Cancer Network Newsletter

July - August 2018

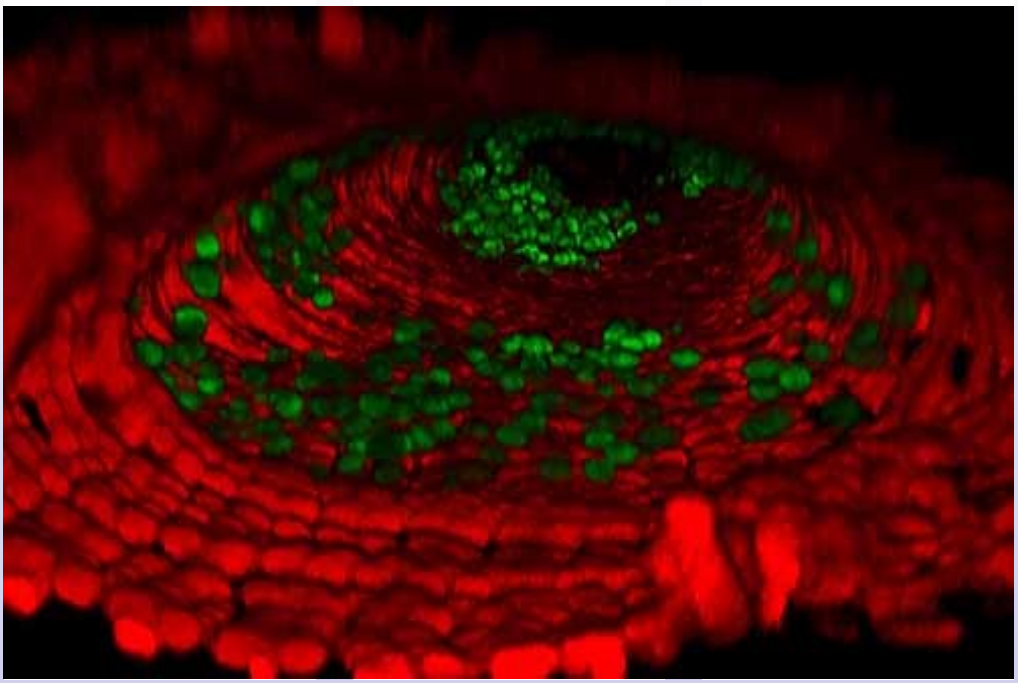
University of BRISTOL
Elizabeth Blackwell Institute for Health Research

£1.4m to investigate cancer growth

Prof Eugenia Piddini (CMM) has been awarded a Programme Foundation Award worth £1.4 million by Cancer Research UK (CRUK) to lead research into how the natural properties of normal non-cancer cells can be harnessed to contain cancer growth.

Cancer has become one of the most common and deadly diseases. It is becoming increasingly clear that the communication between cancer cells and surrounding normal cells plays a pivotal role in cancer growth, and that better understanding the nature and impact of this exchange is key to identifying novel anti-cancer strategies. Using *Drosophila* Prof Piddini's group have shown that cancer cells compete with and kill neighbouring normal 'host' cells, known as "cancer-host cell competition". They have shown that the process fuels cancer growth by allowing cancer cells to clear a space that they can expand into. The team have also revealed how it is possible to contain the growth of these cancers by protecting normal cells from cell competition and therefore from being killed by the cancer. The CRUK award will fund Prof Piddini's research for the next 6 years to investigate further the impact that interfering with cell competition has on cancer growth.

Image shows intestinal tumour masses (green) growing and expanding in the intestinal cavity of a fruit fly (red). © Piddini Group



Inside this issue:

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EVENTS

L&R Postgraduate seminars
24 July 2018, 13.00 - 14.00, Yunfei Li (Year 1, PhD student): *Development and validation of a new ex-vivo model for the study of osteoarthritis using human osteochondral plugs*, and Reham Mashat (Year 2, PhD student): The *role of 27-Hydroxycholesterol in breast cancer cell line*. Seminar rooms A&B, Level 2, Learning and Research Building, Southmead Hospital

Translation Toolkit seminar series: Why Science Policy Matters
7 July 2018, 14.00 - 15.00, Rhiannon Wilson (PolicyBristol) and Dr Hannah Rose-Vineer (Bristol Veterinary School, pictured top right), G13/14 Life Sciences Building

Infection and Immunity Early Career Researchers' Symposium
10 September 2018, 9.45 - 14.00, Life Sciences Building

Cancer in Children and Young People Conference
12 - 14 September 2018, Westminster, London

IDEAL International Conference
13 - 14 September 2018, MShed, Princes Wharf, BS1 4RN

Translation Toolkit seminar series: How to be an Effective Networker
13 September 2018, 14.00 - 17.00, Vox Coaching, venue TBC

CITER Annual Scientific Meeting 2018
17 - 18 September 2018, Keynote: Dr Rhys Jones (Cardiff University, pictured second from top on right), Cardiff University

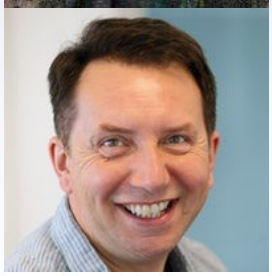
Translation Toolkit seminar series
27 September 2018, 14.00 - 15.00, venue TBC

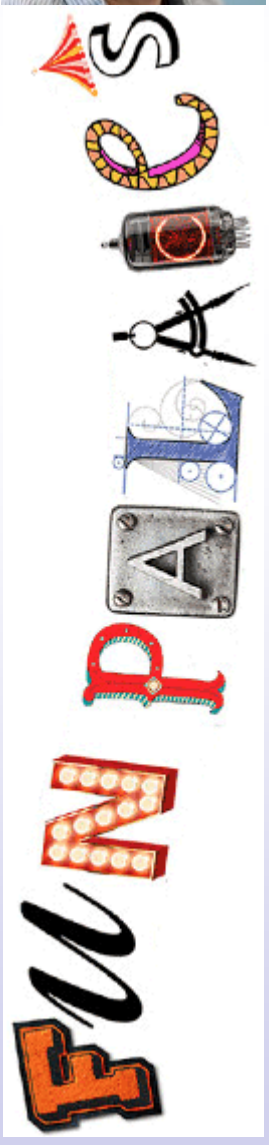
UK CLL Forum Clinical Sciences Day
28 September 2018, 9.15 - 17.05, Cavendish Conference Centre, 22 Duchess Mews, London W1G 9DT

Crick Cancer Research Symposium
1 - 2 October 2018, The Francis Crick Institute, London

Early Detection of Cancer Conference 2018
2 - 4 October 2018, Knight Cancer Research Building, 2720 SW Moody Ave., Portland, OR 97201 (USA)

Come and make a Fun Palace
6 - 7 October 2018, various around Bristol





EVENTS CON'T

Translation Toolkit seminar series
25 October 2018, 14.00 - 15.00, venue TBC

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

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

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

L&R Postgraduate Presentations
13 November 2018, 13.00 - 14.00, Georgina Mortimer (Year 1, PhD student): *Down's syndrome and diabetes – insights into rapid progression to type 1 diabetes* and Amy Howell (Year 1, PhD student): *Risk factors for development and progression of Primary Brain Tumours*, Seminar rooms A&B, Level 2, Learning and Research Building, Southmead Hospital

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

Pumps and Pipes UK Conference
19 February 2019, 8.00 - 18.00, SPE Aberdeen

Biological therapies in cancer - towards cancer cures
7 March 2019, 14.30 - 19.00, Prof Charles Swanton (The Francis Crick Institute), The Francis Crick Institute, London

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




From top: Ahmad Alghamdi, Ophira Ginsburg, Richard Sullivan, Charles Swanton

NEWS

UCRF funded projects

The University Cancer Research Fund (UCRF) approved funding for five projects in the 2018 round:

Jon Lane: *Autophagy-transcriptional crosstalk in tumourigenesis: the LMX1A /LMX1B paradigm.* Purpose: To test the hypothesis that the ATG8 family of autophagy proteins coordinates the expression of autophagy genes by direct binding to and regulation of transcription factors in the nucleus.

Karim Malik and Madhu Kollareddy: *Establishing CARM1/PRMT4 as a novel drug target in high-risk neuroblastoma.* Purpose: RNA sequencing will establish that pharmacological inhibition of CARM1 will modulate E2F/Myconcogenic transcription factors to favour a growth suppressive pro-apoptotic signature rather than a proliferation signature. This will represent key validation data for this axis representing a tractable drug target, thus facilitating future MRC and or CR-UK drug discovery projects.

Harry Mellor and Gemma Cass: Title: *Markers of response to bevacizumab in ovarian cancer*. Purpose: To identify serum markers of response to bevacizumab in patients with ovarian cancer.

Stefan Roberts: *The role of BASP1 in the response of cancer cells to tamoxifen*. Purpose: Recent results from our laboratory suggest that the tumour suppressor BASP1 plays a central role in the action of the anti-cancer drug tamoxifen in breast cancer cells. The purpose of this proposal is to obtain preliminary data for a grant application that will explore how BASP1 regulates the different effects that tamoxifen exerts in endometrial cancer cells.

Kaitlin Wade: *The human gut microbiome in colorectal cancer: causal effects vs. confounded relationships*. Purpose: To support or challenge the role of the human gut microbiome in the development of colorectal cancer using applied epidemiology and Mendelian randomisation methodology.

Researcher profile: Sabina Sanghera

In January 2018 Sabina began her NIHR post-doctoral fellowship in health economics (01/18 - 12/20). The research is entitled *Accounting for the impact of fluctuating health states on quality of life measures included in economic evaluation*. Using chemotherapy treatment for cancer as a case study, she will assess the influence of the timing of assessment, recall and the quality-adjusted life year (QALY) calculation on cost-effectiveness recommendations when health is fluctuating. Sabina will use mixed-methods to understand how patients complete questionnaires, identify how and when to measure quality of life, and investigate the suitability of current valuation methods in recurrent fluctuating states.

Sabina will be collaborating with colleagues from NICE, University of Bristol, other Universities in the UK, and Erasmus University Rotterdam. Her mentors are Joanna Coast, Tim Peters, Dr Axel Walther, and Katherine Payne.

Funding successes

Miss Amy Davies (Bristol Dental School, pictured below right) from the **NIHR - Programme Grant for Applied Research**, £9,628 for *Head & Neck 5000* for one year.

Dr Abderrahmane Kaidi (Cellular and Molecular Medicine, pictured top right) from **Cancer Research UK**, £176,326 for *Understanding and targeting bacterial-driven cancer cell-stemness to overcome chemo-resistance*. Start date 1 June 2018 for two years.

Dr Abderrahmane Kaidi (Cellular and Molecular Medicine) from the **Leverhulme Trust**, £32,068 for *Understanding the role of nuclear actin polymerisation in DNA repair*. Start date 1 June 2018 for one year.

Fighting cancer with nature

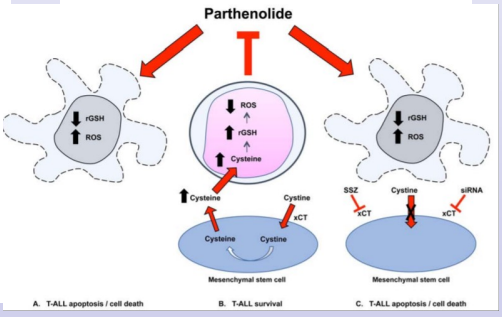
New research led by UoB cancer biologists has shown that bone marrow cells can protect cancer cells from a plant derived anti-cancer agent called Parthenolide.

Current therapies for children suffering from an aggressive type of cancer found in the blood, T-cell acute lymphoblastic leukaemia (T-ALL), 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.

The agent Parthenolide (PTL) is a natural plant extract that has previously shown excellent anti-leukaemia activity with minimal effects on normal blood healthy blood cells. However, some populations of these cancerous cells unfortunately do remain resistant to Parthenolide.

A new study explores the mechanisms for this resistance. The team found that protection against PTL is provided by the release of antioxidants by normal support cells derived from the bone marrow. By blocking the release of antioxidants a significant reduction in leukaemia cell resistance to PTL was seen. These findings indicate that it may be possible to improve the efficacy of PTL, as well as other chemotherapy drugs, by starving childhood T-ALL cells of anti-oxidants. The next step is to fully evaluate if blocking antioxidant release enhances anti-leukaemia drug effects in vivo.

Ede BC *et al*. (2018). Investigating Chemoresistance To Improve Sensitivity Of Childhood T Cell Acute Lymphoblastic Leukemia To Parthenolide. *Haematologica*. 186700.



Link between obesity and smoking behaviour

A study by the International Agency for Research on Cancer (IARC) provides new evidence that increased weight and obesity may result in increased smoking. The team found that increased body mass index (BMI), body fat percentage and waist circumference were associated both with a higher risk of being a smoker and with greater smoking intensity. These results were consistent in both men and women.

In contrast to previous studies evaluating the relationship between body weight and smoking behaviour, this study was based on genetic markers of obesity using UK Biobank data with genetic information on nearly 450 000 participants. Based on genetic markers of obesity, the study allows us to better understand the complex relationship between obesity and important smoking habits such as smoking initiation and intensity, as well as the impact of obesity on smoking cessation, says Dr Paul Brennan. The study also suggests that the link between BMI and tobacco exposure may originate in a common biological basis for addictive behaviours, such as nicotine addiction and higher energy intake.

It is known that smokers have a lower body weight on average than non-smokers, possibly because of a reduced appetite in smokers, but that people tend to gain weight after quitting smoking. However, among smokers, those who smoke more intensively tend to weigh more. This new analysis of genetic variants linked to body mass highlights the complex relationship between obesity and tobacco smoking.

Read more

Health data review

A new landmark report published by the MRC highlights the University's strengths in digital health research and other areas.

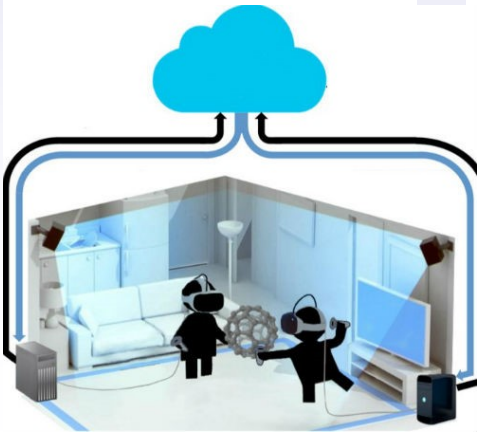
Mapping the Landscape of UK Health Data Research and Innovation is a new landmark report published by the Medical Research Council. The review, commissioned in 2017, encompasses 26 research organisations. The report highlights the complex and flourishing area of health data research in the UK, detailing key activities and major investments made by UK public funders, government, charities and universities from across the country.

Prof John Macleod, Professor in Clinical Epidemiology and Primary Care and Joint Head of CAPC, Bristol Medical School (PHS) said: "This is an important snapshot of the breadth and depth of UK Health Data Research. The fast-moving nature of this sector means that inevitably the report is already out of date. Bristol's unique strengths are clearly described and we will continue to grow these and realise their potential for impact on health improvement".

Read the full report

New drug and material discoveries to be untangled in VR

A joint team of computer science and chemistry researchers, in collaboration with developers at Bristol based start-up Interactive Scientific and Oracle Corporation, have used Oracle's public cloud infrastructure to combine real-time molecular simulations with the latest virtual reality technology. This collaboration has made it possible for researchers to reach out and 'touch' molecules as they move - folding them, knotting them, plucking them and changing their shape to test how they interact. Using cloud computing, several people can interact with the molecules in the same virtual space at the same time.



Industry is already showing interest in using VR in this breakthrough way to change how drugs are designed, and to transform the teaching of chemical structures and dynamics. Anybody wishing to try out the tasks described in the paper can download the software at https://isci.itch.io/nsb-imd, and launch their own cloud-hosted session.

O'Conor M *et al*. (2018). Sampling molecular conformations and dynamics in a multi-user virtual reality framework. *Science Advances*. 4(6), eaat2731.

Research Design Service (RDS)

The National Institute for Health Research (NIHR) has awarded the Research Design Service (RDS) a further five years of funding to continue the work of the RDS South West.

Proposals were invited from NHS organisations and Higher Education Institutions in England with proven expertise in research methodology and design. Ten organisations were successful and the combined Research Design Services will form a national network, liaising with each other to develop a consistent service to the research community across England. The NIHR funding will allow RDS advisers in the South West to continue offering free and confidential advice, drawing on a unique breadth of experience and established track record in improving funding applications.

The RDS have been funded for the ten years prior to this round of funding and the advice offered by us to researchers represents a key contribution to the NIHR's commitment to delivery of high quality health and social care research.

Prof Gordon Taylor, Director of NIHR RDS SW:

We look forward to continuing to support researchers, working in applied health, across the South West of England and to strengthen our engagement with partners in social care.

Find out more about how the RDS could help you by visiting the website or contacting the RDS South West Bristol Office:

The Education & Research Centre - Level 3
University Hospitals Bristol
NHS Foundation Trust
Upper Maudlin Street
Bristol, BS2 8AE
Tel: 0117 342 0233
Email: rds@uhbristol.nhs.uk

A home medical sensing device?

New research that could transform the future of healthcare will investigate whether it is possible to reuse WiFi radio waves as a medical radar system. The research is part of a new £1.5m grant awarded by the EPSRC, Toshiba and Decawave to the OPERA project, a consortium including the universities of Bristol and Oxford; University College London and Coventry University.

The 3-year project, starting in October 2018, will extend the current SPHERE project, which is developing sensors for use in the home to spot health and wellbeing problems, with both projects running until 2021.

Physical activity and behaviour patterns play a significant role in a range of long-term chronic health conditions; the UK currently spends 70% of its entire health and social care budget on these types of conditions. OPERA will attempt to build a complementary passive-sensing platform by reusing existing home technologies; a receiver-only radar network that detects the reflections of ambient radio-frequency signals from people.

Read more

Screening and treatment for prostate cancer

Jenny Donovan, Professor of Social Medicine, on recent findings from two prostate cancer trials:

A recent announcement stated that deaths from prostate cancer exceeded those from breast cancer in England and Wales for the first time – 11,800 per year. Yet screening for prostate cancer is a controversial public health topic. There are strong advocates for or against screening for prostate cancer who draw on the same evidence to reach opposite conclusions. The third and largest ever randomised trial of prostate cancer screening was published, the Cluster Randomized Trial of PSA Testing for Prostate Cancer (CAP), funded by Cancer Research UK and the Department of Health and Social Care. The NIHR-funded Prostate testing for cancer and Treatment (ProtecT) trial – the largest of its type – was embedded in CAP. The main finding of CAP was that after a median of 10 years' follow up, while the number of cases of prostate cancer was higher in men who underwent screening than in the control group, screening had no effect on prostate cancer-specific or all-cause mortality. Meanwhile in the ProtecT treatment trial, prostate cancer mortality was extremely low at around 1% at a median of 10 years. There was no difference in mortality between the groups allocated to surgery, radiotherapy or active monitoring. However, men who underwent radical treatments were half as likely to develop metastases or local disease progression compared with men who underwent active monitoring (2-3% versus 6%). And, for the first time, ProtecT showed that surgery and radiotherapy were equally effective at treating localised prostate cancer.

The outcomes of the CAP and ProtecT trials provide a great deal of information to facilitate individual decision-making and to guide policy and further research. Read the full review

Improving clinical trials

Medicine relies heavily on clinical trials which, while essential, are extremely costly and carry the potential of unintended adverse consequences.

A study, funded by CRUK, re-examined and replicated the results of a $115m US trial conducted in 2001 that aimed to see whether taking vitamin E or a selenium supplement could lower the risk of prostate cancer. The trial had to be abandoned early due to evidence that men taking vitamin E supplements were at elevated risk of prostate cancer and that those taking selenium were at higher risk of developing an aggressive form of the disease. A UoB team used a set of genetic variants known as SNPs to estimate the effect of increasing blood selenium to a similar level as in the trial to see if they could have predicted these results.

SNPs affect variations in the levels of vitamins and minerals we hold. The study looked at these selenium-increasing SNPs in more than 70,000 men who had taken part in other studies, allowing them to recreate the groups from the original trial. They analysed how many of these men had subsequently developed prostate cancer to see what differences there were between the groups. As with the trial researchers found that genetic variants associated with elevated blood selenium levels did not prevent prostate cancer but rather increased rates of advanced prostate cancer and type 2 diabetes.

The study showed that there may have been a way to predict the SELECT trial results in advance, and proposes that Mendelian randomisation could serve as an important time-efficient and inexpensive way of testing interventions for their efficacy and possible adverse effects prior to the design of a randomised trial. The study could have far reaching implications for the way that population health studies are conducted in the future.

Jarmolinsky J *et al*. (2018). Circulating Selenium and Prostate Cancer Risk: A Mendelian Randomization Analysis. *Journal of the National Cancer Institute*. Djy081.

Mendelian Randomisation Studies of Cancer Risk

Pierce BL *et al*. (2018). Mendelian Randomisation Studies of Cancer Risk: a Literature Review. *Current Epidemiology Reports.* 5(2), pp184–196. The paper summarises prior studies that have used Mendelian randomisation (MR) methods to study the effects of exposures, lifestyle factors, physical traits, and/or biomarkers on cancer risk in humans. Many such risk factors have been associated with cancer risk in observational studies, and the MR approach can be used to provide evidence as to whether these associations represent causal relationships. MR methods require a risk factor of interest to have known genetic determinants that can be used as proxies for the risk factor (i.e., "instrumental variables" or IVs), and these can be used to obtain an effect estimate that, under certain assumptions, is not prone to bias caused by unobserved confounding or reverse causality.

Patient prehabilitation gets a boost

Thanks to initial funding from the Elizabeth Blackwell Institute (EBI), we are now close to seeing some real impact from a prehabilitation intervention for cancer patients undergoing major surgery. The project, which aims to identify interventions that improve post-operative recovery, has been awarded further funding to take forward this important research.

Dr Maria Pufulete (Research Fellow, Clinical Trials and Evaluation Unit at the University of Bristol) has been awarded £1,854,558 from the National Institute for Health Research (NIHR) Technology Assessment Programme. The project was part of the Elizabeth Blackwell Institute's 'Research for Health Challenge' scheme.

Improving patients' health and fitness before a major operation can reduce the risk of complications and help recovery, yet its potential has not yet been sufficiently explored. Researchers aim to improve surgical outcomes in cancer patients by boosting health in the vital weeks before surgery. Maria led collaborative research to identify interventions that improve post-operative recovery and decrease the length of hospital stay. Such interventions may include dietary, exercise, psychological and physiological components. The team applied for an NIHR Health Technology Assessment grant to test one prehabilitation intervention (inspiratory muscle training) that was shown to work by the systematic review.

The project received its original funding from the EBI Research for Health Challenge scheme in response to a challenge from Dr Sanjoy Shah, Consultant in Intensive Care Medicine at University Hospitals Bristol NHS Foundation Trust (UHB), to develop a 'prehabilitation' programme for patients having major cancer surgery.

@BristolCancer

The Cancer Research Network is delighted to announce it has set up its first social media feed via Twitter, @BristolCancer. This is an exciting opportunity for PhD students, junior and/or senior staff to become more involved in developing communication channels with the wider Cancer community across the University and externally. If you feel you could contribute to curating the feed, please contact Catherine Brown. If you already have a Twitter account please do follow us and re-tweet at will!

ELIZABETH BLACKWELL FUNDING

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.

University of BRISTOL
Elizabeth Blackwell Institute for Health Research

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**.

Department of Health and Social Care
Global health research programme – research and innovation for global health transformation

Closing date: 01-Aug-18 Award amount: £5m

This supports interdisciplinary applied global health research for the direct and primary benefit of patients and the public in low- and middle-income countries. Research challenges in infection-related cancers are included in this call.

National Cancer Institute, USA

Inter-organelle communication in cancer (R01)

Closing date: 15-Aug-18 Award amount: USD275,000

This supports research projects that examine how inter-organelle communication in cancer cells and tumour-associated cells affects cellular function, adaptation and phenotypic plasticity.

Cancer Research UK
Pioneer award

Closing date: 05-Sep-18 Award amount: £200,000

This supports high-risk, high-reward research projects that have a clear relevance to cancer, and enables the exploration of novel ideas which may lead to new discoveries or approaches. Early-stage ideas from any discipline are welcomed.

Cancer Research UK
Predoctoral research bursary

Closing date: 18-Sep-18 Award amount: £200,000

This allows clinicians and other health professionals to get involved in research projects early in their career. The bursary gives the applicant a greater understanding of research before deciding whether to undertake a PhD or MD, or gives the applicant the time and resources to obtain preliminary data before applying for a PhD or MD.

Cancer Research UK
Early detection programme awards

Closing date: 25-Sep-18 Award amount: £12.5m

These support long-term, integrated and renewable programmes of exceptional science to transform how and when early cancers and pre-cancerous states are detected. Projects may focus on any specific or combination of the following research areas:

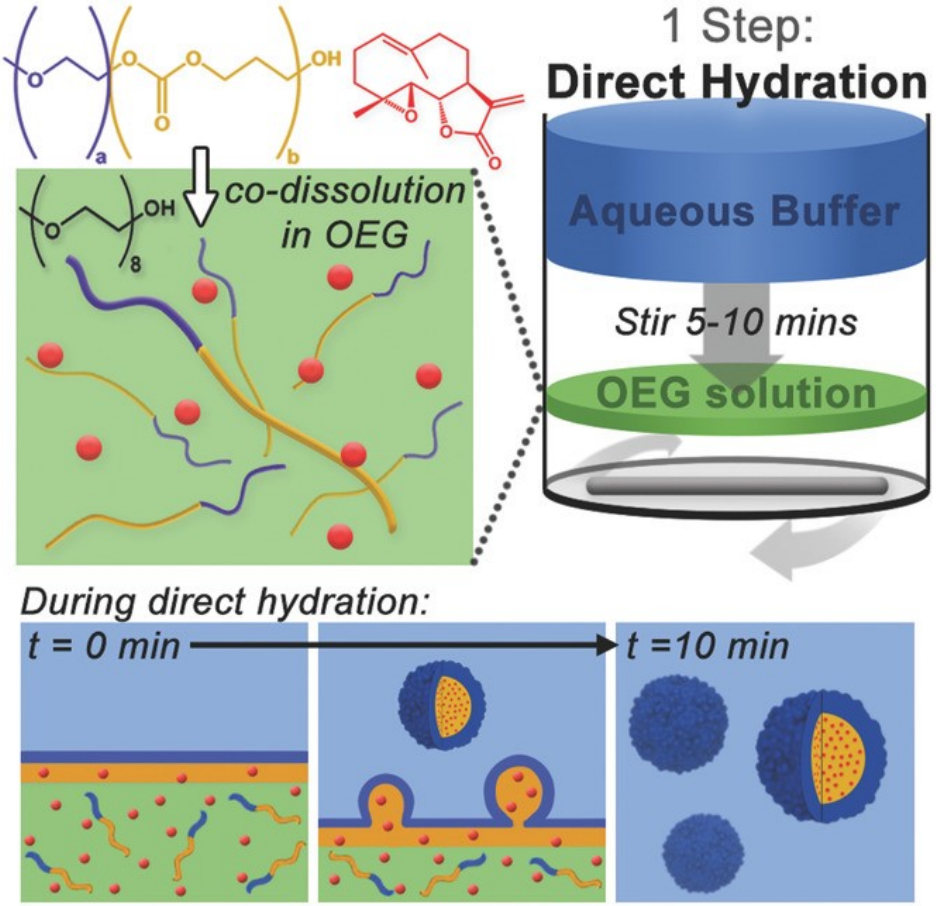
- biological research underpinning early detection and biomarker discovery and validation
- human-based early detection discovery research
- epidemiology and risk stratification for early detection, to inform populations for targeted research or screening
- data and computation-driven approaches to early detection
- development and utilisation of preclinical early detection model systems
- early detection technology development
- translational and clinical early detection research

FEATURED PUBLICATION

Biodegradable, Drug-Loaded Nanovectors via Direct Hydration as a New Platform for Cancer Therapeutics

Ridolfo R, Ede BC, Diamanti P, White PB, Perriman AW, van Hest JCM, Blair A & Williams DS

The stabilisation and transport of low-solubility drugs, by encapsulation in nanoscopic delivery vectors (nanovectors), is a key paradigm in nanomedicine. However, the problems of carrier toxicity, specificity, and producibility create a bottleneck in the development of new nanomedical technologies. Copolymeric nanoparticles are an excellent platform for nanovector engineering due to their structural versatility; however, conventional fabrication processes rely upon harmful chemicals that necessitate purification. In engineering a more robust (copolymeric) nanovector platform, it is necessary to reconsider the entire process from copolymer synthesis through self-assembly and functionalization. To this end, a process is developed whereby biodegradable copolymers of poly(ethylene glycol)-block-poly(trimethylene carbonate), synthesized via organocatalyzed ring-opening polymerization, undergo assembly into highly uniform, drug-loaded micelles without the use of harmful solvents or the need for purification. The direct hydration methodology, employing oligo(ethylene glycol) as a nontoxic dispersant, facilitates rapid preparation of pristine, drug-loaded nanovectors that require no further processing. This method is robust, fast, and scalable. Utilizing parthenolide, an exciting candidate for treatment of acute lymphoblastic leukemia (ALL), discrete nanovectors are generated that show strikingly low carrier toxicity and high levels of specific therapeutic efficacy against primary ALL cells (as compared to normal hematopoietic cells).



Schematic outlining the direct hydration methodology for the production of discrete nanovectors. Codissolution of PEG–PTMC copolymer (chains coloured blue and orange, respectively) and drug (red) in OEG (green solvent phase) is followed by stirring with aqueous buffer to create pristine nanovectors in under 10 min, without use of harmful solvents. During direct hydration, as the two phases coalesce, copolymer and drug undergo rapid hydrophobic co-assembly into micellar constructs.

Cancer Network

CONTACTS

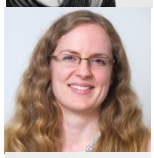
University of BRISTOL
Elizabeth Blackwell Institute for Health Research

Network Co-Lead:
Professor Paul Martin
Professor of Cell Biology

Network Co-Lead:
Dr Axel Walther
Senior Lecturer and Research Lead, Bristol Haematology & Oncology Centre

Catherine Brown, *Network Administrator*

- Dr Sabine Hauert, *Engineering Mathematics*



- Dr Zoë Holland, *RED Facilitator*

- Prof Richard Martin, *Professor of Clinical Epidemiology*

- Prof Anne Ridley, *Head of School of Cellular and Molecular Medicine*

- Prof Caroline Relton, *Professor of Epigenetic Epidemiology*

- Prof Ann Williams, *Professor of Experimental Oncology*

- Dr Emma Vincent, *Research Fellow and Early Career representative*

The Cancer Research Network is led by a Steering Group:

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