Cancer Theme Newsletter

January-February 2016

University of BRISTOL
Elizabeth Blackwell Institute for Health Research

Royal College of General Practitioners Research Paper of the Year Award

Research led by Dr Jonathan Banks has resulted in an award- winning paper which demonstrates an overwhelming preference in members of the public for cancer testing, even when the risk of disease is as low as 1%. The project employed an original approach to engage patients in the research using iPads and vignettes. Patients were involved and engaged by researchers to discover patients' understanding and preferences for cancer diagnosis. The study, which explores views of patients, carries important messages for general practice about working in partnership with patients to discuss risks, treatments and diagnosis pathways.

For the full story, visit the Centre for Academic Primary Care website.

Banks J, Hollinghurst S, Bigwood L, Peters TJ, Walter FM, Hamilton W (2014). Preferences for cancer investigation: a vignette-based study of primary-care attendees. *The Lancet Oncology*. 15(2), pp232-40

New Director of Strategic Alliances

Prof Neil Williams has been appointed the new Director of Strategic Alliances for the Elizabeth Blackwell Institute for Health Research, with the responsibility for implementing the University's new Strategic Alliance Framework in which they will develop productive strategic partnerships with pharmaceutical and biotechnology industries. Together with Director of Regional Health Partnerships Prof Lars Sundström, they will ensure that Bristol's environment and capability for health and biomedical research translation is fully optimised.

Inside this issue:

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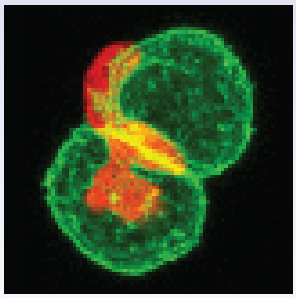
EVENTS



Wound healing and cancer

Body mass index and cancer - the challenges of a large-scale analysis of routinely collected primary care data

26 January 2016, 12.45-13.45. Dr Krishnan Bhaskaran (London School of Hygiene & Tropical Medicine), LG08, Canynge Hall

New and unexpected functions for NF-κB subunits in cancer

26 January 2016, 13.00-14.00. Professor Neil Perkins (Institute for Cell and Molecular Biosciences, Newcastle University), Lecture Theatre C42, Biomedical Sciences Building

Intestinal inflammation and colon cancer

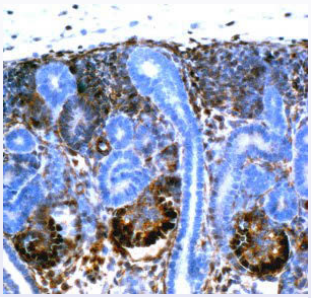
4 February 2016, 13.00-14.00. Professor Fiona Powrie FRS (Nuffield Department of Medicine, University of Oxford), Lecture Theatre C42 Biomedical Sciences Building

Decoding chromatin using chemical biology and proteomic approaches

9 February 2016, 13.00-14.00. Dr Till Bartke (Chromatin Biochemistry Group, MRC Clinical Sciences Centre, Imperial College London), Lecture Theatre C42, Biomedical Sciences Building

Translating genomic discovery into improved therapies for childhood brain tumours

16 February 2016, 13.00-14.00. Professor Steven Clifford (Northern Institute for Cancer Research, Newcastle University), Lecture Theatre C42, Biomedical Sciences Building



Expression of the WT1 gene in the developing kidney; positive cells stain brown

Fellowship Bootcamp 2016

16 February 2016, 12.00-17.00. Room 4.10 35 Berkeley Square. *Deadline for applications 25 January 2016.*

Chromosome dynamics

18 February 2016, 13.00-14.00. Dr Catherine Green (Nuffield Department of Medicine). Lecture Theatre C42, Biomedical Sciences Building.

Transformer proteins: functions for the alternative genome in breast cancer cell survival

23 February 2016, 13.00-14.00. Professor David Elliott (Institute of Human Genetics, University of Newcastle Upon Tyne), Lecture Theatre C42, Biomedical Sciences Building

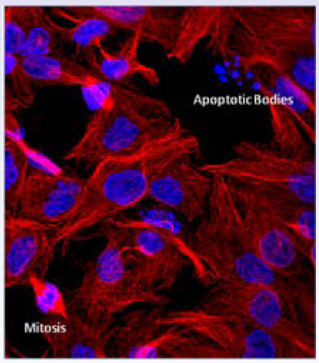
Professors Richard Martin & Caroline Relton
8 March 2016, 12.45-13.45. Professors Richard Martin & Caroline Relton (University of Bristol), LG08, Canynge Hall

Using zebrafish for in vivo cellular analyses and high-throughput screens
8 March 2016, 13.00-14.00. Dr David Lyons (Centre for Neuroregeneration, The University of Edinburgh), Lecture Theatre C42, Biomedical Sciences Building

South West Public Health Scientific Conference 2016
16 March 2016, 9.30-17.00. Mercure Bristol Holland House Hotel and Spa, Redcliff Hill, Bristol, BS1 6SQ

Surgical Trials Showcase 2016
18 March 2016, 9.00-17.00. M-Shed

Chris Jones, Institute of Cancer Research
10 May 2016, 1.00-14.00. Prof Chris Jones (Institute of Cancer Research), Lecture Theatre C42, Biomedical Sciences Building



Colorectal cancer cells

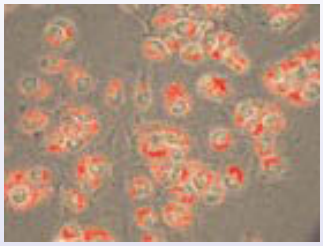
NEWS

An investment of £150,000 on behalf of the Elizabeth Blackwell Institute for Health Research, through its Wellcome Trust ISSF Award (match funded by the University of Bristol), will fund three new posts that will be openly available to help support all health and biomedical researchers across the University in their informatics needs. These posts will come into full effect in the early part of 2016, and will comprise:

i) A *Biomedical Research Computing Analyst* based in the Advanced Computing Research Centre who will enable researchers working with high throughput, multi-omic data and complex modelling to have enhanced access to the University's HPC and Research Data Facilities in order to generate, refine and optimise the research software they specifically need.

ii) A *Genome Informatician* located in the Life Science Building 'Omics Hub' with expertise in Galaxy software and who will support researchers analyse deep sequencing, RNA-seq and CHiP-seq

iii) A *Microscopy Image Analyst* based in the Wolfson BioImaging Facility in the Biomedical Sciences Building to help researchers with their image processing and analysis needs. Dr Stephen Cross has been appointed into this role and is expected to be in post on 1 February 2016.


Insulin-like growth factors in cancer

NEWS

The **Bristol Biobank**, funded by the David Telling Charitable Trust with stakeholders from the University of Bristol and University Hospitals NHS Foundation Trust, stores samples collected from patients and healthy volunteers for use in biomedical research. The samples form a biorepository to which researchers can apply for use in their research. The collection of a wide range of samples will provide a platform for research into complex conditions.

Researchers may request to deposit samples into the Biobank following the end of a NHS Research Ethics Committee approved study. Consent must have been taken using study specific documentation for the storage and use of these samples in research beyond the study. The team will also be happy to receive applications to deposit samples for specific projects you wish to set-up using Biobank permissions and documentation.

The Bristol Biobank is licensed by the Human Tissue Authority (licence 12512) to store human tissue for research and has ethics approval from Wales Research Ethics Committee 3 as a research tissue bank to collect and issue biomaterials for biomedical research across a range of therapeutic areas. If you are interested in finding out more about the opportunities of working with the Biobank please contact Manager Claire Matthews.

- **Grace Edmunds (CMM) has been awarded an EBI Clinical Veterinary Primer** to pursue research into *Proteomic analyses to assess the*

New translational research centre

The £5.3 million **Translational Biomedical Research Centre** (TBRC), currently under construction at Langford, aims to get research out of the laboratory and ensure patients worldwide can access ground-breaking treatments as quickly as possible. Funded by UoB, MRC and BHF, the centre's 'topping-out' was celebrated in September, led by the Centre's Director, Professor Raimondo Ascione.

TBRC will use experimental models relevant to human disease and anatomy and procedures will be tracked in living animals using non-invasive scanning techniques. This will help test new treatments to NHS standards while reducing the number of animals needed. It will operate under the One-Health concept for the benefit of people, animals and environment. This is a key development in the University's vision for a research culture that feeds directly and rapidly into tangible and lasting benefits for the health and welfare of humans and animals alike.

NEWS

effects of adenosine on CD8+ tumour-infiltrating lymphocytes: A step towards the restoration of effective anti-tumour immunity.

University Policy on Open Access to research publications

Senate has approved a mandate for the institutional policy on Open Access to research publications, and this will take effect from 1 October 2015. Academics and research students are required to deposit, at the point of acceptance from the publisher, eligible research outputs in the institutional repository (Pure). The mandate is to ensure that all research outputs that will be submitted to the post-2014 REF are eligible, under new requirements from HEFCE. Further information about the mandate and help available. For the full policy please see the Institutional Policy web page.

- **Adam Chambers, a higher surgical trainee** in the East Midlands Deanery and a recent Elizabeth Blackwell Clinical Primer fellow, has been awarded a **Clinical Research Training Fellowship by the Medical Research Council** (MRC). This highly competitive and prestigious fellowship is designed to support clinically active professionals within the UK to undertake a higher research degree.

Adam is aiming to specialise in bowel (colorectal) surgery with the goal of practising as an academic colorectal surgeon. He used his EBI Clinical Primer award to undertake a formal laboratory-based period of research, with the Colorectal Tumour Biology Group run by Professors Ann Williams and Chris Paraskeva. The MRC fellowship will allow him to combine his interests of colorectal cancer and inflammation by completing a PhD with the group. This will build on his work examining the role of inflammation and the response of bowel cancer to radiation.

- **Researchers at Bristol** can **recruit participants online** via ***Call For Participants***, an advertising platform focused on bringing opportunities for taking part in academic research to the general public. A dedicated notice board will advertise surveys, interviews and other research studies. The company will also provide support and guidance on how to advertise research and communicate to the public. To post an advert go to https://www.callforparticipants.com/researcher.

NEWS

- **Tissue damage has been implicated as a possible trigger in the development of various cancers**. Until now, little was known about how local wounding following cancer surgery, biopsy collection or ulceration, might impact on disease progression. A recent study, led by researchers from the Universities of Bristol and Århus, investigated how inflammatory cells react to cancerous wounds. The team first used zebrafish larvae that were genetically modified to sporadically produce pre-cancerous cells in their skin. They found that their inflammatory cells, primarily a type called neutrophils, were rapidly diverted from wounds to the pre-cancerous cells and this led to increased growth at the pre-cancerous site.

Results showed the process was dependent upon these inflammatory immune cells and was, at least in part, due to the release of a factor called prostaglandin-E_2 derived from the immune cells promoting cancer cell growth, which is, interestingly, a key target of the anti-inflammatory action of aspirin. In an adult Zebrafish model of chronic wounding, they also showed that repeated wounding led to a greater incidence of local melanoma formation.

NEWS

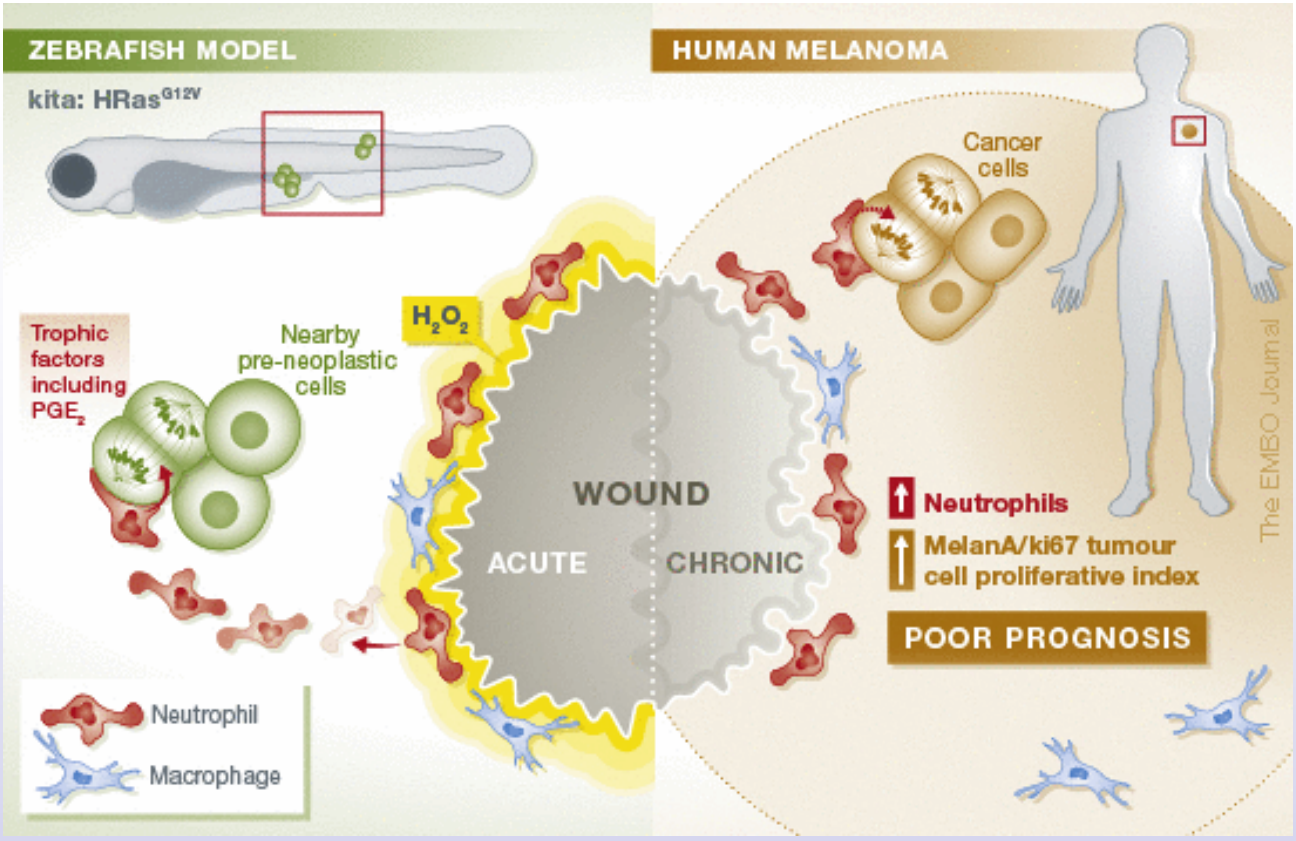
The Bristol lead was Prof Paul Martin, Main author of the paper was Nicole Antonio who graduated with a PhD from the School of Biochemistry in 2015.

Antonio N, Bønnelykke-Behrndtz ML, Ward LC, Collin J, Christesen IbJ, Steiniche T, Schmidt H, Feng Y, Martin P. (2015). The wound inflammatory response exacerbates growth of pre-neoplastic cells and progression to cancer. *The EMBO Journal*. 34, pp.2219-2236 (*see image below)*

Integrative Cancer Epidemiology Programme

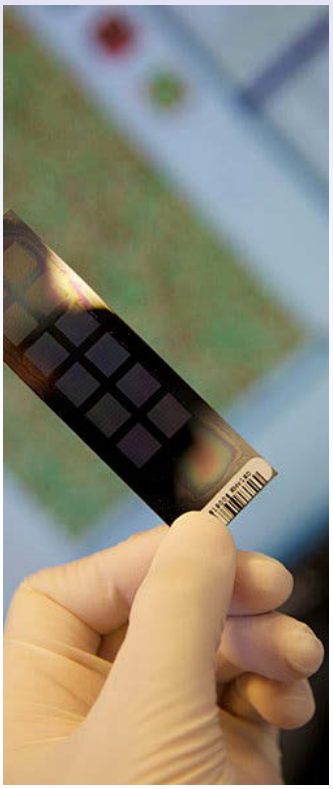
launched 21 October 2015

The £4.1M study will focus on new ways to prevent and predict cancer development and progression. Funded by Cancer Research UK (CRUK) and the University of Bristol, the five-year Integrative Cancer Epidemiology Programme (ICEP) will use advances in genetics and molecular technology to



The study reveals how innate immune cells, in particular neutrophils, that are initially drawn to a wound can subsequently be attracted away to nearby early- & late-stage cancer cells and drive their proliferation.

NEWS



understand the causes of the disease, and to inform the development of preventative interventions in people at risk of, or diagnosed with, cancer.

The programme will carry out research into identifying novel markers that accurately define cancer risk and prognosis by analysing large quantities of genetic data of populations.

Studies will include research into biomarker tests, which look at an individual's genetics and their risk of developing the disease, and could help improve early diagnosis and our ability to tailor treatments to patients. Other studies will focus on finding out if it is possible to confidently identify aspects of diet or lifestyle or physiology, which if altered, could help reduce the risk of cancer or its progression. Research will drill down to the molecular level to investigate new ways of intervening to prevent cancer. The programme is co-directed by Professors Richard Martin and Caroline Relton.

The Wellcome Trust new Strategic Framework

Wellcome's new framework consists of three complementary approaches across science, research and engagement with society:

1. Advancing Ideas. Wellcome will continue to respond to great ideas and inspired thinking that address the fundamental health challenges of our time.
2. Seizing opportunities. Wellcome brings ideas together to make a big difference, providing intensive support that creates real change. They identify times when concerted intervention can accelerate progress towards better health. Priorities will evolve as new challenges arise, drawing on insights from a rich history of achievement and a network of experts from different disciplines around the world. Initial priorities include Science education.
3. Driving reform. Wellcome changes ways of working so more ideas can flourish, leading by example and campaigning for wider reform. Their record in areas like open access to research results, public engagement, and research careers has earned us the credibility to challenge ways of working, and to propose better alternatives. One area on which reform will concentrate is Science to health- insights most improve health when they are applied to diagnosis, prevention and therapy. They will work to improve intellectual property and translation systems so business and academia are encouraged to innovate for better health.

MINI MD

The Mini MD programme trial was successfully completed at the start of the 2015-2016 academic year. This new initiative by the Cancer Theme, led by Dr Axel Walther, gave five postgraduate students the opportunity to spend time in various clinical settings. It is expected that experiencing clinical issues, treatments and pathways will help inform the projects of these early-career basic scientists. PhD students spent five days over three weeks 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. Initial feedback from the pilot programme has been very positive, and the Theme expects to expand it in the coming years. There are no costs associated with this programme. PIs with any students expected to start in October 2016 should contact Axel Walther for details.

ELIZABETH BLACKWELL FUNDING SCHEMES

EBI Workshops Funding

Support for interdisciplinary workshops in health research at a new or emerging interface between two or more disciplines. Applications are reviewed on a rolling basis.

EBI Catalyst Fund

Pump priming awards can support the most promising and ambitious ideas across the widest interdisciplinary boundaries. These projects will be identified largely through the running of workshops to explore new possibilities and identify the big questions. Applications are reviewed on a rolling basis.

Returning Carers Scheme

UoB has introduced a Returning Carers' Scheme (RCS) to support academic staff across all faculties in re-establishing their independent research careers on return from extended leave (16 weeks or more) for reasons connected to caring - such as maternity leave, adoption leave, additional paternity leave, or leave to care for a dependant.

The deadline for applications is 30 April and 31 October each year.

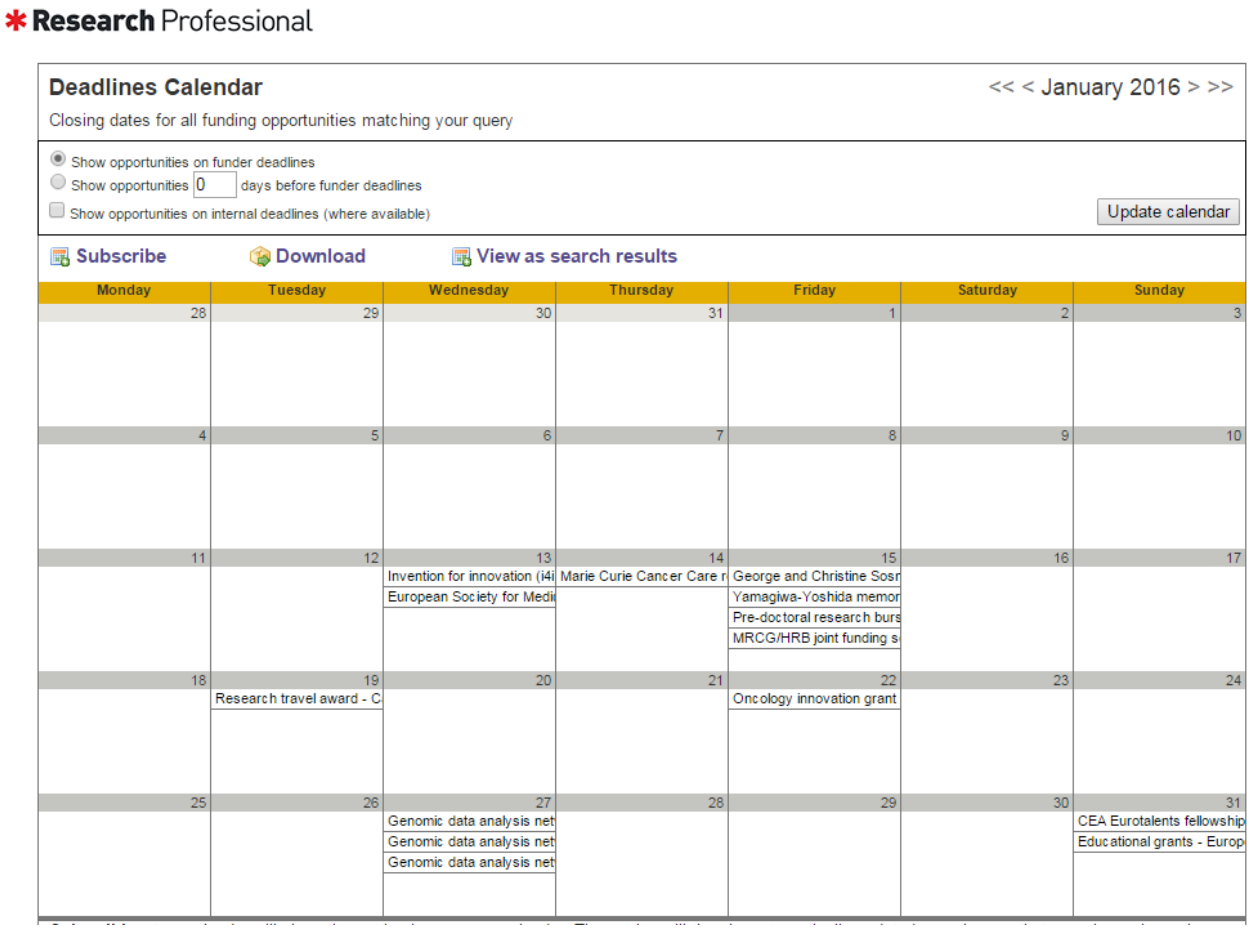
EBI Early Career Fellowships

Designed to support exceptionally talented and motivated researchers who wish to further their career by applying for prestigious, independent, externally-funded fellowships to be held at Bristol. This scheme is available to internal and external applicants.

Closing date: 12 February 2016

FUNDING OPPORTUNITIES

Calendar of potential Funding Opportunities for Cancer



A calendar of potential funding opportunities for cancer has been set up via Research Professional. Subscribing to a calendar will place the entries in your own calendar, which will update automatically according to pre-specified search criteria. Staff and students have **FREE** access to Research Professional online from all computers on the University network. You can create your own personalised funding opportunity e-mail alerts by registering with RP. Find out all about it on the RED website.

H2020: 2016-2017 Societal Challenges and LEIT Work Programmes published

The Societal Challenge Work Packages reflect the policy priorities of the EC and address shared concerns across Europe. The challenge-based approach is expected to bring together resources and knowledge across different fields, technologies and disciplines. Topic areas include Health, Food Security, Energy, Transport, Climate, Security and Inclusive, Innovative and reflective societies. A minimum of three partners from three different EU countries are required for both Societal Challenges and LEIT proposals, with a variety of deadlines over the next two years (starting February 2016). If you are

interested in discussing involvement in one of these calls, either as a lead or partner, or would like more details about what is available in your area of interest please contact Tiernan Williams.

Medical Research Council
Radiation oncology and biology - HIGHLIGHT NOTICE

Closing Date: none Award amount: depends on scheme

Proposals may cover the spectrum of research from studies that explore important cellular and molecular mechanisms, through to more translational medical research that would underpin the development of new health interventions. Research is particularly sought on improving the therapeutic effects of radiation in the treatment of cancer; studies of approaches to improve long term health and minimise morbidity after radiation exposure; understanding the fundamental processes associated with radiation injury from initial damage to pathogenesis, at the molecular, cellular, tissue and organ levels; research into the pathways involved in radiation carcinogenesis; development of novel biological approaches from radioprotection to treatment of radiation toxicity.

Cancer Research UK
Conferences and meeting support

Closing Date: none Award amount: £15,000

Supports specialist conferences and meetings that are run by CRUK grant holders and researchers. The lead applicant must be directly involved in organising the meeting or conference and it must take place in the UK. There are three types of funding from £100 to £15,000.

Laura Crane Youth Cancer Trust
Research grants

Closing Date: none Award amount: not fixed

On cancer affecting teenagers and young people between the age of 13 and 24. The aim is to bring increased understanding of cancer in this age group, better prevention, improved treatments and more saving of lives.

Cancer Research UK
Pioneer awards

Closing Date: none Award amount: £200,000

Support high-risk, high-reward research that, due to its novelty and lack of supporting data, would be unlikely to secure funding through traditional mechanisms. Projects must have a clear relevance to cancer and enable the exploration of novel ideas, which may lead to new discoveries or approaches.

Applications are invited from all backgrounds and vocations.

NIHR
Fellowship Programme

Closing date: 20-Jan-16 Award amount: not specified

Open to all professions and offer five levels of fellowship. Cover the salary, research costs, and training and development costs. The following are available on an annual basis:

- Doctoral Research Fellowship (PhD) funding
- Post-Doctoral Fellowship (<3 yrs)
- Career Development Fellowship (postdoc <7/8 yrs)
- Senior Research Fellowship
- Transitional Research Fellowship (postdoc <5 yrs)

University of Bristol
International Strategic Fund

Closing date: 22-Jan-16 Award amount: travel and subsistence

To establish or develop sustainable research partnerships across all university faculties, providing opportunities for postgraduates and researchers to develop their skills and international profile. Eligible partners include: Kyoto University; University of Heidelberg; Newton Fund countries; WUN Universities.

University of Bristol
University Research Fellowships

Closing date: 12-Feb-16 Award amount: not specified

Enable academic staff to carry out a dedicated research project lasting twelve months.

Cancer Research UK
Grand Challenge

Closing date: 12-Feb-16 Award amount: not specified (total budget £20M)

To tackle one of seven specific 'grand challenges':

1) To develop vaccines to prevent non-viral cancers
2) To eradicate EBV-induced cancers from the world
3) To discover how unusual patterns of mutation are induced by different cancer-causing events
4) To distinguish between lethal cancers that need treating, and non-lethal cancers that don't
5) To find a way of mapping tumours at the molecular and cellular level

6) To develop innovative approaches to target the cancer super-controller MYC
7) To deliver biologically active macromolecules to any and all cells in the body

Teams should be interdisciplinary and include a patient advocate. Commercial collaboration is encouraged. If you are likely to be part of a collaboration, please Zoe Holland.

Cancer Research UK
Population research catalyst award

Closing date: 19-Feb-16 Award amount: unspecified

Supports capacity building and collaboration, enabling research groups to unite to deliver impact. Aims to boost progress aligned to RCUK strategic priorities, build new collaborations and build capacity in population research. Applicants need to establish a hub across at least three locations creating a new collaboration with either national or international institutions, support a new research direction for the hub within RCUK strategic priority areas, commit to data sharing and plan for sustainability beyond the lifetime of the award.

Established independent researchers, industry researchers, clinicians, health professionals, non-clinical researcher and nurses are eligible to apply. Funding is flexible but applications may cover the following activities: central coordination of the hub across the collaborating institutions; discretionary fund to be spent on pilot or development studies for innovative and high risk work, or for bridge-funding exceptional early career researchers; recruitment of rising star or senior expert into the hub, where expertise is currently lacking; infrastructure, including data or sample curation and management; multidisciplinary research projects.

Cancer Research UK
Science committee programme grants

Closing Date: 23-Feb-16 Award amount: £2.5M

Provide long-term support for broad, multidisciplinary research where the aim is to answer questions spanning basic and translational research. Research proposals should address the following areas:

- basic biological research relating to cancer
- preclinical studies that will generate biological data to underpin therapeutic development
- biomarkers
- imaging
- radiotherapy research
- the application of engineering and physical sciences to cancer

Cancer Research UK
Programme foundation awards

Closing date: 23-Feb-16 Award amount: £1.5M

Enable cancer researchers with eight to 14 years' experience post-PhD to establish or further develop their independent research group. Research proposals should address the following areas:

- basic biological research relating to cancer;
- preclinical studies that will generate biological data to underpin therapeutic development;
- biomarkers;
- imaging;
- radiotherapy;
- the application of engineering and physical sciences to cancer

Cancer Research UK
Career development fellowship

Closing Date: 29-Feb-16 Award amount: salary for Fellow, RA, technician plus £25,000 for equipment

Offers support in setting up an independent cancer research group. Applications can cover any area of CRUK's funding remit, with the exception of drug discovery and clinical trials. Applicants should have between 3 and 8 years' postdoctoral research experience and should not have received prior fellowship funding to set up a research group or have a core-funded group leader position at one of CRUK's institutes.

Cancer Research UK
Bupa Foundation fund innovation grants

Closing Date: 29-Feb-16 Award amount: unspecified

Aim to catalyse new multidisciplinary collaborations and develop innovative research in cancer prevention via sandpit workshops. Applications are welcome from a wide range of disciplines. Applicants must be willing to engage with policymakers, community organisations, government agencies, business and other stakeholders. Early- and mid-career researchers are particularly welcome.

Cancer Research UK
Career establishment awards

Closing Date: 29-Feb-16 Award amount: salary for RA, technician plus £25,000 for equipment

Support new group leaders in enhancing their cancer research. Applications from any area of CRUK's funding remit, with the exception of clinical trials and drug discovery, will be considered. Applicants should have at least 3 and no more than 8 years' postdoctoral experience. If applicants are clinicians,

they should have completed their specialist training, obtained their PhD or MD and have at least three years of postdoctoral experience.

Cancer Research UK
Senior cancer research fellowship

Closing Date: 29-Feb-16 Award amount: salary for Fellow, 2 RAs, technician, PhD student plus £50,000 for equipment

This enables scientists to establish or further develop an independent cancer research group. Applications are considered from any area of the CRUK's funding remit, with the exception of drug discovery and clinical trials. Applicants should have between 8 and 14 years' postdoctoral experience. Clinicians must have obtained a PhD or MD and have extensive postdoctoral research experience.

Cancer Research UK
Multidisciplinary project award

Closing Date: 01-Mar-16 Award amount: £500,000

Supports collaborations between cancer researchers and scientists from engineering and physical science disciplines. The research themes within remit for this award include: direct application of physics, engineering, chemical or mathematical concepts to address the underlying physical processes of cancer, including tumour initiation, growth and metastasis; development of new transformational approaches or the translation of technologies for direct applications in, or a clear path to, a direct application in the prevention, diagnosis or treatment of cancer. Proposals across all engineering and physical science disciplines are welcome, and those which demonstrate potential clinical applicability are encouraged.

NIHR CLAHRC West
Implementation projects and research proposals

Closing date: 07-Mar-16 Award amount:

Funds will go towards projects that address two key issues: (a) Integrated working across the health system; (b) Effective and efficient optimal care

British Academy
Newton Mobility Grants / Newton Research Collaboration Programme

Closing date: 02-Mar-16 Award amount: unspecified

Eligible partner countries are Brazil, Malaysia, Mexico, South Africa, Thailand, Turkey. Provide support for international researchers based in a country covered by the Newton Fund to establish and develop

collaboration with UK researchers around a specific jointly defined research project. Are intended to strengthen the research capacity/capability of, and contribute to promoting economic development and social welfare in, the overseas country.

Cancer Research UK
Postdoctoral research bursary for clinical trainees

Closing Date: 08-Mar-16 Award amount: £35,000

This supports clinical trainees to undertake a research project after completion of a PhD. Applications from any area of CRUK's funding remit, with the exception of clinical trials and drug discovery, will be considered. Clinicians, postdocs, early career researchers and health professionals may apply. Applicants must hold a higher degree, such as MD or PhD, in a cancer relevant research area, a national training number at the time of the award, and have secured protected time and salary for their research.

British Medical Association
Research grants

Closing date: 09-Mar-16 Award amount: £50,000

Aim to encourage and further medical research in a variety of subject areas. Several awards are available:

- TP Gunton grant (£50,000): proposals on public health relating to cancer
- Helen H Lawson grant, (£50,000): proposals on novel technologies and IT in patient care, primary care or public health
- Strutt and Harper grant (£40,000): proposals on the development or implementation of clinical outcome measures

Lady Tata Memorial Trust
International awards

Closing Date: 15-Mar-16 Award amount: £35,000

Support individuals conducting leukaemia research, restricted to studies of the leukaemogenic agents, the epidemiology, pathogenesis, immunology and genetic basis of leukaemia, and related diseases. Priority will be given to those researchers intending to move to other centres with a view to establishing scientific collaboration between laboratories. One or more MPhil or PhD studentships may be granted, normally for two years with renewal possible for a third year on the basis of the eighteen-month progress report.

Bayer, DE
Grants4Targets

Closing Date: 31 Mar 16 Award amount: €125,000

Aims to encourage research on novel targets and disease-related biomarkers in the fields of oncology, gynecology, cardiology, haematology and ophthalmology. The following different types of grants, depending on the specifics of the target and its development phase will be awarded:

- support grants €5,000- €10,000 to advance research on targets that are at a very early stage of discovery
- focus grants €10,000- €125,000 for more mature ideas, such as addressing specific aspects of a target as a first step towards transferring it to the drug discovery process

Cancer Research UK

Drug development project award

Closing date: 06-Apr-16 Award amount: unspecified

Supports the development of new cancer treatments from preclinical development through to early phase patient trials. Funding is available for the following projects:

- development of potential new cancer treatments, including preclinical safety toxicology, drug manufacture, clinical formulation, assays, biomarkers, first in class, first in man, phase one clinical trials, combinations of unregistered and registered agents, early phase two proof of principle, non critical path trials with agents in active commercial development, and trials focusing on safety data, pharmacokinetics, biological endpoints and modulation of target biomarkers
- for approved novel agents, including managed preclinical and clinical development, compiling regulatory documents, trial sponsorship, and patients treated in a UK-wide network of clinical centres with world-leading scientific investigators and expertise in early clinical trials.

Established independent researchers, clinicians, industry researchers or non-clinical researchers may apply. Applicants are required to have a novel agent for cancer needing preclinical or clinical development.

Cancer Research UK

New agents committee trial grants and endorsements

Closing date: 08-Apr-16 Award amount: £150,000

Support early phase patient trials of new cancer treatments, including combinations of treatments and radiotherapy. Funding is available for the following projects:

- UK phase I/IIa oncology clinical trials of new treatments including new combinations and radiotherapy
- anything associated with the trial
- endorsement trials funded by companies or other funding bodies that have the same level

of confidential expert peer review
- early phase oncology clinical trials reviewed by the experimental cancer medicine centre Combinations Alliance joint steering committee

Applicants must be clinical investigators with early clinical oncology trials expertise based at a UK academic institution. Trials must be run and the patients recruited at UK clinical centres, and the proposed treatment or combination of treatments must be novel.

Department of Health

Health services and delivery research programme – researcher-led workstream

Closing Date: 14-Apr-16 Award amount: not specified

Supports research into the quality, effectiveness and accessibility of health services, including evaluations of how the NHS might improve delivery of services. For this round, proposals around the organisation and quality of care in the last year are encouraged. This includes research to identify cost-effective models of specialist palliative care and evaluation of other promising service innovations to provide joined up, person-centred care to those at the end of life. Applicants may submit either a standard outline proposal or an evidence synthesis full proposal. The workstream has a continued interest in the following research areas: surgical and implantable devices; primary care interventions; very rare diseases; long-term conditions in children.

NIHR will fund HEIs at a maximum of 80 per cent of full economic costs, except for equipment worth over £50,000, and non-HEIs at 100 per cent of full economic costs.

Worldwide Cancer Research

Project grants

Closing date: 29-Apr-16 Award amount: £250.000

Support fundamental and translational research into the causes, mechanisms, diagnosis, treatment and prevention of cancer. PIs should have at least three years' post-PhD research experience, or equivalent qualification.

British Council

BIRAX regenerative medicine initiative

Closing Date: 12-May-16 Award amount: £400,000

Enables scientists in both the UK and Israel to carry out collaborative research which furthers advances in the field of regenerative medicine. The scheme funds research that: explores the use of stem cell technology and tissue engineering in the context of fundamental disease processes; discovers new mechanisms that might be targeted to develop novel therapeutic applications of regenerative medicine;

advances understanding of stem cell biology, using lessons learnt from developing tissues and organs, or the mechanisms underlying cell fate and the principles of cellular pluripotency for the development of stem cell-based therapies; advances cell and gene therapies.

Cancer Research UK
Clinician scientist fellowship

Closing date: 23-May-16 Award amount: unspecified

Enable scientists to develop their clinical academic research career through a period of postdoctoral training, and will enable successful fellows to make the transition from doctoral research training to an independent clinical academic post. Applications will be considered from any area of CRUK's funding remit, with exception of clinical trials and drug discovery. The following areas will be considered, but fellowships are not restricted to one area and may span multiple areas of research:

- basic biological research relating to cancer
- preclinical studies
- biomarkers
- imaging
- radiotherapy research
- engineering and physical sciences applied to cancer
- population research

Cancer Research UK
Advanced clinician scientist fellowship

Closing date: 23-May-16 Award amount: unspecified

Offers clinician scientists the opportunity to develop independence and leadership in their field of academic research alongside their clinical practice. Applications will be considered from any area of CRUK's funding remit, with exception of clinical trials and drug discovery. The following areas will be considered, but fellowships are not restricted to one area and may span multiple areas of research:

- basic biological research relating to cancer
- preclinical studies
- biomarkers
- imaging
- radiotherapy research
- engineering and physical sciences applied to cancer
- population research

Cancer Research UK
Population Research Committee project grants

Closing date: 27-May-16 Award amount: £300,000

Support projects that address cancer aetiology, early diagnosis, epidemiology, behavioural research, cancer prevention, statistics and methodology. Applications are open to scientists, clinicians or healthcare workers based in UK universities, medical schools, hospitals and eligible research institutions. Applicants must have three years' postdoctoral experience or equivalent, or a tenured post.

PUBLICATIONS

Neville P, Waylen A & Cole-Hawkins H (2015). Head and Neck Cancer. *The SAGE Encyclopedia of Cancer and Society.* Colditz G (ed.). Thousand Oaks, CA: Sage, pp. 530-531

Love S & Hanley JG (2015). Protein interacting with C kinase 1 suppresses invasion and anchorage independent growth of astrocytic tumour cells. *Molecular Biology of the Cell*. Published online 14 October 2015.

Zeng L, Zielinska HA, Arshad A, Shield JP, Bahl A, Holly JMP & Perks CM (2016). Hyperglycaemia-induced chemo-resistance in breast cancer cells: role of the estrogen receptor. *Endocrine-Related Cancer*. 23, pp125-134

Banki F, Thomas S, Main B & Waylen A (in press). Communication of information about oral and oropharyngeal cancer: the quality of online resources: Quality of online resources for oral cancer. *Oral surgery*.

Metcalfe C, Peters T & Hamdy F (2015). *Prostate Testing for Cancer and Treatment (ProtecT) Study: Statistical Analysis Plan*. 1.0 ed. University of Bristol. 22 p.

Nunan R, Campbell J, Mori R *et al.* (2015). Ephrin-Bs Drive Junctional Downregulation and Actin Stress Fiber Disassembly to Enable Wound Re-epithelialization. *Cell Reports*. 13(7), pp1380–1395

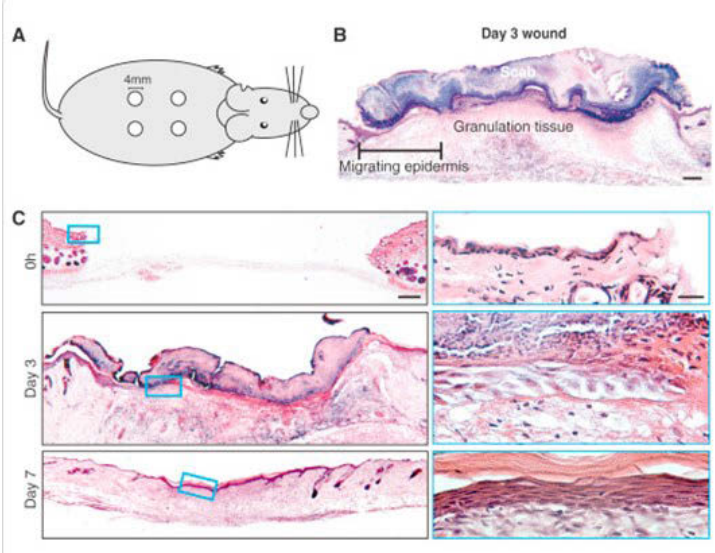


Image caption: Ephrin-B1 and Associated EphB Receptors Are Upregulated following Skin Wounding

(A) Schematic illustrates the location of full-thickness skin

(B) wounds (4 × 4mm diameter) made on adult mice. (B) H&E-counterstained image of a day 3 wound section illustrates the extent of epidermal migration.

(C) (C) H&E-counterstained sections from wounds at the indicated time points, with magnified insets of the epidermal tongue within the boxed areas, are shown.

Vieira GC, Chockalingam S, Melegh Z et al. (2015). LGR5 regulates pro-survival MEK/ERK and proliferative Wnt/β-catenin signalling in neuroblastoma. *Oncotarget*.

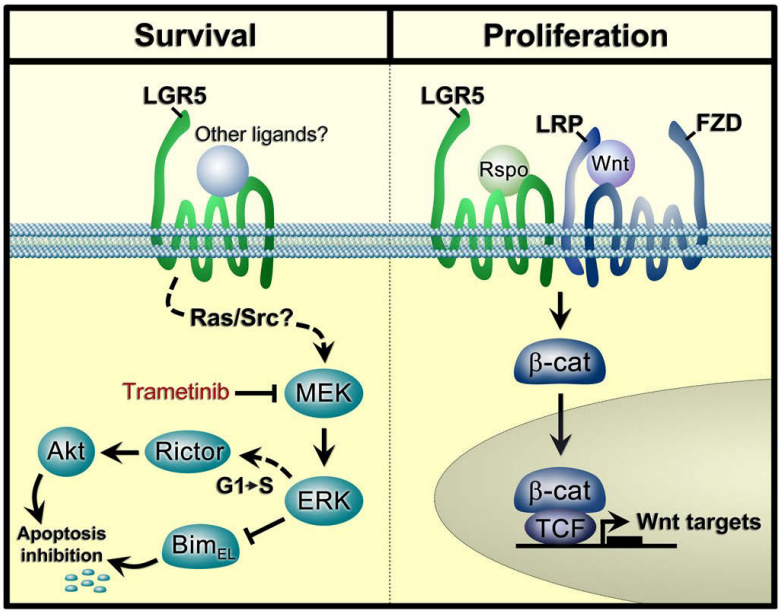


Image caption: A model showing regulatory modalities for LGR5 in neuroblastoma. Pro-survival signalling of MEK/ERK activities which are R-Spondin independent are shown on the left, and may be inhibited by MEK/ERK inhibitors such as Trametinib. Proliferative Wnt signalling in the presence of Wnt/Rspos is shown on the right. FZD: Frizzled receptors; LRP: Low Density Lipoprotein Receptor-Related Proteins, β-cat: β-catenin, TCF: T-cell factor/lymphoid enhancer factor.

Vincent EE, Sergushichev A, Griss T, *et al.* (2015). Mitochondrial Phosphoenolpyruvate Carboxykinase Regulates Metabolic Adaptation and Enables Glucose-Independent Tumor Growth. *Molecular Cell*. 60 (2), pp195-207

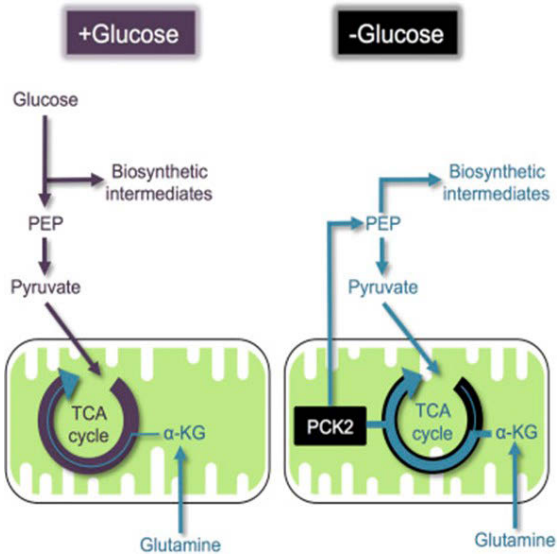


Image caption: a role for mitochondrial phosphoenolpyruvate (PEP) carboxykinase (PEPCK-M or PCK2) in mediating tumour cell adaptation to glucose limitation, which facilitates tumour growth in vivo.

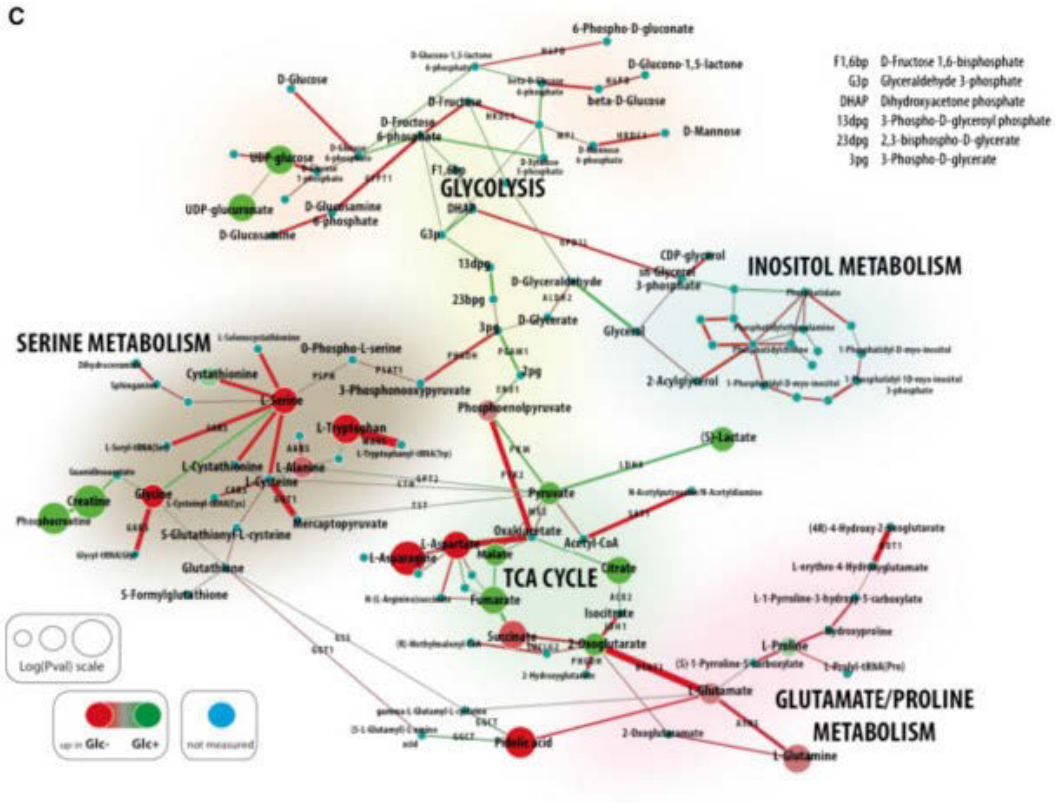
UK10K Consortium, Min JL, Timpson NJ, *et al.* (2015). The UK10K project identifies rare variants in health and disease. *Nature*. 526(7571), pp82-90

Potter S, Holcombe C, Ward JA, Blazeby JM & BRAVO Steering Group (2015). Development of a core outcome set for research and audit studies in reconstructive breast surgery. *British Journal of Surgery*. 102(11), pp1360-71

THIS ISSUE'S SHOWCASED ARTICLE

Mitochondrial Phosphoenolpyruvate Carboxykinase Regulates Metabolic Adaptation and Enables Glucose-Independent Tumor Growth

Vincent EE, Sergushichev A, Griss T, *et al.* (2015). *Molecular Cell.* 60(2), pp195-207



Cancer cells adapt metabolically to proliferate under nutrient limitation. Here we used combined transcriptional-metabolomic network analysis to identify metabolic pathways that support glucose-independent tumor cell proliferation. We found that glucose deprivation stimulated re-wiring of the tricarboxylic acid (TCA) cycle and early steps of gluconeogenesis to promote glucose-independent cell proliferation. Glucose limitation promoted the production of phosphoenolpyruvate (PEP) from glutamine via the activity of mitochondrial PEP-carboxykinase (PCK2). Under these conditions, glutamine-derived PEP was used to fuel biosynthetic pathways normally sustained by glucose, including serine and purine biosynthesis. PCK2 expression was required to maintain tumor cell proliferation under limited-glucose conditions in vitro and tumor growth in vivo. Elevated*PCK2* expression is observed in several human tumor types and enriched in tumor tissue from non-small-cell lung cancer (NSCLC) patients. Our results define a role for PCK2 in cancer cell metabolic reprogramming that promotes glucose-independent cell growth and metabolic stress resistance in human tumors.

Image caption: Integrated metabolic network analysis for A549 cells cultured in the presence (Glc+) or absence (Glc–) of glucose for 48 hr. The direction and magnitude of the fold change in enzyme expression or metabolite abundance between conditions is indicated on a red (enriched in Glc–) to green (enriched in Glc+) color scale. Enzymes are represented by edges (connecting lines between metabolites), with the color of the edge indicating the fold change and the thickness reflecting the significance of differential expression. Round nodes represent metabolites, with the differential abundance of each metabolite indicated by the size of the node. Major features of glucose deprivation identified by the network analysis are highlighted by bold titles and background shading.

Hackshaw L, Perry R, Leach V, Qandil S, Jeffreys M, Martin R & Lane A (2015). A systematic review of dietary, nutritional, and physical activity interventions for the prevention of prostate cancer progression and mortality. *Cancer Causes Control*. 26(11), pp1521-1550

Antonio N, Bønnelykke-Behrndtz ML, Ward LC, Collin J, Christensen IJ, Steiniche T, Schmidt H, Feng Y & Martin P (2015). The wound inflammatory response exacerbates growth of pre-neoplastic cells and progression to cancer. *EMBO Journal*. 34(17), pp2219-2236

Chamberlain C, Collin SM, Hounsome L, Owen-Smith A, Donovan, JL & Hollingworth W (2015). Equity of access to treatment on the Cancer Drugs Fund: A missed opportunity for cancer research? *Journal of Cancer Policy*. 5, pp 25-30

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Feng Y & Martin P (2015). Imaging innate immune responses at tumour initiation: new insights from fish and flies. *Nature Cancer Reviews*. 15(9), pp556-562

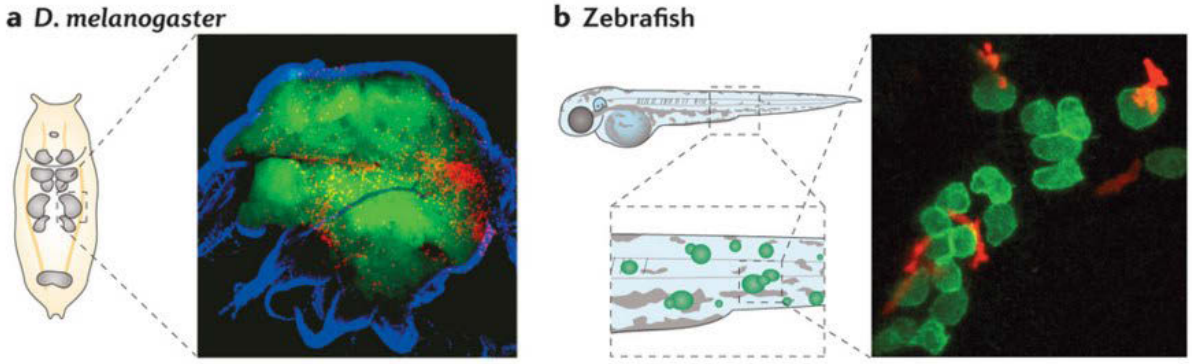
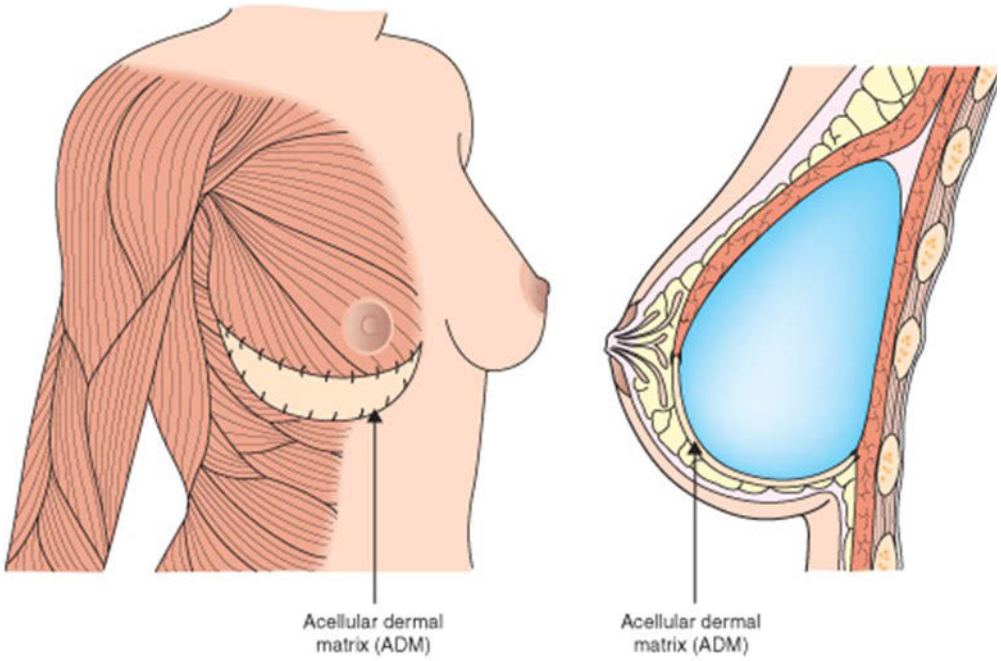


Image caption: Drosophila melanogaster *and zebrafish are both genetically tractable and so offer opportunities for insights into cancer that are not available in mice or humans.* D. melanogaster *has been instrumental in identifying several cancer genes and dissecting signalling pathways upstream and downstream of these genes, and zebrafish is providing insight in large part because of its capacity for large-scale genetic and small-molecule screens. Moreover, zebrafish tumours resemble human cancers at histological, transcriptomic and epigenetic levels. Perhaps of equal importance, both of these models are also translucent at various stages in their development, which enables imaging of the early stages of cancer initiation. (a) In* D. melanogaster, *most of these studies involve clones of transformed cells (green) within the epithelium of the larval imaginal discs, which will become the body parts of the adult fly. The imaginal discs are only amenable for imaging after removal from the larva and so live imaging of the haemocyte (red) response is only possible for brief periods, and these studies are generally of fixed whole-mount preparations. (b) Zebrafish embryos and larvae are accessible and translucent, and thus very amenable for imaging throughout development (although less so in the adult zebrafish without mutations for deleting pigment cells), and so interactions between immune cells (red) and pre-neoplastic cells (green) can be live imaged from when these cells first develop, and for long periods of up to 24 hours or more.* D. melanogaster *imaginal disc image courtesy of M. Vidal, Beatson Institute for Cancer Research, Glasgow. The zebrafish image is from the authors' own library.*

Ramani P, Sowa-Avugrah E & May MT (2015). High proliferation index, as determined by immunohistochemical expression of Aurora kinase B and geminin, indicates poor prognosis in neuroblastomas. *Virchows Archiv*. 467(3), pp319-327

Potter S, Browning D, Savovic J, Holcombe C & Blazeby JM (2015). Systematic review and critical appraisal of the impact of acellular dermal matrix use on the outcomes of implant-based breast reconstruction. *British Journal of Surgery*. 102(9), pp1010-1025

Image caption: Acellular dermal matrices (ADM) can be used to create a lower-pole sling, which augments the inferior aspect of the subpectoral pocket and provides inferolateral implant coverage. The ADM is sutured between the lower border of the pectoralis muscle and the chest wall



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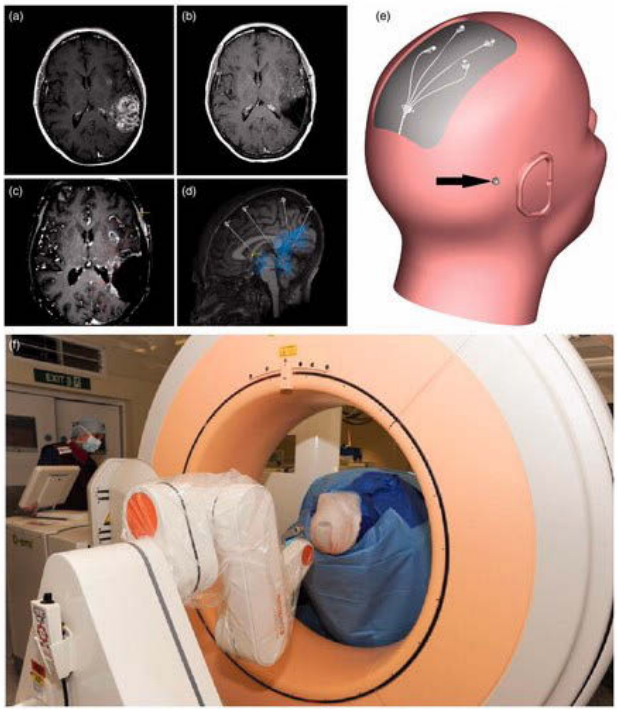

Image caption: Progression of both the left parietal and left insular tumor masses occurred following treatment with PCV (a). A macroscopic resection of the parietal lesion was undertaken prior to catheter implantation (b). In the four-week interval between resective surgery and catheter implantation, significant tumor progression occurred with new enhancement around the resection cavity as well as progression of the insular lesion (c). Using an in-house modification to neuro | inspire™ stereotactic planning software, the volume of tumor enhancement was delineated (shown in outline) and four catheter trajectories were planned (d) as well as the site for implantation of the TBAP (e; black arrow). Targeting accuracy was determined by performing intra-operative O-arm imaging (f).

Ramani P, Taylor S, Miller E, Sowa-Avugrah E & May MT (2015). High Phosphohistone H3 Expression Correlates with Adverse Clinical, Biological, and Pathological Factors in Neuroblastomas. *Journal of*

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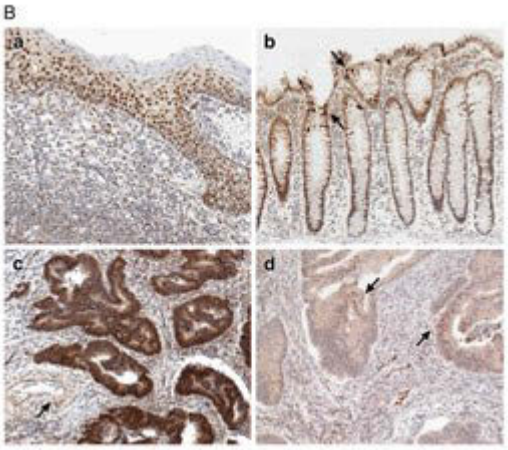

Image caption: (B) Immunohistochemistry (IHC) staining: (a) tonsil positive control for BCL-3 immunoreactivity yields strong nuclear staining of all but superficial keratinocytes, along with a scattered subset of inflammatory cells. (b) Normal colon showing moderate BCL-3 immunoreactivity in epithelial cell cytoplasm, with occasional strong positive cells (arrows). (c) Area of carcinoma showing strong cytoplasmic and nuclear BCL-3. The endothelium of the artery shows nuclear and cytoplasmic immunoreactivity (arrow). (d) In this tumour sample, the bulk of the tumour glands show weak or absent BCL-3 immunoreactivity, although foci of nuclear positivity are present (arrows). Original objective magnification; a×20; b–d×10.

Winters Z, Balta V, Afzal M, Llewellyn-Bennett R, Rayter Z, Cook J, Greenwood R & King M (2015). Long-term clinical and patient reported outcomes (PROs) after immediate latissimus dorsi breast reconstruction and adjuvant treatment in multicentre prospective cohort study. *European Journal of Surgical Oncology*. 41(6), ppS17–S18

Perks CM, Holly JM & Perks C (2015). Epigenetic regulation of insulin-like growth factor binding protein-3 (IGFBP-3) in cancer. *Journal of cell communication and signaling*. 9(2), pp159-66

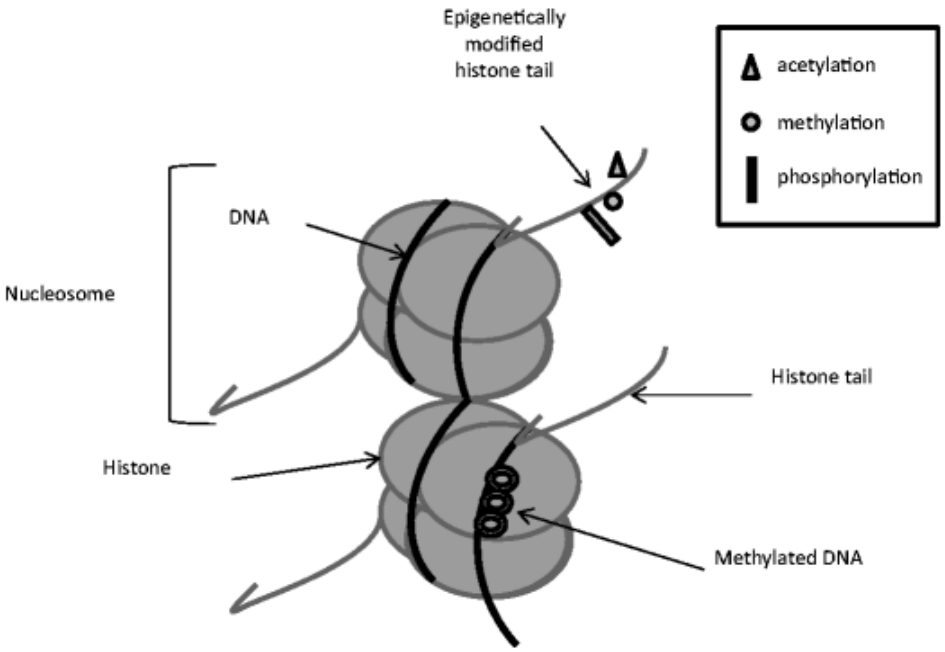

Image caption: Different types of epigenetic modifications. Histones can undergo phosphorylation (▮) methylation (○) and acetylation (△) amongst other modifications that are involved in chromatin remodelling and transcriptional regulation. DNA molecules are methylated which inhibits gene expression

Zeng L, Perks CM & Holly JMP (2015). IGFBP-2/PTEN: A critical interaction for tumours and for general physiology? *Growth Hormone and IGF Research*. 25(3), pp103-7

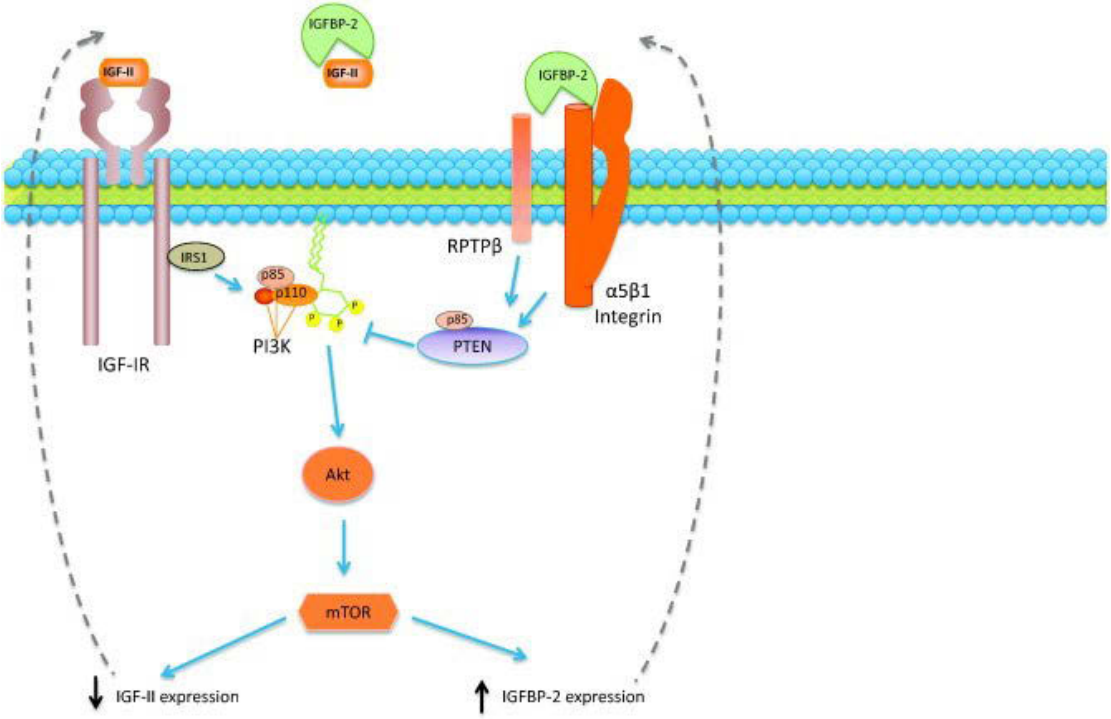

Image caption: A proposed autoregulatory feedback loop of IGFBP-2/PTEN interaction. Binding of IGF-II to the IGF-IR activates the PI3K pathway. Induction of PI3K activates Akt and mTOR signalling and leads to cell proliferation and cell survival. The regulatory subunit of PI3K, p85, also binds and activates PTEN through dephosphorylation. This increased PTEN subsequently blocks IGF-II production to avoid overstimulation. On the other hand, activated PI3K pathway induces IGFBP-2 expression, which when unbound to IGF-II, suppresses PTEN via an interaction with integrin receptors and/or the receptor protein tyrosine phosphatase β (RPTPβ). Thus the negative control of PTEN on PI3K signalling is counteracted. These feedback loops enable the extrinsic balance between IGF-II and IGFBP-2 to be tightly integrated to the intrinsic balance between PI3K and PTEN.

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Oltean S (2015). Modulators of alternative splicing as novel therapeutics in cancer. *World Journal of Clinical Oncology*. 6(5), pp92-95

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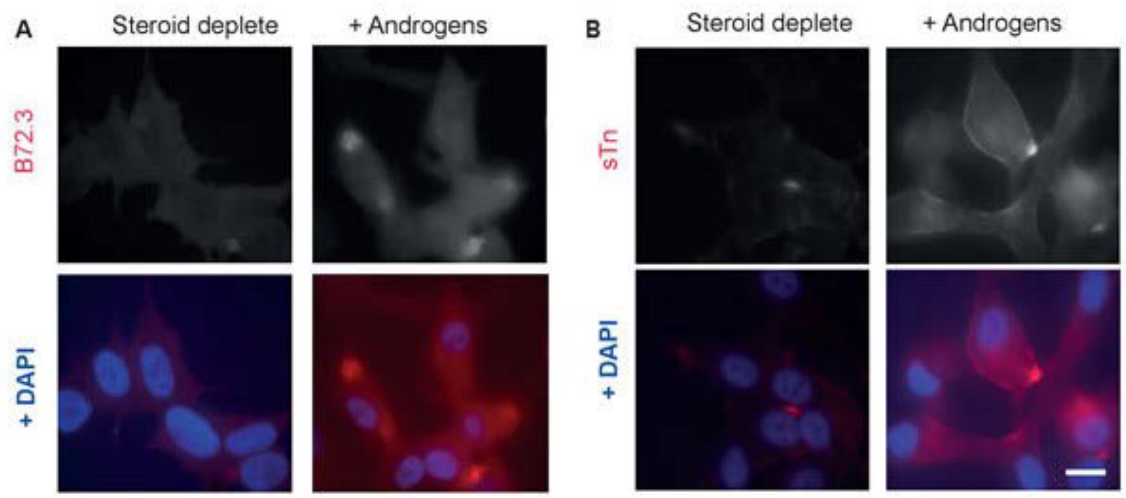

Image caption: The sialyl-Tn antigen is androgen-regulated in LNCaP cells. Analysis of glycosylation in LNCaP cells grown in the presence or absence of androgens (10nM R1881) for 72 hours by immunofluorescence. Androgen-mediated up-regulation of sTn antigen (formed by ST6GalNAc1 catalysed sialylation of GalNAc residues) is observed using two different antibodies A., B. Induction of sTn by androgens is inhibited by the presence of 10μm Casodex® (bicalutamide)

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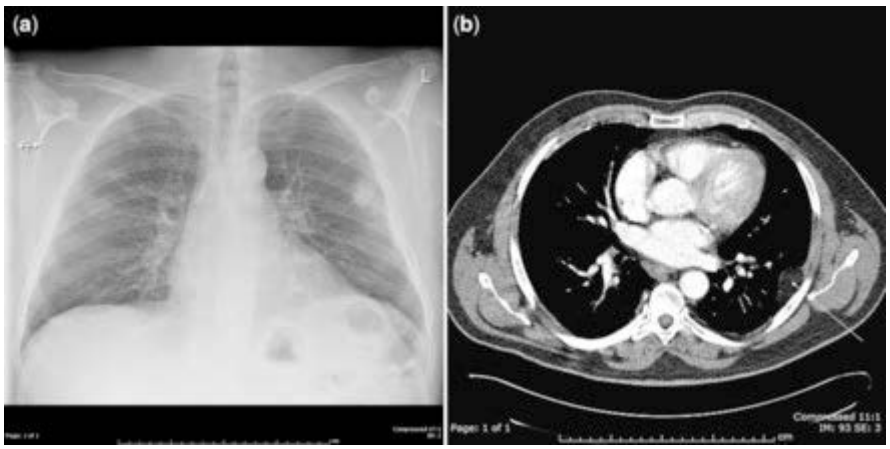

Image caption: (a) CXR demonstrating apparent mass in left lung field. (b) CT thorax (lung windows) demonstrating a pleural based fatty lesion 28 × 42 mm posterolaterally in the left mid chest (arrowed) which merges with the extrapleural fat. There are also multiple discrete pleural plaques in keeping with asbestos exposure.

Cancer Theme

University of BRISTOL

Elizabeth Blackwell Institute for Health Research

Theme Co-Lead:

Professor Paul Martin

Professor of Cell Biology

Theme Co-Lead:

Dr Axel Walther

Senior Lecturer and Head of Research, Bristol Cancer Institute

The Cancer Theme is led by a Steering Group:

- Catherine Brown, Research Development Administrator
- Dr Stephen Falk, *Consultant Clinical Oncologist*
- Dr Elinor Griffiths, *Senior Lecturer*
- Zoe Holland, RED lead
- Mr Andrew Hollowood, *Surgeon, University Hospitals Bristol*
- Prof Jeffrey Holly, *Professor of Clinical Sciences*
- Miss Ann Lyons, *General Surgery, North Bristol NHS Trust*
- Dr Nick Maskell, *Reader in Respiratory Medicine*
- Prof Richard Martin, *Professor of Clinical Epidemiology*
- Prof Catherine Nobes, *Professor of Cell Biology and Head of School (Biochemistry)*
- Prof Christos Paraskeva, *Professor of Experimental Oncology and Head of School (Cellular and Molecular Medicine)*
- Mr Rob Pitcher, *Clinical Lead of Cellular Pathology, North Bristol NHS Trust*
- Ms Anne Pully-Blank, *Director of Surgical Services, North Bristol NHS Trust*
- Prof Stefan Roberts, *Professor of Cancer Biology*
- Dr Stephen Robinson, *Haematological oncology, United Bristol Healthcare Trust*
- Dr Rebecca Smith, *Research Management, prostate cancer*
- Dr Nicholas Timpson, *Reader in Genetic Epidemiology*
- Prof Ann Williams, *Professor of Experimental Oncology*