Cancer Network Newsletter

September - October 2018

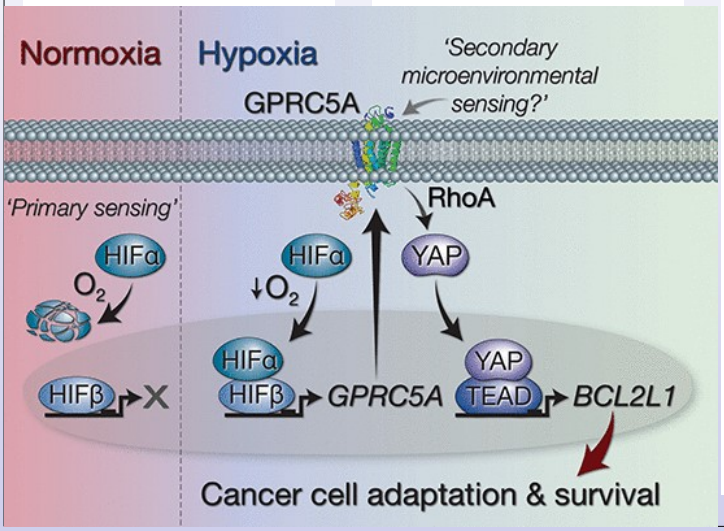
University of BRISTOL
Elizabeth Blackwell Institute for Health Research

Hypoxia could eliminate cancers

A method of targeting cancer without harming healthy tissue has been discovered by a Cancer Research UK-funded team led by Dr Alexander Greenhough and Profs Ann Williams and Chris Paraskeva.

Hypoxia occurs during the development of many common cancers and drives their progression and spread; it arises as tumours often grow faster than their blood supply, causing oxygen deprivation, which forces cancer cells to adapt — thus makes their behaviour more aggressive. The team sought to understand how cancer cells adapt to hypoxic conditions. Using human cancer cells grown in dishes and proteomics techniques, they examined all the proteins that are 'switched on' by cancer cells in hypoxia. The results identified a new signalling mechanism that could be therapeutically targeted to kill cancer cells without harming the surrounding normal cells. Using genetic techniques to stop cancer cells 'switching on' a specific receptor (GPRC5A) when oxygen levels are low triggered cancer cell death. This work advances our knowledge of hypoxic cancer cell behaviour and take us a step closer towards developing novel therapies that could allow clinicians to exploit hypoxia and improve patient treatments.

Identifying the proteins most important for cancer cell survival in hypoxia that are also 'druggable' has remained an unmet challenge. GPCR receptors are considered to be among the best drug targets for many diseases; further investigations would look into whether this receptor serves as a biomarker for more aggressive cancers that are resistant to therapy, and whether it has roles in other diseases where hypoxia or inflammation is implicated.



Greenhough A *et al.* (2018). Cancer cell adaptation to hypoxia involves a HIF-GPRC5A-YAP axis. *EMBO Molecular Medicine*. E8699.

Inside this issue:

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EVENTS

The way we die now - The over medicalisation of death in the 21st century
26 October 2018, 18.00 - 19.00, We The Curious, Anchor Road

Coffee Morning with Brigstow
29 October 2018, 9.00 - 12.00, Library Room, Ground Floor Royal Fort House

Engagement Bites: Tips & Tricks for Public Engagement
31 October 2018, 13.00 - 14.00, Knowle West Media Centre, Seminar Room, Beacon House

Statistics Clinic - 31 October 2018
31 October 2018, 14.00, - 15.30, SM3 Mathematics Building

Sir Anthony Epstein lecture: Nuclear transfer and its contribution and understanding of cell differentiation
1 November 2018, 17.00 - 19.00, Sir John Gurdon (The Gurdon Institute, University of Cambridge), E29 Biomedical Sciences Building

2018 NCRI Cancer Conference
4 - 6 November 2018, SEC Glasgow

Fifty Years of UK Poverty Research - What Have We Learned?
5 November 2018, 9.30 - 17.00, Reception Room, Wills Memorial Building

Rise of Experimental Government
5 November 2018, 15.00 - 17.00, Institute for Government, 2 Carlton Gardens London SW1Y 5AA

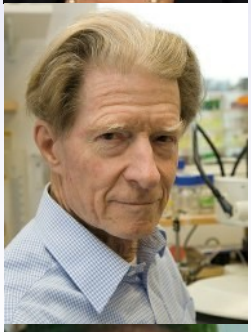
The effect of the IGF binding proteins in the progression of breast cancer
6 November 2018, 13.00 - 14.00, Ahmad Alghamdi (Year 3, PhD student), Seminar rooms A&B, Level 2, Learning and Research Building, Southmead Hospital

Tableau Workshop
7 November 2018, 10.00 - 12.00, Anna Tankel (Academic Marketing Coordinator, Tableau), Ground Floor Seminar Room, Beacon House

UK Myeloma Forum Autumn Day
8 November 2018, 9.00 - 16.00, Cavendish Conference Centre, 22 Duchess Mews, London W1G 9DT

Clinical Academics in Training Annual Conference 2018
8 November 2018, 9.30 - 17.30, The Royal College of Physicians Edinburgh

Focus on the individual: The importance of chromosomespecific biology in


From top: Jane Blazeby (Lead: The Value of Death Network), Sir John Gurdon, David Gordon (Bristol Poverty Institute), Catherine Hewitt (York Trials Unit, speaker at Rise of Experimental Government event), Ahmad Alghamdi

EVENTS CON'T

generating aneuploidy patterns in cancer
8 November 2018, 13.00 - 14.00, Dr Sarah McClelland (Barts Cancer Institute, Queen Mary University of London), C42 Biomedical Sciences Building

Afternoon Tea with Brigstow
9 November 2018, 14.00 - 17.00, Library Room, Royal Fort House

West of England: Healthcare Innovation Expo – making and maximising opportunities
14 November 2018, 9.00 - 17.00, UWE Exhibition and Conference Centre

South West Doctoral Training Programme Conference 2018 – Beyond Research: Society, Collaboration & Impact
14 November 2018, 9.00 - 17.00, Brunel's SS Great Britain

Introduction to Involving Patients and the Public in Research
14 November 2018, 10.00 - 13.00, Biomedical Research Centre PPI team in collaboration with People in Health West of England

Introduction to IRAS, HRA Approval and Research Ethics
14 November 2018, 12.00 - 13.00, Jess Bisset (Research Operations Manager, UHB R&I), Lecture room 3, Education & Research Centre, Upper Maudlin Street, BS2 8AE

Life Sciences- Careers Beyond Academia series: Policy and Funding
14 November 2018, 13.00 - 14.00, Ceri-Wyn Thomas (BBRSC) and Zoë Holland (UoB), E29 Biomedical Sciences Building

Statistics Clinic - 14 November 2018
14 November 2018, 14.00 - 15.30, SM3 Mathematics Building

Data analysis best practice workshop
15 November 2018, 9.00 - 17.00, Ground Floor Seminar Room, Beacon House

Building collaborations in global cancer care: from fragile conflict ecosystems to emerging economies
19 November 2018, 8.00 - 18.00, keynote speakers: Prof Richard Sullivan & Dr Ophira Ginsburg, Royal Society of Medicine, 1 Wimpole Street, London, W1G 0AE

NEWS AND EVENTS ARE REGULARLY UPDATED ON THE CANCER RESEARCH NETWORK WEBSITE

From top: Sarah McLelland, Ceri-Wyn Thomas, Zoë Holland, Richard Sullivan, Ophira Ginsburg

NEWS

Anti-cancer drug alternative to liver transplant

Patients suffering sudden liver failure could benefit from a new treatment that could reduce the need for transplants. A study in mice by researchers at the University of Edinburgh MRC Centre for Regenerative Medicine and the Cancer Research UK Beatson Institute in Glasgow found liver injury triggers a process called senescence, which is usually associated with aging or chronic disease.

Using a class of drugs being developed as anti-cancer therapy to block the spread of this process, they found that in mouse models the organ was able to regenerate after treatment, preventing death from liver injury. Most patients with this type of critical liver injury are otherwise physically healthy, and have accidentally or intentionally taken an overdose of paracetamol. While transplant offers incredible life-saving opportunities for these patients, it does mean a major operation and a lifetime of medication and with around 300 adults and children in the UK in need of a liver transplant at any one time, it cannot be guaranteed. New treatments like this, which set liver regeneration free and may prevent the need for liver transplants, would make a huge difference for these patients. They may also allow us to use the livers available for transplantation for other patients with different forms of liver disease who might otherwise die whilst waiting for a suitable liver donor.

The next step is to explore the potential of the new drugs in the clinic on patients with liver failure.

Bird TG *et al*. (2018). TGFβ inhibition restores a regenerative response in acute liver injury by suppressing paracrine senescence. *Science Translational Medicine*. 10(454), eaan1230.

Reproducibility Network

A new Reproducibility Network that aims to improve the rigour and reliability of UK-led scientific research was launched on 12 September 2018. The Network aims to reinforce the leading position of UK science by co-ordinating shared training and best practice across research-intensive universities.

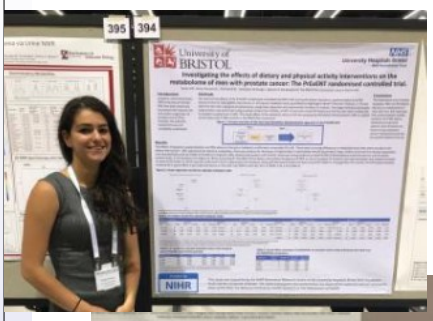
Prof Marcus Munafò, who contributed to the recently-published Manifesto for Reproducible Science, called on universities to do more to improve research rigour by setting out a range of measures for scientists that will optimise key elements of the scientific process.

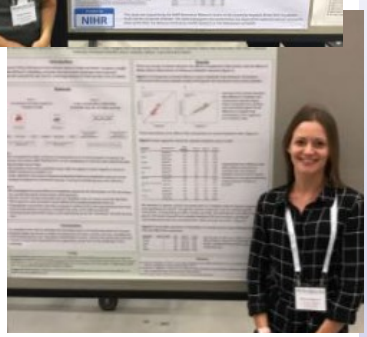
Nearly all researchers go into science wanting to find out something new, and perhaps which has the potential to improve health, lives, and tackle some of society's major challenges. However, while UK science has an enviable reputation for being world-leading, to remain so we need to ensure the research we conduct is innovative, high quality and high integrity. The Network aims to support this through a series of measures that place extra emphasis on research rigour and reliability.

If you are interested in finding out more about the Network and its plans to improve scientific practices through targeted changes to research methods, reporting and dissemination, reproducibility, evaluation and incentives, contact Marcus.

External engagements

PhD students Meda Sandu and Rhona Beynon presented posters at the **14th Metabolomics Society Conference** held in Seattle on 24-28 June 2018. The conference's theme of *Making Connections* included presentations on systems biology, big data, technology advances, precision medicine and translational science. Meda's poster was entitled *Investigating the effects of dietary and physical activity interventions on the metabolome of men with prostate cancer: The PrEvENT randomised controlled trial* (below) and Rhona's was *Investigating the effects of lycopene and green tea on the metabolome of men at risk prostate cancer: The ProDiet randomised controlled trial* (bottom).





Lesley C Booth MSc MBE, Lead - Patient & Public Involvement in Research at Bowel & Cancer Research , visited the Colorectal Tumour Biology research group on 20 July 2018.

Lesley Booth with Prof Ann Williams and Dr Adam Chambers in the CTB lab

Prof Richard Martin and Dr Sarah Lewis attended the annual Prostate Cancer Association Group to Investigate Cancer Associated Alterations in the Genome (**PRACTICAL**) meeting in Stockholm on 14-15 May 2018. Sarah presented *Diet and Prostate Cancer: A Mendelian Randomization study* and Richard presented *Setting up a Mendelian randomization working group in PRACTICAL*. Representatives from Prostate Cancer Studies around the world were present at the meeting.

On 28 June 2018 the Integrative Cancer Epidemiology Programme (ICEP) team at Southmead Hospital hosted the biannual **Cancer Research UK** (CRUK) **Lab Tours**. The event hosted the supporters and fundraisers for CRUK, who had travelled from as far as Cornwall for the experience. They listened to talks about cancer and the work done in ICEP from Jeff Holly, Claire Perks and Nic Timpson. The groups then went on interactive tours of the laboratories, organised and run by Kalina Biernacka. Feedback from the public included "wonderful people doing wonderful research" and "To see technology which was used during my diagnosis was eye opening".

The Cluster Randomised Trial of PSA Testing for Prostate Cancer (CAP) Trial has been nominated for the Office for National Statistics (ONS) **Research Excellence Awards** 2018 which recognise and celebrate outstanding innovative research carried out using research data to deliver a public benefit to the UK, whilst protecting data confidentiality. The winner, chosen from 10 shortlisted submissions, will be announced in November.

Funding successes

UH Bristol Radiographer Pauline Humphrey is a consultant therapeutic radiographer working at the Bristol Cancer Institute. Her area of expertise is brachytherapy, a type of internal radiotherapy. She has just been awarded a Clinical Research Doctoral Fellowship, funded by the **National Institute of Health Research** and Health Education England, as part of the Integrated Clinical Academic Programme. She started the 4 year part-time fellowship in May 2018 and is being supervised by Prof Fiona Cramp and Dr Emma Dures at UWE and Professor Peter Hoskin at The Christie, Manchester and Mount Vernon Hospital. She will also be continuing her consultant radiographer role on a part-time basis. Her research aims to develop an intervention to reduce distress caused by brachytherapy for locally advanced cervical cancer. It will consist of a UK survey of brachytherapy practice followed by semi-structured patient interviews at four UK centres. From this information an intervention will be developed and a proof of concept study with a small number of women will be carried out to test the intervention.

Dr Paul Race has been awarded an Innovate UK grant for *Bioprocess for the manufacturing of affordable pharmaceuticals to prevent and treat cancers, obesity and age-related diseases*; £42k over 1 year.

The latest round of successful funding applications to the **GW4 Alliance** were announced on 31 July 2018. These collaborative research communities will tackle some of society's biggest questions and global challenges. One Accelerator award went to GW4-BCR (Brain Cancer Research), Sep '18 to Apr '19. Leads from all four GW4 institutions include Bath: Lorenzo Caggiano (PI) and Julien Licchesi, Bristol: Kathreena Kurian, Cardiff: Chris Marshall & Stephen Paisey, Exeter: Jacqueline Whatmore. *From Daffodils to Drugs* – this community will be investigating synthetic analogues of compounds found in daffodil bulbs to treat brain tumours.

Academic Clinical Research Fellow in general practice in the Bristol Medical School, Department of Population Health Sciences, Dr Sam Merriel has been awarded a **PhD studentship** to study the use of MRI in prostate cancer diagnosis in primary care at the University of Exeter Medical School.

Wellcome Board of Governors visit

Dr Jeremy Farrar, Director of the Wellcome Trust, visited Bristol on 25 September 2018 to meet senior staff and researchers and understand how Wellcome funding is used, explore issues of joint concern in the UK science base, and discuss future opportunities with the University. Dr Farrar, who delivered a talk on Wellcome's strategy and future directions to Bristol senior staff and researchers, was joined by other members from Wellcome's Board of Governors and senior leadership team. During the day, the Wellcome team met researchers from across the University to discuss their work on a wide range of topics.

Serum calcium's role in prostate cancer

Prostate cancer is the most frequently diagnosed cancer among men and is a common cause of male cancer death. Global variation in mortality and findings from migration studies provide support for a role of modifiable risk in prostate carcinogenesis. Dietary calcium intake has been associated with an increased risk of prostate cancer in prospective epidemiological studies. Similarly, high calcium intake has been linked to an increased risk of advanced and fatal prostate cancer. Establishing a causal role of elevated serum calcium in prostate carcinogenesis could have therapeutic implications for the prevention or treatment of prostate cancer.

The availability of germline genetic variants robustly associated with serum calcium and prostate cancer in separate and independent genome-wide association studies (GWAS) can permit examination of the causal effect of increased serum calcium on prostate cancer risk using a "two-sample Mendelian randomization" framework. Given uncertainty surrounding the role of serum calcium in prostate cancer aetiology and progression, data from two GWASs were used to perform a two-sample Mendelian randomization analysis to examine the causal effect of elevated serum calcium with risk of overall and advanced prostate cancer.

Yarmolinsky J *et al*. (2018). Mendelian randomization does not support serum calcium in prostate cancer risk. *Cancer Causes and Control*. Online 10 October 2018.

Inflammation as a predictive tool for cancer

Head and neck squamous cell carcinoma (HNSCC) is often associated with chronic systemic inflammation (SI). A team from the Integrative Cancer Epidemiology Programme (ICEP) assessed if DNA methylation-derived SI (mdSI) indices: Neutrophil-to-Lymphocyte ratio (mdNLR) and Lymphocyte-to-Monocyte ratio (mdLMR) are associated with the presence of HNSCC and overall survival (OS).

The team observed an elevated methylation-derived circulating neutrophil and monocyte count and a decreased lymphocyte count in HNSCC cases compared to controls. Similarly, HNSCC cases with poor OS showed elevated neutrophil and monocyte cell counts and a lower lymphocyte count.

The similarities between DNA methylation and cell count based inflammation indices strengthens the utility of mdSI indices as a valuable research tool to estimate SI in the absence of cell count based measurement, especially in prospective studies. They demonstrated that systemic inflammation indices are associated with the presence of HNSCC. Further, the mdSI indices are sufficient to distinguish HNSCC case and controls. In the HNSCC survival dataset, lower mdLMR was associated with poorer OS. The mdSI indices may be useful as a research tool for predicting high-risk HNSCC, especially HPV-negative HNSCC where there is a lack of reliable biomarkers of detection, although this would require rigorous validation in large prospective studies.

Ambatipudi S *et al*. (2018). DNA methylation derived systemic inflammation indices are associated with head and neck cancer development and survival. *Oral Oncology*. 85, pp. 87-94.

Elizabeth Blackwell Institute updates

Rachael Gooberman-Hill, Director of the EBI, describes the Institute's innovative **approach to global health challenges** in a blog as part of the Bristol Firsts series, celebrating Bristol-based innovations in the NHS's 70th year.

Through its Wellcome Trust ISSF Award, EBI is delighted to support a new post to help researchers with the experimental design and statistics associated with fundamental biology research and pre-clinical studies. **Michelle Taylor**, Senior Research Associate in **Statistics and Experimental Design**, will provide expert advice on appropriate statistical methods for a diverse range of experimental approaches. She will work primarily with researchers during the planning stages of their projects as well as providing help with grant applications. This will include contributing expert input into calculating sample size estimates, methods to avoid bias, and appropriate statistical analyses.

Contact her on michelle.l.taylor@bristol.ac.uk.

Treatment for diffuse intrinsic pontine glioma

Diffuse intrinsic pontine glioma (DIPG) is a lethal, high-grade, paediatric glioma that accounts for up to 85% of all brainstem gliomas and 100-150 new cases are recorded each year in the USA. DIPG is difficult to treat due to the heterogeneity generated from the various mutations associated with the disease, as well as its sensitive location in the brainstem. Chemotherapies have proved ineffective and new treatments are urgently required.

Palbociclib is a novel DIPG treatment that restricts the proliferation of rapidly dividing cancer cells via selective inhibition of cyclin-dependent kinase (CDK) 4 and CDK6. However, implementing it as a monotherapy for DIPG is unfeasible, as CDK4/6 inhibitor resistance is commonplace and palbociclib does not readily cross the blood–brain barrier (BBB) or persist in the central nervous system. To inhibit the growth of DIPG cells, a team from the Functional Neurosurgery Research Group in the Bristol Medical School aimed to use palbociclib in combination with the rapamycin analog temsirolimus, which is known to ameliorate resistance to CDK4/6 inhibitors and inhibit BBB efflux. They tested palbociclib and temsirolimus in three patient-derived DIPG cell lines. Analyses revealed palbociclib and temsirolimus inhibited CDK4/6 and mammalian target of rapamycin (mTOR) signalling through perturbation of phosphorylation of the retinoblastoma (RB) and mTOR proteins, and demonstrated that palbociclib and temsirolimus inhibited cell proliferation in all three DIPG cell lines, acting synergistically in combination to further restrict cell growth.

Asby DJ *et al*. (2018). Combined use of CDK4/6 and mTOR inhibitors induce synergistic growth arrest of diffuse intrinsic pontine glioma cells via mutual downregulation of mTORC1 activity. *Cancer Management and Research*. 10, pp. 3483-3500.

New Faculty of Life Sciences

Created on 1 August 2018, the new faculty brings together the Schools of Biochemistry, Biological Sciences, Cellular and Molecular Medicine, Physiology, Pharmacology and Neuroscience and Psychological Science to deliver research and teaching activity at all scales of the life sciences, from molecular to societal. Its creation is part of the University's Vision and Strategy to become a life sciences destination for students, academics and research funding. The Faculty of Life Sciences will deliver a range of challenging, research-focused, undergraduate and postgraduate programmes taught in the context of world-leading research environments. It will also make significant contributions to three professional programmes (Medicine, Dentistry and Veterinary Science) which are run by the Faculty of Health Sciences. Research in the new faculty will address a range of the important challenges in the life sciences. From tackling ecosystem and global change, to innovation in fundamental biosciences for better human, animal, plant and ocean health; from understanding animal and human behaviour and wellbeing to developing future synthetic biotechnologies and so driving the UK's bioeconomy. The Faculty is led by Prof Jeremy Tavaré as Dean.

University joins UK BioIndustry Association

The UK BioIndustry Association (BIA), the UK's trade association for innovative life sciences, represents over 300 companies including start-up and established bioscience and pharmaceutical companies, academic, research and philanthropic organisations, service providers to the biosciences sector as well as health advocacy groups, government agencies, economic development groups and overseas trade associations. Facilitating engagement of Bristol researchers with the life industries is part of the Elizabeth Blackwell Institute's remit to support growth of partnerships and alliances with industry across the health arena, led by Dr Richard Seabrook MBA, Advisor on Business Development.

A proud member of BIA UK BioIndustry Association

This membership offers researchers at the University of Bristol the opportunity to:

- influence policy ensuring your voice is heard and the University is represented on the matters that are critical for the life sciences sector success
- connect with the sector and grow your network through the BIA industry-leading events and expert committees
- save money through the BIA business solutions purchasing programme
- provide visibility and showcase your research, advertise your jobs, share your news, events and other information through the BIA website.

To benefit from access to BIA full online content, log in using your**@bristol.ac.uk** email address and create your personal account.

Prostate cancer screening

A team investigated the efficacy and safety of prostate-specific antigen (PSA) testing to screen for prostate cancer through a systematic review and meta-analysis of randomised controlled trials comparing PSA screening with usual care in men without a diagnosis of prostate cancer. Included in the review were five randomised controlled trials, enrolling 721 718 men; among them the Cluster Randomised Trial of PSA Testing for Prostate Cancer (CAP) Trial conducted by UoB.

When considering the whole body of evidence, screening probably has no effect on all-cause mortality and may have no effect on prostate-specific mortality. Sensitivity analysis of studies at lower risk of bias also demonstrates that screening seems to have no effect on all-cause mortality but may have a small effect on prostate-specific mortality. This corresponds to one less death from prostate cancer per 1000 men screened over 10 years. Using modelling, they estimated that for every 1000 men screened, approximately 1, 3, and 25 more men would be hospitalised for sepsis, require pads for urinary incontinence, and report erectile dysfunction, respectively.

Ilic D *et al*. (2018). Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. *BMJ*. 362, k3519.

Biomarker tool for cancer immunotherapy

New immunotherapies which help the immune system to recognise and destroy cancer cells are promising, but some patients don't respond to the new treatments. With the help of an Elizabeth Blackwell Institute Clinical Primer Scheme award, Dr Emily Milodowski (pictured) has been developing a new tool as a step towards being able to identify people who can be helped by these new therapies.

The body's immune system plays a major role in regulating cancer development, and can identify and destroy many cancers - except when the cancers can prevent these cells from functioning effectively. Using flow cytometry she has started to look at patterns of co-inhibitory receptors on the surface of immune cells to see if these could potentially be used as biomarkers to determine which patients will respond to the treatments for melanoma and which will not. The technique allows her to study individual immune cells which she can label with different antibodies, tagged with fluorescent markers, and identify the different combinations of receptors found on the surface of each cell. She has designed a new antibody panel to look at the expression of 16 different cell markers simultaneously. Over the course of the six month project, Emily has been testing how different experimental conditions can affect how co-inhibitory receptors are expressed by T lymphocytes. So far, she has been developing the new panel to look for co-inhibitory receptors on T lymphocytes in healthy donors. The next step is to use the panel in blood and tumour samples from people with malignant melanomas, to help understand why some people don't respond to checkpoint inhibitor immunotherapies.

Tobacco and alcohol at diagnosis of head and neck cancer

Tobacco smoking and alcohol consumption are well-established risk factors for incidence of head and neck cancer but what is their prognostic role at time of diagnosis?

Head and neck cancers (HNCs) are a group of tumours that arise from the mucosal epithelium of the upper aerodigestive tract and represent the sixth leading cause of cancer worldwide. Around 75% of HNCs have been attributed to the combined effects of tobacco and alcohol use. The prognostic role of smoking status and alcohol intake at the time of cancer presentation remains unclear and it has yet to be established whether smoking and alcohol use provide any additional prognostic information beyond the tumour, node, metastasis (TNM) staging system, which currently forms the basis for clinical decision making in people with HNC. The major finding is that, even after adjusting for a wide-range of prognostic factors, smoking status at the time of an HNC diagnosis is associated with worse survival. Current smokers had a 70% higher all-cause mortality risk compared to people who had never smoked; former smokers were 40% more likely to die during follow-up. Drinking behaviour around the time of diagnosis was not associated with overall mortality risk in this analysis.

Beynon RA *et al*. (2018). Tobacco smoking and alcohol drinking at diagnosis of head and neck cancer and all-cause mortality: Results from head and neck 5000, a prospective observational cohort of people with head and neck cancer. *Cancer Epidemiology*. Online 5 April 2018.

EBI Research Strands

The newly created Elizabeth Blackwell Institute (EBI) Research Strands are cross-faculty initiatives that build on the existing research base in Bristol to tackle challenges that can only be addressed by multi-disciplinary teams of researchers. The research strands align with research priorities of the University of Bristol and create a shared vision in key thematic areas. They aim to support capacity development and provide exciting new research opportunities for researchers, including those who have never previously felt their skills and expertise were relevant to a particular health or biomedical area.

Current strands include:

Bioethics, Biolaw and Biosociety
Establishing Bristol as a leader in interdisciplinary and multi-disciplinary research into the ethical, legal and social dimensions in the biosciences, including health and social care.

Medical Humanities
Opening the door to new arts-science collaborations by connecting researchers from all faculties together with clinicians and external partners for research focusing on philosophy and humanities.

Bristol AMR
Building on clear areas of success and expanding the research network in antimicrobial resistance, across disciplines and linked to global health challenges. The Strand is co-lead by Profs Matthew Avison and Adrian Mulholland.

Digital Health
Increasing visibility of digital health research, bringing together teams around health challenges, developing external partnerships and engaging undergraduate students.

How Bristol research has helped shape the NHS

This year we honour the 70th anniversary of the National Health Service (NHS). Since it was established in 1948, the NHS has played a vital role in UK society. As part of the celebrations, UoB shone a spotlight on how our research and teaching has helped to shape the NHS and improve people's health.

Examples include:

Studying Bristol families to improve the health of future generations

The Children of the 90s study has been charting the lives of people born in the early 1990s in the greater Bristol area. Data from the has been used by more than 600 academics, leading to important discoveries that are helping treat and prevent ill health. For example, mothers who consume less fish during pregnancy have children with lower IQs.

Growing blood in a laboratory

The NIHR Blood and Transplant Research Unit has successfully grown red blood cells from adult stem cells. It's being trialled in humans for the first time this year to assess the performance of laboratory-grown cells compared to donated red blood cells. This research has the potential to improve the health of people who need regular transfusions throughout their life for conditions such as thalassemia, sickle cell and certain cancers.

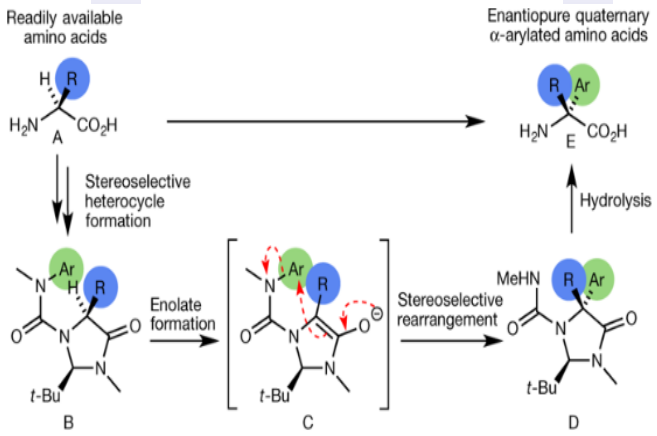
Read more

Modification of amino acids

A team in the School of Chemistry has invented a new way to modify amino acids by attaching a ring of carbon atoms at the very centre of the amino acid molecule.

The unusual reaction that introduces this new ring was previously of limited application, but the work showed that introducing new molecular structural features makes it compatible with a much wider range of chemical structures than previously suspected. For example, it is now possible to add rings that also carry a whole range of other atoms around their periphery.

The reaction involves the migration of the ring from the nitrogen atom of the amino acid to a carbon atom, and because amino acids exist in two mirror image forms, importantly it retains a memory of the starting mirror image structure in the structure of the product. The chemistry is also very easy to carry out on large scale, making it potentially very valuable for the practical synthesis of new drug molecules. The work has allowed us to turn what was a scientific curiosity into a really practical new way of making an important new group of chemical building blocks. It will provide scientists with a whole new set of modified amino acid molecules for making new medicines or modified proteins, enabling advances in understanding natural biochemical systems or tackling disease.



Leonard D and Clayton J (2018). Asymmetric α-arylation of amino acids. *Nature*. 562, pp 105–109.

ELIZABETH BLACKWELL FUNDING

EBI MRC Proximity to Discovery Industry Engagement Fund (PtoD)

With support from the MRC, funding for short term two-way people exchanges between industry and academia which align to MRC strategic priorities in population health, cardiovascular research, infection and immunity, neuroscience and cancer.

Closing date: **29 October 2018**

EBI Clinical Primer scheme

This scheme is aimed at exceptionally motivated clinically qualified medical, veterinary and dental trainees who are at an early stage of their career.

Closing date: **8 November 2018**

EBI Research Strands Funding opportunities (Bioethics, Biolaw, Biosociety)

The Bioethics, Biolaw, Biosociety Research Strand invite applications to support for research activities. Proposals should seek to advance the strand themes, facilitate new multidisciplinary connections, and lead to follow-on work.

Closing date: **16 November 2018**

EBI Identifying Candidates for Wellcome Trust Investigator Awards

This scheme is designed to support a small number of permanent academic staff at UoB within the first five years of their appointment, who are planning to apply for an Investigator Award from the Wellcome Trust. Applications will be accepted on a rolling basis.

Heads of Schools are asked to nominate members of staff who can be eligible for this scheme by emailing ebi-health@bristol.ac.uk

EBI Workshops Funding

Support interdisciplinary workshops in health research at new or emerging interface between two or more disciplines. Applications reviewed all year.

Returning Carers Scheme

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 (e.g. maternity leave, adoption leave, additional paternity leave, leave to care for a dependant.).

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

EBI Bridging Funds for Senior Fellows

This scheme is designed to support a small number of academic staff at the University of Bristol who currently hold an externally funded research fellowship. Applications accepted on a **rolling** basis.

FUNDING OPPORTUNITIES

Would you like to receive timely, tailored funding opps information?
Do you want to know what funding opportunities come up in your research area?
Get tailored funding alerts?

Research Professional provides access to an extensive database of funding opportunities, and can send out tailored alerts based on keywords that you input, ensuring that the funding alerts you receive are the ones you want to hear about. UoB staff and students have **FREE** online access to the database from any device – once you've registered then you can view upcoming funding opportunities from home or away, not just while on the University network.

You can search for funding information by discipline, sponsor, database searches, by recent calls or by upcoming deadlines. If you register for the site and log in, you'll be able to:

- **Set up automated funding opportunity email alerts** - **tailored according to your discipline and research interests**, an easy process that will take just a few minutes to set up through the use of keywords
- **Save searches and bookmarks** - store items of interest for future reference, download and email to colleagues
- **Sign up for higher education news bulletins** – want to hear about what is going on in the broader HE environment? Latest news on the REF, setting up of UKRI etc? Sign up for the 8am playbook or the Research Fortnight news publications and stay up to date with the latest news.

Alternatively, a full calendar of funding opportunities for neuroscience research has already been set up and is available online. Subscribing to the calendar will place the entries in your own calendar, which will automatically update according to pre-specified search criteria. Find out more about **Research Professional** on the RED website. Note that some calls may have an internal process; do always remember to check the major bids webpage here to see if there is an internal process.

The following listings represent a *brief selection* of available funding for the Cancer Research community. **Full listings of opportunities** are sent out via Faculty Research Directors and/or School Research Directors, and **are available on the Research Development website**.

Nuovo-Soldati Foundation for Cancer Research
Fellowships

Closing date: 01-Dec-18 Award amount: €40,000

These support young doctors in pursuing a research project on cancer cells with the main aim being to support innovative techniques or novel therapeutic approaches. Medically qualified candidates or medical students at the end of their training who work in specialities such as pathology, oncology, radiotherapy or surgery, may apply. Preference will be given to projects that take place outside the fellows country of origin or within centres of excellence with their home country.

Cancer Research UK
Biomarker project awards

Closing date: 06-Dec-18 Award amount: £100,000

These provide funding for biomarker assay development, validation and qualification for use in the clinical setting. Proposals may use invasive or imaging techniques and cover all types of biomarkers, including predisposition, screening, diagnostic, prognostic, predictive, pharmacological and surrogate response types.

Marie Curie Cancer Care
Research grants

Closing date: 10-Dec-18 Award amount: £750,000

This supports research with the potential to improve quality of life for people with terminal illnesses and their carers, families, friends and communities. Projects may address the following topics:

- out of hours palliative and end of life care
- support for carers and families
- continuity of care
- bereavement
- incontinence
- follow-on and implementation studies building on research previously supported by the organisation
- interventional research
- motor neurone disease
- terminal primary brain cancer

National Cancer Institute, USA
Investigator-initiated early phase clinical trials for cancer treatment and diagnosis (R01 clinical trial required): AIDS-related

Closing date: 07-Jan-19 Award amount: USD 2.5 million

This supports projects that implement early phase – phase 0, I and II – investigator-initiated clinical trials focused on cancer-targeted diagnostic and therapeutic interventions. Types of clinical trials that can be supported include single site clinical trials; multi-site clinical trials; mechanistic clinical trials; feasibility clinical trials; pragmatic trials; ancillary clinical trials; pharmacodynamic trials; bio-marker driven trials; co-clinical trials.

Cancer Research UK
Accelerator award

Closing date: 10-Jan-19 Award amount: £5 million

This supports cross-institutional research teams in bringing together resources and expertise to accelerate progress in cancer research that could not be delivered in isolation.

FEATURED PUBLICATION

Investigating Chemoresistance To Improve Sensitivity Of Childhood T-Cell Acute Lymphoblastic Leukemia To Parthenolide

Ede BC, Asmaro RR, Moppett JP, Diamanti P & Blair A (2018). *Haematologica*. 103, pp1493-1501.

Current therapies for childhood T-cell acute lymphoblastic leukaemia have increased survival rates to above 85% in developed countries. Unfortunately, some patients fail to respond to therapy and many suffer from serious side effects, highlighting the need to investigate other agents to treat this disease. Parthenolide, a nuclear factor kappa (κ)B inhibitor and reactive oxygen species inducer, has been shown to have excellent anti-cancer activity in paediatric leukaemia xenografts, with minimal effects on normal hemopoietic cells. However, some leukaemia initiating cell populations remain resistant to parthenolide. This study examined mechanisms for this resistance, including protective effects conferred by bone marrow stromal components. T-cell acute leukaemia cells co-cultured with mesenchymal stem cells demonstrated significantly enhanced survival against parthenolide (73±11%) compared to cells treated without mesenchymal stem cell support (11±9%). Direct cell contact between mesenchymal cells and leukaemia cells was not required to afford protection from parthenolide. Mesenchymal stem cells released thiols and protected leukaemia cells from reactive oxygen species stress, which is associated with parthenolide cytotoxicity. Blocking cystine uptake by mesenchymal stem cells, using a small molecule inhibitor, prevented thiol release and significantly reduced leukaemia cell resistance to parthenolide. These data indicate it may be possible to achieve greater toxicity to childhood T-cell acute lymphoblastic leukaemia by combining parthenolide with inhibitors of cystine uptake.

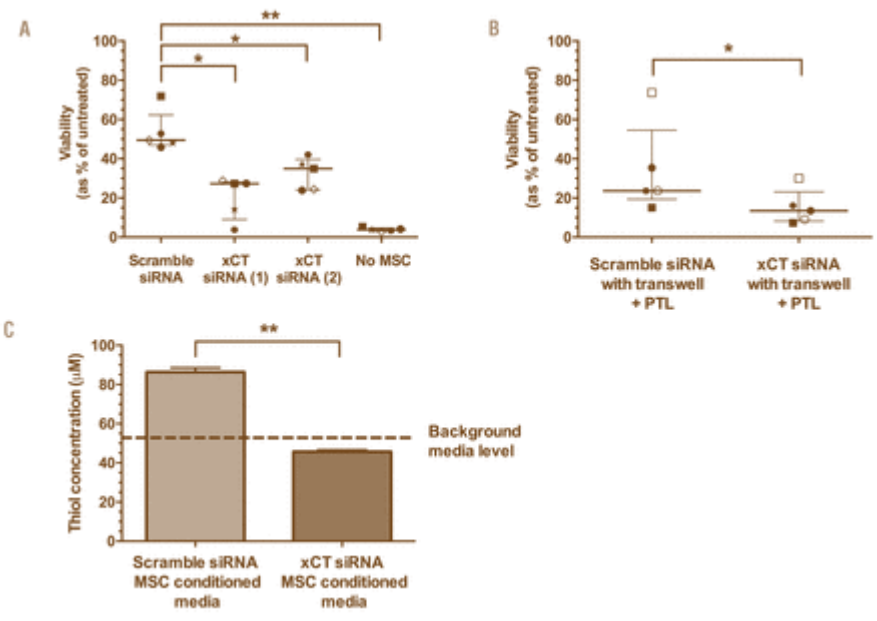


*Image: xCT knockdown in mesenchymal stem cells (MSC) overcomes MSC mediated resistance to parthenolide (PTL). Viability of T-cell acute lymphoblastic leukemia (T-ALL) samples (patients 5, 6, 8-10) treated with 10 μM PTL for 24 hours (h) in the presence of MSC pre-treated with xCT or scramble control siRNA, in direct contact (A) or samples (1, 2, 6, 8, and 10) in transwell inserts (B). Symbols represent the average viability in duplicate samples. Each symbol represents an individual patient. Lines represent median and interquartile range. (C) Thiol concentration in media following 24-h incubation with MSC pre-treated with xCT or scramble control siRNA compared to background media. Data represent mean±Standard Deviation. (n=4). Results were analyzed by one-way ANOVA (A) or paired t-tests (B and C). *P≤0.05, **P≤0.01.*

Cancer Network

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