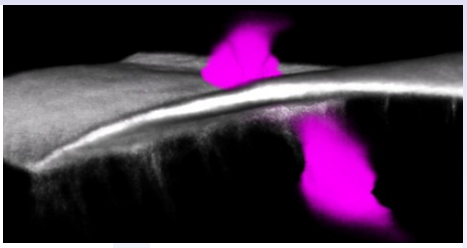
Cancer Network Newsletter
July - September 2019

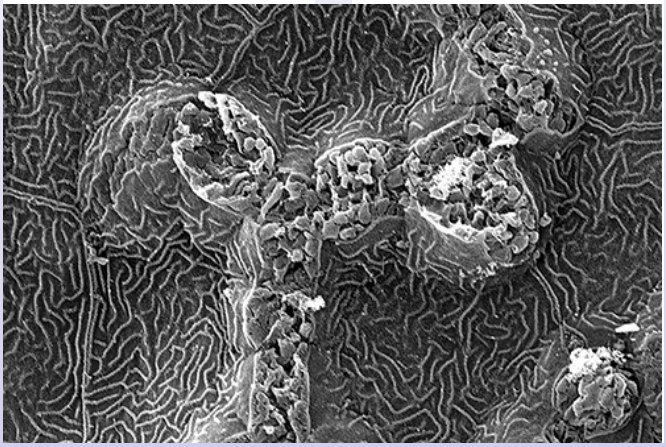
University of BRISTOL
Elizabeth Blackwell Institute for Health Research

Zebrafish capture the cancer process

Cancer-related inflammation impacts significantly on cancer development and progression. Research has observed in zebrafish, for the first time, that inflammatory cells use weak spots or microperforations in the extracellular matrix barrier layer to access skin cancer cells. The use of translucent zebrafish allowed the team to model several sorts of skin cancer and live image how inflammatory cells find the growing cancer cells in the skin. To access the cancer cells, the immune cells need to first breach the basement membrane zone. They observed weak spots in the membrane which the inflammatory cells use as easy routes to access the cancer. Those clones of cancer cells nearest to the weak spots tend to receive more inflammatory cell visits and as a consequence they grow faster. Now we know these microperforations exist we can target them with cancer therapeutics. The study's findings have clear clinical relevance to cancer patients as microperforations in the basement membrane zone have been shown to occur in human airways and guts and so could act as similar portals to let inflammatory cells gain access to the cancer.



Below: micrograph of a region of zebrafish skin where a track of cancer cells has disrupted the epithelium much like a mole burrowing beneath a lawn of grass



Above: an immune cell (magenta) breaches the basement membrane to access cancer cells. The basement membrane separates different tissues in the body and plays an important role as a barrier in confining tumours

Watch the video explaining the process

Van den Berg MCW *et al*. (2019). Proteolytic and Opportunistic Breaching of the Basement Membrane Zone by Immune Cells during Tumor Initiation. *Cell Reports*.

Inside this issue:

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EVENTS

Workshops: Above and Beyond (A&B) and Research Capability Funding (RCF) grants
6 August 2019, 12.00 - 13.00, Research & Innovation, Education & Research Centre, Interview Room, Level 4

Clinical Research Network Open day
8 August 2019, 13.00 - 16.00, Level 5, Whitefriars Centre, Lewins Mead, BS1 2NT

GW4 GCRF Clusters Call Networking Event
12 August 2019, 1400 - 16.30, Clock Tower Room, Engine Shed, Bristol

Science Policy: Improving the Uptake of Research into UK Policy
19 - 21 August 2019, Wellcome Genome Campus

Workshops: Above and Beyond (A&B) and Research Capability Funding (RCF) grants
20 August 2019, 12.00 - 13.00, Research & Innovation, Education & Research Centre, Interview Room, Level 4

STARS School 2019: Embedding the Industrial Perspective
8 - 13 September 2019, Darlington

EDIS Symposium 2019: Inclusive Research and Experimental Design
9 September 2019, 9.30 - 16.30, Keynote: Londa Schiebinger (Director of the EU/US Gendered Innovations in Science, Health & Medicine, Engineering, and Environment, Stanford University), Francis Crick Institute, London

New Directions in Immuno-Oncology Conference
10 - 12 September 2019, Bush House East Wing, King's College London, Bush House, 30 Aldwych, London, WC2B 4BG

Parliament for Researchers
11 September 2019, 10.30 - 15.30, Bath Spa University

Frontiers in Cellular, Viral and Molecular Microscopy - with Cryo-specimen Preparation Techniques
16 - 17 September 2019, Plenaries: John Briggs (MRC-Laboratory of Molecular Biology) & Ari Helenius (ETH Zurich), Wills Memorial Building

Writing for a lay audience
17 September 2019, 10.00 - 12.00

Above & Beyond
Fundraising for Bristol city centre hospitals

UK Clinical Research Collaboration

GW4

edis
Equality, Diversity and Inclusion in Science and Health

CANCER RESEARCH UK | KING'S HEALTH PARTNERS CENTRE

SEE ALL EVENTS ON THE CANCER RESEARCH NETWORK WEBSITE

EVENTS CON'T

Bristol Endothelial meeting 2019

19 September 2019, 9.00 - 17.30, The FOUNDATION, Lower Ground Floor, St George's Road, Bristol, BS1 5BE (see programme below)

JOIN US FOR THE

Cancer Research Network: Translational Pathway (Part 2) and Metastasis

5 February 2020, 13:15 - 17:00

Seminar Room 4, Learning and Research Building, Southmead Hospital, Bristol BS10 5NB

registration closes 15 January 2020

REGISTER NOW

VIEW THE FULL PROGRAMME

Research IT drop-in session

19 September 2019, 11.00 - 13.00, Room 2.10, 31 Great George Street

GW4 BBSRC Mock Board Meeting as an Early Career Researcher Training Opportunity

20 September 2019, 10.00 - 14.00

CRUK Early Detection of Cancer Conference

24 - 26 September 2019, Canary Center, Stanford University, Palo Alto, California, USA

Research ethics committees - here to help, not hinder

24 September 2019, 12.00 - 13.00, Chris Foy (Senior Adviser, Research Design Service South West) Tutorial Room 1, Education & Research Centre, Upper Maudlin Street, Bristol BS2 8AE

Translation toolkit: Spin-out or licencing your research - pro's and con's of both

26 September 2019, 14.00 - 15.00

Cardiff-Bristol clinical cancer meeting

19 September 2019, 10.00 - 14.00

Cardiff & Vale University Health Board (Heath Hospital), Cardiff, CF14 4XW

The Universities of Cardiff and Bristol are holding a joint symposium with the purpose of highlighting potential areas of clinical collaboration. Topics to be covered include phase I trials, other clinical trials research, imaging, radiotherapy, screening, population genetics.

REGISTER NOW

SEE ALL EVENTS ON THE CANCER RESEARCH NETWORK WEBSITE

NEWS

Operation at Clifton Down Shopping Centre

The Biomedical Research Centre's Surgical Innovation Theme set up a giant game of Operation in Clifton Down Shopping Centre on 20 May 2019. Members of the public were invited to compete against surgeons Prof Jane Blazeby and Dr Natalie Blencowe (both Bristol Medical School); as well as testing the steadiness of their hands against the surgeons, participants were asked questions about surgery, such as what information do you think you would want to know before you have an operation? Would this be different if it was a new type of operation? How do you feel about robotic surgery, where a surgeon controls a robot?. The surgeons were interviewed on BBC Radio Bristol and featured on BBC Points West.

Almost a third of hospital admissions involve a surgical procedure. With 4.7 million operations carried out in the UK each year and numbers rising, surgery is one of the most important life-saving treatments offered to patients. With over 17,000 surgeons in the UK carrying out thousands of different procedures from replacing joints and removing tumours to repairing organs and reconstructing after injury, developing new techniques and procedures to help speed patient recovery are essential to improve patient care and reduce the risk of complications. The challenge, however, lies in doing so safely and transparently.

Funding successes: Part 1

To Prof Ann Williams (Cellular and Molecular Medicine) from the **Medical Research Council**, £351,685 for *Investigating the function of the BCL-3/Beta-catenin complex in promoting intestinal tumorigenesis and acquisition of therapeutic resistance.*

A Collaborator Agreement has been put in place between the **International Agency for Research on Cancer** (IARC) and the MRC Integrative Epidemiology Unit (IEU) under Prof Nic Timpson (Bristol Medical School) for *Metabolomic data collection and analysis of renal cell carcinoma* to a value of £86,000.

A **National Institute for Health Research** (NIHR) Doctoral Research Fellowship has been awarded to Prof Nick Maskell for David Arnold to pursue a project on *Ambulatory Strategies in Pleural Infection*.

Ms Alison Denny, Manager of the Integrative Cancer Epidemiology Programme (Bristol Medical School) received £7,500 support from **Cancer Research UK** to host a Nutrition and Cancer Workshop.

Dr Karim Malek (Cellular and Molecular Medicine) was awarded £99,956 from the **Children's Cancer and Leukaemia Group** for *Evaluating a novel protein methyltransferase inhibitor for poor-prognosis rhabdomyosarcoma therapy*. The project will run from April 2019 to December 2020.

University Cancer Research Fund awards

The University Cancer Research Fund (UCRF) seeks out the most innovative ideas in cancer research through an annual seed funding call. The Research Committee selects projects and ideas in their early stages that have the promise to develop into high impact research. By funding the most imaginative and promising research at this early stage, the fund is able to promote the most exciting and potentially important discoveries that could result in important breakthroughs in cancer research.

The latest round awarded funding to:

- Dr Bernadette Carroll (Vice Chancellor's Fellow, Biochemistry), £4,809 for *Targeting the mTORC1 pathway to block melanoma*
- Dr Sabine Hauert (Engineering Mathematics), £5,000 for *Controlling cancer cell cooperation using a dynamic optical microenvironment (dome)*
- Dr Lindsay Nicholson (Bristol Medical School), £4,950 for *A study of differential gene expression of tolerant CD8 cells from tumours vs persistent autoimmune inflammation*
- Prof Christoph Wuelfing (Cellular and Molecular Medicine), £5,000 for *The regulation of cytotoxic T cell infiltration into tumour spheroids by adenosine and Tim3*
- Prof Linda Wooldridge (Bristol Veterinary School), £4,942 for *Defining the mechanism of anti-PD1 antibody mediated tumour regression.* The project will utilise CRISPR/Cas9 technology to knockout the expression of the co- inhibitory receptor (Co-IR) PD-1 amongst tumour specific CD8+ cytotoxic T lymphocytes (CTL).

The next round of the UCRF is expected to open in March 2020 and will be announced via the Network's mailing list.

The Translational Pathway symposium debrief

On 17 June 2019 the Cancer Research Network hosted its first half-day symposium in the Learning and Research Building at the University Hospitals Bristol NHS Foundation Trust. A packed room (over the 60 person capacity- whoops!) welcomed twelve invited speakers including a gastroenterologist, a senior surgical research photographer, the head of bioengineering of UHBristol, an epidemiologist, a physicist working in radiotherapy, a translation manager at CRUK, an engineering mathematician working in nanotech and the head of the SW Genomics Laboratory. Three of the 18 poster presenters were awarded prizes, and we extend our congratulations to:

- 1st: Natasha Clayton (Senior Research Associate, CMM), *Roles of RhoU, RhoV and p21-activated kinases in prostate cancer cells*
- 2nd: Chris Parker (PhD student, CMM), *Developing* in vitro *models to investigate the role of the proto-oncogene BCL-3 in therapeutic resistance*
- 3rd: Anne Germon (MSc student, Biochemistry), *Identification of Protein Disulphide Isomerase A3 Dependent Proteins from the Secretome of MDA-MB-231 Breast Cancer cells*

Image shows Tom Creed giving his presentation

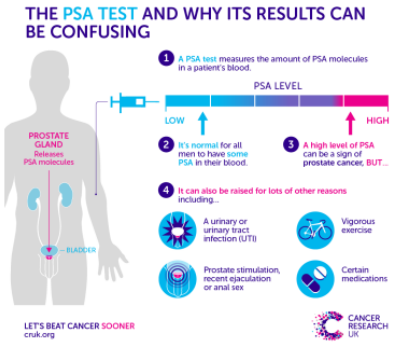
Funding successes: Part 2, awards and engagements

Dr Bernadette Carroll (Biochemistry) has received £87,149 from the **British Skin Foundation** for the project Exploring B-RAFV600E-dependent changes that cause mTORC1 and autophagy dysregulation in melanoma.

Prof Varinder Aggarwal (Chemistry) has been awarded the prestigious **Davy Medal** from the **Royal Society** for his outstanding contribution to the field of chemistry. A methodology he developed has been applied to the synthesis of a broad range of natural products and biologically active molecules possessing, for example, anticancer, antibacterial or antifungal properties.

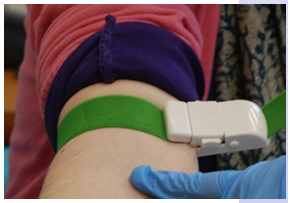
Dr Emma Turner attended the National Cancer Research Institute Annual Trials Meeting held on 17 June 2019 in London to present findings from the Cancer Research UK-funded Comparison Arm for ProtecT (Prostate Testing for Cancer and Treatment), or CAP, study which evaluated the effectiveness and cost effectiveness of population screening using prostate-specific antigen testing.

Read more about the CAP trial



Inflammatory marker tests to rule out serious conditions

Blood tests that detect inflammation are not sensitive enough to rule out serious underlying conditions and GPs should not use them for this purpose, according to Bristol's Centre for Academic Primary Care, University of Exeter and the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care West (NIHR CLAHRC West). Many diseases cause inflammation in the body, including infections, autoimmune conditions and cancers. Millions of inflammatory marker tests are done each year and rates of testing are rising. Although many of these tests will be done appropriately for different reasons, GPs are increasingly using them as a non-specific test to rule out serious underlying disease. Using data from the Clinical Practice Research Datalink, researchers analysed the records of 160,000 patients who had inflammatory marker tests in 2014 and compared these with the records of 40,000 patients who had not had the test. Overall, 15% of raised inflammatory markers were caused by disease: 6.3% the result of infections, 5.6% caused by autoimmune conditions, and 3.7% due to cancers. No relevant disease could be found in the remaining 85% of patients with 'false positives'. The researchers calculated that, for every 1,000 inflammatory marker tests performed, there would be 236 false positives. They also calculated that these false positives would lead to 710 GP appointments, 229 blood test appointments and 24 referrals in the following six months. Half of patients with a relevant disease had normal test results, or a 'false negative', meaning that GPs should not rely on a normal test result as proof of good health or to 'rule out' disease. **Read more**



£9 million boost for health research

Health researchers in the west country have been awarded £9 million from the Department of Health and Social Care (DHSC) to tackle the area's most pressing problems. The funding will enable new research projects including forecasting demand in hospitals, increasing people's physical activity levels, supporting people who self-harm and improving outcomes for children in care. The investment will help develop better health and care through research that aims to address the immediate issues facing the health and social care system. The money is part of a larger £135 million award over five years to 15 pioneering research teams across the country, known as NIHR Applied Research Collaborations (ARCs). These ARC teams build on the success of the NIHR Collaborations for Leadership in Applied Health Research and Care (CLAHRCs), which the ARCs replace from 1 October 2019. The team in the West, NIHR CLAHRC West has a strong track record of producing impactful research with a range of collaborators. The CLAHRC West team has worked on diverse projects including evaluating patient safety tools and the roll out of an intervention to reduce cerebral palsy in premature babies, exploring the experiences of Somali families affected by autism, creating harm reduction materials with people who inject drugs and improving how healthcare professionals respond to signs of domestic violence and abuse.

£100 million to drive 'tech for better futures'

A new £100 million institute, based in the centre of Bristol, is set to transform the way we create, utilise and evaluate new digital technologies to benefit our society now and in the future. In a unique collaboration, Bristol engineers will work with social scientists and with tech giants, corporations, local government and community partners to answer these big questions and create transformational technologies for the future. The Bristol Digital Futures Institute (BDFI) will be based at the University's new Temple Quarter Enterprise Campus in the heart of the City of Bristol's buzzing new Enterprise Zone.

This international leading research facility is being funded by a £29 million grant from the Research England UK Research Partnership Investment Fund (RPIF), which has received more than double that in £71 million of match funding (£16 million philanthropy and £55 million from 27 partners including organisations such as BT, Dyson, BBC, Airbus and Aardman).

The Institute will aim to generate 30 new collaborative projects per year. It will be jointly led by Profs Susan Halford, a social scientist and professor of sociology, and Dimitra Simeonidou, an engineer and professor of high-performance networks.

The new research facilities are vitally important to understand our digital futures. They will allow a step-change in socio-technical research and help us to gain new insights on the challenges and opportunities brought by disruptive digital technologies.

"These insights will enable us create new technologies and deliver our vision for a future digital society based on opportunity, trust, human control, resilience, openness, diversity and inclusion.

Prof Dimitra Simeonidou

CRUK supporters lab visit

On 24 May 2019 supporters of Cancer Research UK (CRUK) were hosted by the research laboratories at Southmead Hospital. Members of the Integrated Cancer Epidemiology Programme including Kalina Biernacka, Claire Perks, James Yarmolinsky, Aayah Nounu and colleagues spent a couple of hours entertaining volunteers of the charity and explaining how their support goes towards furthering advances in preventing and treating cancer.

Top: a volunteer entering the ICEP "mystery box", a public engagement tool used to start discussions about cancer with members of the public

Bottom: Kalina Biernacka demonstrating the pipette challenge

Making the immune system better at recognising cancer

Prof Linda Wooldridge (Bristol Veterinary School) and colleagues used an Elizabeth Blackwell Institute Translational Acceleration and Knowledge Transfer (TRACK) award to explore new ways to manipulate immune cells to 'see' cancers and attack the cells more efficiently. Cytotoxic (CD8+) T-cells are a white blood cell that kill infected cells. However, their ability to kill cancerous cells in particular is compromised by the immunosuppressant environment that tumours create, and the fact that the T-cells express quite low affinity receptors at their surface. CD8+ T-cells have receptors on their surface (TCRs) that can recognise molecules on their target cells called antigens, which in turn trigger an immune response. These antigens are carried to the cell surface by MHCI (Major Histocompatibility complex Class I) molecules. As well as the TCR, CD8+ T-cells also express a molecule called CD8. Once the TCRs have recognised an antigen, it is CD8 that binds to the MHCI on the target cell, although they bind with weak affinity. Prof Wooldridge's team is developing novel CD8 molecules which are capable of binding much more strongly to the MHCI and so increasing the ability of the CD8+ T-cells to fight cancer. Firstly, the new higher affinity CD8 molecules needed to be designed; molecular modelling based on the structure of CD8, by team member Dr Richard Sessions (Biochemistry), produced five candidate mutations. These then needed to be evaluated and then inserted into viruses, to get the molecules onto the surface of the T-cells. They found that at least one of the five candidate mutations results in increased recognition of MHCI at the cell surface. As a result of these findings Linda and Richard secured a European Research Council International Training Network Grant involving ten European partners, all experts in cancer immunotherapy and collaborations with industry.

Read more

Career inspirations podcast

The Medical Research Council hosted a series of podcasts interviewing seven scientists, each working in different area of medical research. In each episode the interviewee was asked to share their career highlights, what makes them tick, and their advice for forging a career in medical research. The June episode had Prof Caroline Relton (Integrative Cancer Epidemiology Programme) baring all.

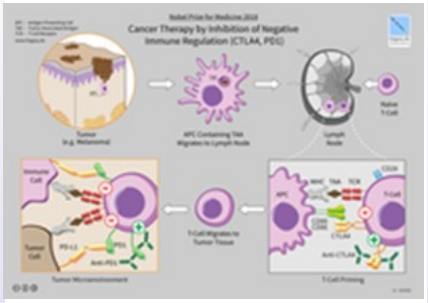
Before going into research Caroline's love of science led her to study for a degree in applied biology and nutritional science, followed by the pursuit of a different passion – teaching. After completing her PGCE and teaching in a secondary school for five years, she decided that academia was her true calling and returned to university to do a PhD in molecular genetics. She and her research group use the tools and methods of population-based research for understanding the role of epigenetics – changes to the way genes are read by cells – in health and disease. In the interview she shares how educating teenagers equipped her with valuable skills as a scientist, her tips on forging a successful career and why she believes in a whole team approach to science.

Listen to the podcast, or read the full transcript

Meeting of minds with a Nobel laureate

Prof Paul Martin (Cancer Network co-Lead, Biochemistry, on the left in the image with Honjo to his right) met immunologist and joint winner of the Nobel Prize in Physiology / Medicine 2018 Tasuku Honjo (本庶 佑) at the RIKEN Center for Integrative Medical Sciences - Japanese Society for Immunology International Symposium on Immunology 2019, *Genetic Craft Immunity and Biology Networks*, held on 24-25 June 2019 in Tokyo. Paul spoke in the Inflammation, Resolution, and Repair session on *Imaging inflammation and it consequences in wound repair and cancer.*

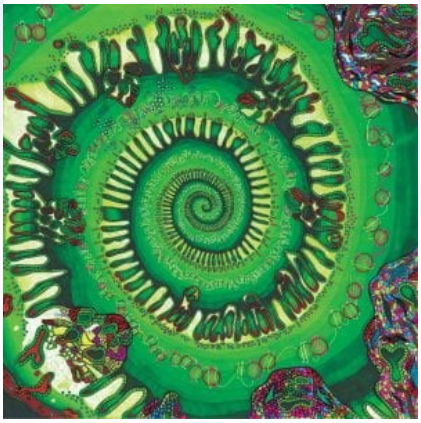
Prof Honjo is best known for his identification of programmed cell death protein 1 (PD-1) and his molecular identification of cytokines: IL-4 and IL-5, as well as the discovery of activation-induced cytidine deaminase (AID) that is essential for class switch recombination and somatic hypermutation. He was elected as a foreign associate of the National Academy of Sciences, USA (2001), as a member of German Academy of Natural Scientists Leopoldina (2003), and also as a member of the Japan Academy (2005).



In 1992, Honjo first identified PD-1 as an inducible gene on activated T-lymphocytes, and this discovery significantly contributed to the establishment of cancer immunotherapy principle by PD-1 blockade.

Why we should be talking about bowel cancer

Prof Ann Williams' (Cellular and Molecular Biology) research looks into the effect of aspirin in helping to prevent bowel cancer by an unknown mechanism. We know that aspirin inhibits cyclooxygenases, a class of enzymes that produce prostaglandins such as PG2 which can promote cancer. However, drugs that inhibit selective cyclooxygenases are not as effective as aspirin at inhibiting cancer. This suggests that aspirin is doing something else to protect against bowel cancer. The research we are doing is looking at the effects of aspirin that do not involve cyclooxygenase inhibition. We are modelling human tumour progression, to investigate the effects of long-term aspirin exposure on the proteins made by our cells. The long-term goal of this research is to help inform how people should be taking aspirin.



Creative Reactions, a collaboration between artists and Pint of Science scientists, resulted in *Progression of Colorectal Cancer* by Claudia Stoker, pictured left, inspired by Ann's research.

Helping to prevent bowel cancer is hugely important to me, especially as my father died from the disease when he was only 55

Prof Ann Williams

Read the full blog on the Faculty of Life Sciences website

Focus on: taking part in a research study

Since 2008 the creator of this newsletter (Catherine Brown, see contacts) has been a participant in the Generations Study, funded by Breast Cancer Now. This UK-wide study into the causes of breast cancer began 15 years ago and now has over 110,000 women who regularly complete questionnaires and submit blood samples to the research team.

Nearly 50,000 women are diagnosed with breast cancer each year in the UK and the numbers are increasing. Many of these could, in principle, be prevented, but to do so we need to gain a better understanding of the causes. Scientific evidence indicates that the causation of breast cancer involves a complex mixture of factors - some to do with behaviour, such as lack of exercise, some to do with environment and some genetic (inherited). These factors act at many different stages of life, starting in childhood and perhaps even before birth, and continuing to the menopause and beyond. To find out what these factors are, and how they combine with each other to cause breast cancer, this study was established in which information about the factors, and how they change through life, is related to the risks of subsequent breast cancer. The last few years have seen over a hundred scientific papers published by the team, who are also studying the causes of breast cancer in men; around 350 men are diagnosed with the disease in the UK every year.

My mother survived breast cancer and its treatments, including radiotherapy, chemotherapy and a mastectomy; the small part I play acknowledges those who have succumbed to the disease, and the hope that fewer will suffer.

Catherine Brown

Take part in a research study:

- NIHR
- Alzheimer's Society
- Cancer Research UK

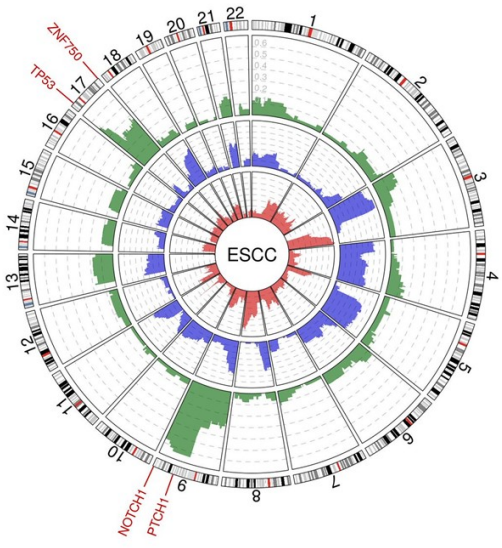
Parental exposures and childhood cancers

Data from the Avon Longitudinal Study of Parents and Children (ALSPAC) was one of the sources accessed to study parental occupational exposures to pesticides, animals and organic dust and their association with an increased risk of childhood cancer. The International Childhood Cancer Cohort Consortium evaluated parental occupational exposures and risk of childhood leukaemia and central nervous system (CNS) tumours by pooling data on 329,658 participants from birth cohorts in five countries (Australia, Denmark, Israel, Norway and United Kingdom). Risk of childhood (<15 years) acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML) and CNS tumours was estimated. Paternal exposures to pesticides and animals were associated with increased risk of childhood AML but not ALL or CNS tumours. Paternal exposure to organic dust was positively associated with AML, inversely associated with ALL and not associated with CNS tumours. This analysis provides evidence for paternal agricultural exposures as childhood AML risk factors.

Patel DM *et al*. (2019). Parental occupational exposure to pesticides, animals and organic dust and risk of childhood leukemia and central nervous system tumors: Findings from the International Childhood Cancer Cohort Consortium (I4C). *International Journal of Cancer*.

Identifying regions of uniparental disomy in cancer

Uniparental disomy (UPD) is defined as the occurrence of inheriting a pair of homologous chromosomes from the same parental origin, caused by segregation errors mostly in meiosis and leads to the development of several genetic disorders through the gain or loss of imprinted regions, or the presence of two identical copies of an abnormal gene. Advances in molecular genetics has provided the opportunity to systematically identify regions of somatic UPD in cancer, known as somatically-acquired UPD (aUPD). Recent reports have shown that aUPD events are non-randomly distributed across cancer types, pointing out common genomic profiles of aUPD in a tumour-type specific manner, which typically coincide with regions of genomic losses, both in solid tumours and haematological malignancies. In addition, the identification of cancer-specific minimal regions of aUPD has led to the discovery of inactivating mutations in cancer-related genes, which might increase the functional relevance of such events in the development of cancer. Several studies have provided evidence that aUPD could act as the "second hit" and inactivate tumour suppressor genes. A substantial amount of literature suggests that aUPD represents an unquestionable event to achieve a "second hit" alteration during tumorigenesis and its identification might be a useful resource in early detection and targeted therapy.



Erola P *et al*. (2019). The non-random landscape of somatically-acquired uniparental disomy in cancer. *Oncotarget*. 10(40): pp3982–3984.

The unintended consequences of healthcare apps

People are living longer, but often with multiple long-term health conditions. Maintaining people's quality of life in these circumstances requires a lot of support from the NHS.
At the same time, GPs are under pressure to improve patients' access to healthcare while coping with their own workloads and growing patient demand. Policymakers are proposing new ways to relieve the strain by using digital technologies such as phone apps to improve the convenience and reduce the cost of healthcare. The move towards 'digital first' care is explicit in the new NHS Long Term Plan. Hundreds of thousands of health apps are already available in app stores, targeting fitness, wellbeing and general health as well as specific conditions. These developments are set against a backdrop of well-known challenges for healthcare app innovation. For example, evidence exists that some apps can help patients, but many have not had their effectiveness rigorously tested or the reliability of the information they provide assured. Some other possible consequences are less well understood, for instance, whether digital health tools will close or widen existing health inequalities, as well as what the impact will be on people's relationships and communication with their GP, on GP workload and how GPs use health apps with patients. The DECODE study aims to produce guidance on the unintended consequences of digital health tools for all stakeholders.

Partnership with Kenya to build data science expertise

A collaboration between the University of Bristol's Jean Golding Institute for Data Science and the Strathmore University Business School in Kenya, will focus on using data science to address contemporary challenges facing Kenya and other African countries. The partnership will involve an exchange of ideas and people between the two institutions, sharing expertise, connecting researchers across disciplines and facilitating research projects. The aim is to produce high-quality academic research which addresses societal challenges in an African context, across sectors as diverse as healthcare, agriculture, wildlife conservation, disaster response, geospatial modelling, communications and economics.

Prof Kate Robson Brown, Director, Jean Golding Institute, with Dr George Njenga, Executive Dean of Strathmore University Business School

Gender imbalance in cancer research funding

Within the European Union women represent nearly half of the workforce and more than half of all university graduates, but are under-represented in senior positions in the workplace. In science, research and development, the attrition rate among women exceeds that of their male counterparts at every stage of career progression, with women representing 46% of PhD graduates, 33% of career scientists and 22% of grade A researchers. Previous studies have explored gender imbalance and suggested that only a fifth of countries worldwide have achieved gender parity in scientific research. A team used data from several sources on public and philanthropic cancer research funding bodies including the Medical Research Council, Department of Health, Wellcome Trust, European Commission and medical research charities, awarded to UK institutions between 2000 and 2013. They compared research investment totalling £2.3bn as well as the mean and median research award between male and female primary investigators (PIs). Analysis showed 69% of grants, total value £1.8bn, were awarded to male primary investigators compared with 31% grants with total value £0.5 billion awarded to female PIs.

Zhou CD *et al.* (2017). A systematic analysis of UK cancer research funding by gender of primary investigator. *BMJ Open.*

Cancer Research UK's obesity campaign

Cancer Research UK (CRUK) states that their latest obesity campaign aims to stimulate a government policy response to 'junk food' advertising to children. Focusing on policy change rather than individual behaviour change is a laudable aim. However, the charity's approach has been challenged by the public, researchers, and healthcare professionals. CRUK's national public facing ad campaign frames obesity as "the new smoking" with the tagline "obesity is a cause of cancer too". They aren't on their own: the CEO of the NHS, Simon Stevens, frequently uses the phrase "obesity is the new smoking". But CRUK's public facing campaign doesn't make any reference to children or junk food, which are the stated target of the campaign. Experts are warning that comparing obesity to smoking is flawed and ultimately serves to stigmatise people perceived to be overweight or obese, and have a negative impact on their health.

A group of experts, including Dr James Nobles (Bristol Medical School) met with CR UK's marketing and policy teams in November to outline their concerns about the charity's previous "OB_S_ _Y" campaign. At the meeting, the experts clearly stated their position: this campaign would likely deepen prejudice against people perceived to be obese or overweight rather than supporting them, and was likely to have a negative impact on their future health.

Read the full article

Partnership with the UK Reproducibility Network

The University of Bristol has announced their support of and official partnership with the UK Reproducibility Network (UKRN). UKRN is a peer-led consortium that aims to ensure the UK retains its place as a centre for world-leading research. As part of this collaborative partnership, the University has created an Academic Lead for Research Integrity and Improvement role, working closely with the Pro-Vice Chancellor for Research to improve the robustness of Bristol's research activity. The University already has an active local network of researchers at all career stages – one of over 40 local networks supported by UKRN across the country – that works to share best practice across disciplines and discuss relevant topics such as open research practices. Formal support for UKRN builds on this activity and demonstrates Bristol's commitment to world-leading research. As the number of institutions supporting UKRN increases, so will opportunities for coordinating activity and sharing best-practice and training.

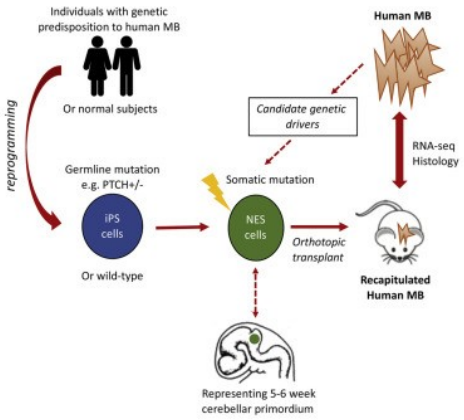
Considering the diagnosis of a brain tumour

A team of researchers evaluated the utility of different symptoms, alone or combined, presented to primary care for an adult brain tumour diagnosis. All presentations within 6 months of the index diagnosis date (cases) or equivalent (controls) were coded into 32 symptom groups. Sensitivity, specificity, positive predictive values (PPVs) and positive likelihood ratios (PLR) were calculated for symptoms and combinations of symptoms with headache and cognitive features. Diagnostic odds ratios were calculated using conditional logistic regression, adjusted for age group, sex and Charlson co-morbidity. Stratified analyses were performed for age group, sex and whether the tumour was of primary or secondary origin. 8,184 cases and 28,110 controls were included in the study. Seizure had the highest PPV of 1.6% followed by weakness 1.5% and confusion 1.4%. Combining headache with other symptoms increased the PPV. For example, headache plus combined cognitive symptoms PPV 7.2%; plus weakness 4.4%, compared to headache alone PPV 0.1%.The diagnostic odds ratios were generally larger for patients <70 years; this was most marked for confusion, seizure, and visual symptoms. They found seizure, weakness and confusion had relatively higher predictive values than many other symptoms. Headache on its own was a weak predictor but this was enhanced when combined with other symptoms especially in younger patients. Clinicians need to actively search for other neurological symptoms such as cognitive problems.

Cookson M *et al*. (2019). The usefulness of symptoms alone or combined for general practitioners in considering the diagnosis of a brain tumour: A case control study using the Clinical Practice Research Database (CPRD) (2000 2014). *BMJ Open*.

Genetic brain tumour predisposition

Neural stem cell culture systems could potentially advance our understanding of human brain development and disease. The capture of self-renewing neural progenitor cells *in vitro* provides scalable cell populations for biochemical or genetic studies. Importantly, neural stem cells can be genetically manipulated or differentiated in a controlled environment and therefore allow functional studies that would not be possible in human brain. It has been postulated that brain tumours could develop from neural progenitors that deviate from their developmental pathway. In this study, the team demonstrate that defined genetic perturbations in a specific class of human progenitor cells lead to the formation of a distinct human cancer phenotype.



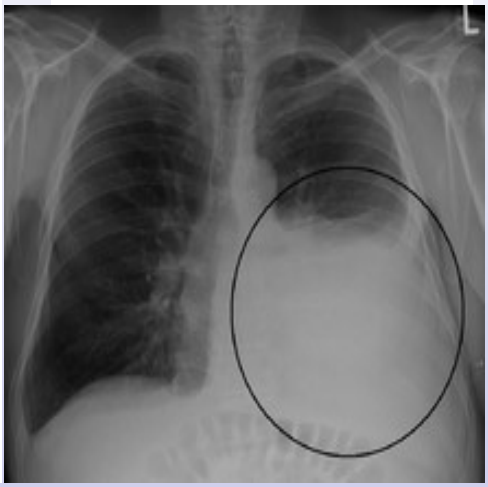
Huang M *et al*. (2019). Engineering Genetic Predisposition in Human Neuroepithelial Stem Cells Recapitulates Medulloblastoma Tumorigenesis. *Cell Stem Cell*. Available online 13 June 2019.

Treatment of malignant pleural effusions

Malignant pleural effusions (MPEs) affect up to 15% of cancer patients, with the majority being symptomatic, most commonly with breathlessness. The presence of MPE signifies advanced disease with a reduced life expectancy; median survival 3-12 months. Treatment is therefore aimed at reducing symptoms to optimise quality of life. Many patients with MPE will experience re-accumulation of fluid after initial therapeutic aspiration. Definitive pleural intervention is therefore often preferable to avoid repeat thoracocentesis.

Inducing pleurodesis with a chemical agent to prevent fluid build-up is a well established and reliable practice, with a recent meta-analysis confirming that graded talc is both efficacious and safe and data consistently suggesting that around 80% of patients will achieve success. However, this approach necessitates inpatient hospital admission. Indwelling pleural catheters (IPCs) can be inserted as a day case procedure and offer an alternative which focuses on symptom control rather than prevention of fluid formation. Evidence shows that patients treated with an IPC spend fewer days in hospital and have symptoms controlled as effectively as those receiving a chest drain and talc pleurodesis. Used in isolation, however, IPCs do not confer the same likelihood of achieving pleurodesis as instilling a chemical agent.

Dipper A, Bhatnagar R and Maskell N (2019). Outpatient talc administration via indwelling pleural catheters for malignant effusions. *Current Opinion in Pulmonary Medicine*. 25(4): pp380–383.



Immersive VR documentaries

The Virtual Realities: Documentary Encounters project, funded by the Engineering and Physical Sciences Research Council, showcased three non-fiction works on 25 June 2019. The project investigates the use of Virtual Reality (VR) for journalism and documentary, and the impact the platform has on storytelling and audience experience. The three projects were chosen from among over 150 applications based on their originality and innovation.

The Waiting Room:VR

The Waiting Room, from Bafta Award winner Victoria Mapplebeck tells the story of her own breast cancer from diagnosis through treatment to recovery. Her first exploration of VR; this project explores the cultural myths and language of chronic illness, asking us to confront what we can and what we can't control when our bodies fail us.

Read the full story

Understanding how cancer cells eat

Dr Emma Vincent (Cellular and Molecular Medicine and Bristol Medical School) works on the link between type 2 diabetes, obesity and cancer. People with type 2 diabetes and obesity have an increased risk of developing cancer across their lifetime; she and her team want to find out why this occurs to stop it happening. By studying cell metabolism they hope to better understand how cancer cells eat and fuel themselves in order to divide.

Sophie Rae created an artwork based on this research entitled *Pathways* (image bottom right), which represents the team's desire to show that by treating, managing and improving type 2 diabetes and obesity, it is possible to do something positive to help prevent disease progression and to lower cancer risk. Eating more healthily and exercising more can help adjust your path towards a healthier life. I was thinking there are parallels between how cells change their pathways to determine their fate and how people can also change the decisions they make to positively influence their health.

...the most valuable thing I have got out of this experience is that it made me reflect on how what I do is perceived by other people – I don't do that very often.

Emma Vincent

Image left: Amy Holt (1st year PhD), Emma Vincent, Aleksandra Ryk (MREs) and Danny Legge (Postdoc)

Read the full interview

ELIZABETH BLACKWELL FUNDING

EBI Seed Fund: Public Engagement with Health Research

Seed funding is available for health researchers who would like to deliver public engagement events and activities. Applications will be considered on a rolling basis.

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 Workshop support

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 Research 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.

The Elizabeth Blackwell Institute for Health Research is officially a member of **Equality, Diversity and Inclusion in Science and Health**, or EDIS, an initiative set up by the Wellcome Trust, the Crick Institute and GSK.

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**.

Cancer Research UK
Career development fellowship

Closing date: 20-Aug-19 Award amount: £ unspecified

This enables scientists without a salaried independent position to set up their own independent research group in any area of CRUK's funding remit, with the exception of drug discovery and clinical trials. Postdoctoral and early-career researchers may apply.

Cancer Research UK
Programme Foundation Awards

Closing date: 22-Aug-19 Award amount: £1.5 million

These 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
Pioneer Award

Closing date: 03-Sep-19 Award amount: £200,000

This supports innovative, higher-risk ideas that could revolutionise the understanding of cancer. Early-stage ideas from any discipline are welcomed, including: molecular and cellular biology; optimising treatments and diagnostics; device and software development; behavioural and population studies.

View all CRUK funding schemes and deadlines

Children's Cancer and Leukaemia Group
Little Princess Trust innovation grant

Closing date: 06-Sep-19 Award amount: £1 million

This supports basic science and translational and clinical research in paediatric cancer. Projects may focus on a specific childhood cancer or a range of cancer types, and should focus on new approaches to treatment, in particular the following:

- more effective treatments with fewer side effects for the patient while on treatment
- approaches to treatment that may lead to a reduction in short and long-term sequelae of treatment
- chronic health conditions and disabilities as late side effects of treatment

De Duve Institute, Belgium
Postdoctoral fellowships

Closing date: 15-Sep-19 Award amount: €70,000

These enable young scientists to pursue postdoctoral research within one of the research groups in the institute. The research groups are: cancer; genetics and development; infections and inflammation; metabolism and hormones. Candidates must hold a PhD not obtained at a Belgian university or a MD and must not have resided in Belgium for more than 12 months in the three years prior to application. It is mandatory to contact the group leader of the laboratory of choice before any application.

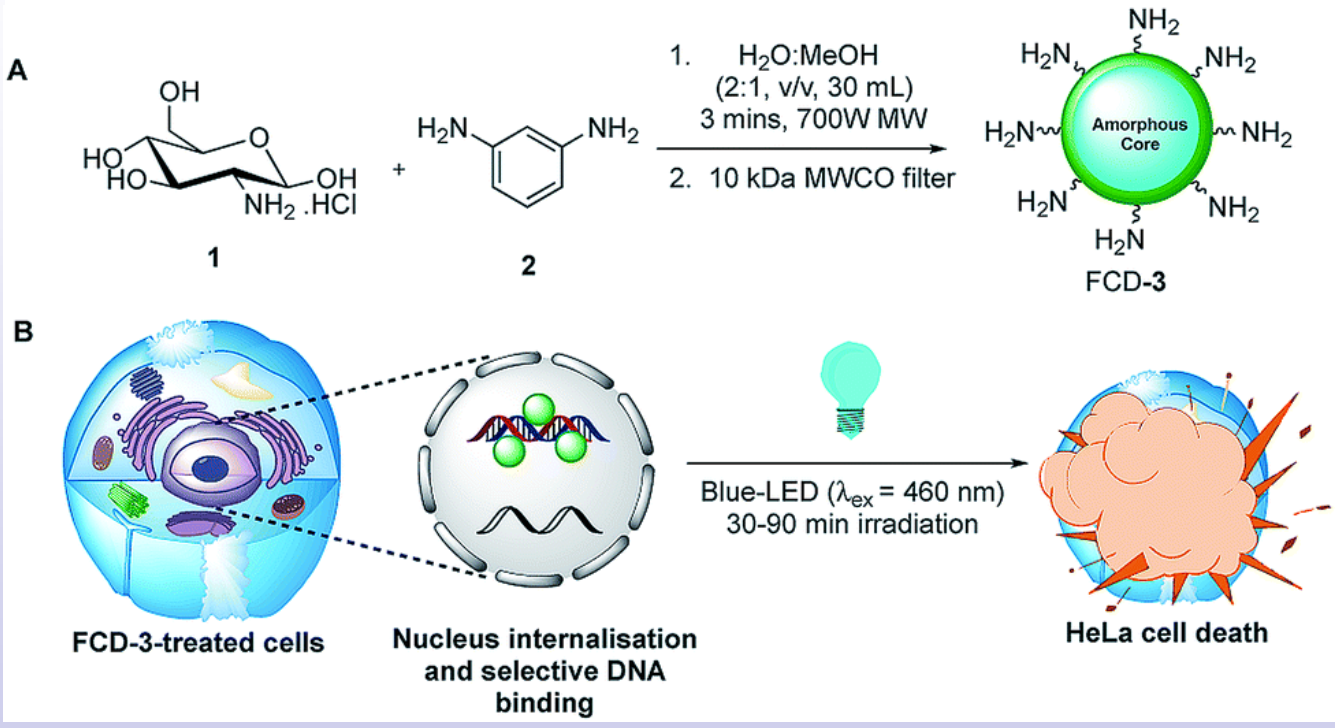
FEATURED PUBLICATION

Selective Photothermal Killing of Cancer Cells Using LED-Activated Nucleus Targeting Fluorescent Carbon Dots

Hill SA, Sheikh S, Zhang Q, Ballesteros LS, Herman A, Davis SA, Morgan DJ, Berry M, Benito-Alifonsoa D and Galan MC. *Nanoscale Advances*. Published 15 July 2019.

The development of effective theranostic probes in cancer therapy is hampered due to issues with selectivity and off-target toxicity. We report the selective LED-photothermal ablation of cervical (HeLa) cancer cells over human dermal fibroblasts (HDF) using a new class of green-emissive fluorescent carbon dots (FCDs). The FCDs can be easily prepared in one pot using cheap and commercial starting materials. Physico-chemical characterisation revealed that a surface coating of 2,5-deoxyfructosazine on a robust amorphous core gives rise to the nanomaterial's unique properties. We show that intracellular uptake mostly involves passive mechanisms in combination with intracellular DNA interactions to target the nucleus and that cancer cell selective killing is likely due to an increase in intracellular temperature in combination with ATP depletion, which is not observed upon exposure to either the “naked” core FCDs or the surface components individually. The selectivity of these nanoprobes and the lack of apparent production of toxic metabolic by-products make these new nanomaterials promising agents in cancer therapy.

(A) Three minute synthesis of green emitting FCD-3 and (B) FCD-3 nuclear targeting leading to photothermal cancer cell ablation after blue-LED irradiation.



Cancer Network

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