**

**Feasibility Study Project Grants**
Fund investigator-led studies testing aspects of feasibility, tolerability or efficacy.

Award Amount: £150,000  
Deadline: 25-Mar-15

**Cancer Research UK**

**Phase III Clinical Trial Grant**
Support studies for cancer treatment directed at the tumour, such as chemotherapy, radiotherapy and surgery, with the principal objective of improving survival. Grants are for a maximum of 10 years.

Award Amount: £100,000  
Deadline: 25-Mar-15

**Bone Cancer Research Trust**

**Research Grants**
Support novel research proposals that will lead to interventions to improve the time to diagnosis for patients with bone cancer. BCRT offers small grants worth up to £10,000, pump-priming grants of up to £30,000 and project grants of up to £75,000.

Award Amount: £75,000  
Deadline: 28-Mar-15

**Cancer Research Institute**

**Irvington Postdoctoral Fellowships**
Support young scientists at leading universities and research centres around the world who wish to receive training in cancer immunology. Projects should be hypothesis driven, mechanistic studies in both immunology and tumour immunology that directly impact understanding of the immune system’s role in cancer risk, tumour initiation, progression, metastasis, host response to tumours or the treatment of cancer.

Award Amount: US$164,500  
Deadline: 01-Apr-15

**Cancer Research UK**

**New Agents Committee Trial Grants**
Support early phase patient trials of new cancer treatments including combinations of treatments and radiotherapy.

Award Amount: £300,000  
Deadline: 03-Apr-15
Wellcome Trust

Research Career Development Fellowships in Basic Biomedical Science
Enable postdoctoral scientists to become independent research scientists and undertake research at an institution in the Republic of Ireland. Scientists must work across the remits of specific funding streams, including cellular, developmental and physiological sciences; genetic and molecular sciences; infection and immunobiology; neuroscience and mental health; population health.

Award Amount: not specified                           Deadline: 17-Apr-15

Worldwide Cancer Research

Project Grants
Support fundamental and translational research into the causes, mechanisms, diagnosis, treatment and prevention of cancer. Proposals that demonstrate a small clinical element as an essential part of a basic or translational research project may be permitted.

Award Amount: £250,000                           Deadline: 24-Apr-15

European Society for Medical Oncology

Translational Research Fellowships
Support research in oncology through training, career development and translational research projects. Each applicant must be: full or junior ESMO member, or apply for membership; an oncologist with at least one year experience in medical, radiation or surgical oncology; be under the age of 40; be proficient in English.

Award Amount: €72,000                           Deadline: 01-May-15

Cancer Research UK

Cancer Immunology Project Awards
Aim to to catalyse research and build the UK’s research base in cancer immunology by funding immunologists in non-cancer fields. Proposals may address any area of immunological research including any of the following key areas: cellular and molecular immunology; inflammation, allergy, transplantation and auto immunity; the immune response to infection; the interaction of immune cells with tissues; immunity and disease susceptibility or resistance.

Award Amount: £300,000                           Deadline: 18-May-15

NOTE: Paul Martin is on this CRUK panel and welcomes discussions with anyone thinking of applying to this call.
**Department of Health**

**Research for patient benefit – including mesothelioma themed call**

Supports high-quality research that will be of direct benefit to users of the NHS in England. Proposals covering a wide range of health service issues and challenges are encouraged, including:

- studies of the provision and use of NHS services;
- evaluations of the effectiveness and cost effectiveness of interventions;
- examinations of the resource utilisation of alternative means for healthcare delivery;
- scrutinising of innovations and developments;
- feasibility studies

In addition, funding is available for clinical and applied health research into mesothelioma, including prevention, earlier diagnosis, treatment and care.

Award Amount: £350,000                           Deadline: 21-May-15

**Medical Research Council**

**UK-Thailand joint health research call**

The scientific remit includes studies into Cancer, particularly those outlined below which are major causes of death in Thailand: Lung cancer: basic research to understand the disease mechanisms, and research and development related to biological markers for disease detection, monitoring and treatment; Cholangiocarcinoma: basic research on early diagnostic markers, and potential new more effective therapies; Oesophageal cancer: basic research related to disease development mechanism, and biological marker for treatment.

Award Amount: £444,000                           Deadline: 02-Jun-15

**Cancer Research UK**

**Population Research Committee Project Grants**

Support projects that address clinical and public health epidemiology, educational and behavioural research in areas of prevention, screening and early diagnosis, clinical trials methodologies or statistics, and secondary physical effects of treatment.

Award Amount: £300,000                           Deadline: 19-Jun-15

**Cancer and Polio Research Fund**

**Research Grants**

Support research into cancers, with particular reference to the causes, development and treatment of these diseases, or research into polio and other crippling diseases. Grants may be used for direct costs of research and to support research symposia or lectures for the dissemination of findings.

Award Amount: not specified                           Deadline: 15-Oct-15
Cancer Research UK

**CRUK and Bupa Foundation Cancer Prevention Fund**
Supports postdoctoral researchers and healthcare professionals who conduct research into behavioural and lifestyle changes that can prevent people from getting cancer. Applications must have the potential to be translated into practice or influence policy.

Award Amount: not specified  Deadline: 23-Oct-15

Leukemia and Lymphoma Research

**Bennett Fellowships**
Awarded to outstanding clinical and non-clinical qualified postdoctoral researchers to establish themselves as independent investigators in any aspect of haematological research relevant to the charity’s mission. Fellowships are up to five years in duration together with one research assistant or postdoctoral post.

Award Amount: not specified  Deadline: 01-Nov-15

Royal Society

**Research Professorships**
Enable world-class scientists to be relieved from teaching and administration duties in order to focus on research. Research in any of the natural and applied sciences, including medical science, engineering and interdisciplinary research, may be supported.

Award Amount: £1.1M  Deadline: 03-Nov-15

Cancer Research UK

**Clinician scientist fellowship**
This enables scientists to develop their clinical academic research career. The fellowship provides salaries for the fellow and one research assistant, and associated running expenses for up to four years.

Award amount: Not specified  Deadline: 20-Nov-15


Image caption: Diagram describing collider bias. a If we condition on circulating vitamin D levels (box), we could create an association of SNPs with confounders (dashed line). b If we condition on sun exposure (box), the association between SNPs and confounders is not generated because the SNPs are not associated with sun exposure (dashed line is removed).


Exogenous expression of VEGF cDNA from a VEGF promoter rescues the effect of SRPK1-KD on tumour growth in vivo. (a) Tumour growth curves for four groups of mice injected subcutaneously with the following stably transfected cells: open circles, control shRNA and VEGF165 plasmid; filled circles, SRPK1-KD and VEGF165 plasmid; open squares, control shRNA and empty vector; filled circles, SRPK1-KD and empty vector. *P<0.05. (b) Examples of tumour growth in all mice groups (tumours outlined in black).


Inhibiting LGR5 glycosylation results in reduced localisation within the cis-Golgi network. Confocal laser scanning microscopy Z-sections showing intracellular LGR5 expression in fixed and permeabilised (A) LoVo and (B) LS174t-LGR5 cells following 24 h treatment with DMSO control or 1 μg ml⁻¹ TMC.