## Cancer Network Newsletter January - March 2020



### Smart needles in cancer diagnosis

A multidisciplinary team of experts has developed a groundbreaking 'smart needle' probe that uses light to pinpoint cancerous tissues or cells almost instantaneously.

The machine uses Raman spectroscopy, which measures the light scattered by tissues when a lowpower laser is shone onto it. Light is scattered differently from healthy or diseased tissues, so health professionals are able to detect whether there are concerns within seconds. The results show it is possible to

show a fingerprint of the disease that can be used to diagnose cancer within a few seconds, producing near instantaneous results for the clinician and reducing patient anxiety. The team believe that the new technique could significantly improve the rate of detection and diagnosis of cancers, and particularly lymphoma, the sixth most common cancer in the UK.

The 'smart needle' probe is comprised of fibre-optics encased within a fine needle that can look for cancer under the skin's surface – for example, in neck glands. Dr John Day (Physics), who built the first prototypes and continues to work on optimising the design:

If our probe is successful in clinical trials for lymphoma, then it opens the door to applying it to many other cancers in the body.

The team has already proved that it is able to differentiate between healthy and diseased tissue, having demonstrated its accuracy in the lab. They are now embarking on a 3--year project to initiate a clinical trial with the device in patients.

#### Inside this issue:

| Events                  | 2-3   |
|-------------------------|-------|
| News                    | 4-19  |
| EBI Funding             | 20    |
| Funding Opps            | 21-22 |
| Featured<br>Publication | 23    |
| Contacts                | 24    |
|                         |       |
| @BristolCancer          |       |



## EVENTS

## Workshops: Above and Beyond (A&B) and Research Capability Funding (RCF) grants

13 February 2020, 12.30 - 13.30, Research & Innovation, Education & Research Centre, Tutorial Room 1, Upper Maudlin Street

Digital Inclusion and Exclusion 13 February 2020, 12.30 - 14.00, central campus

Physician Associate Talk with Q and A13 February 2020, 18.00 - 19.15, Chemistry Lecture Theatre 2

Graphic Medicine – An Evening with Aneurin Wright 13 February 2020, 19.00 - 21.00, Aneurin Wright (illustrator and graphic novelist), Café Kino, 108 Stokes Croft, Bristol, BS1 3RU

#### **CReSS: Excess Treatment Costs and the SoECAT form**

18 February 2020, 12.30 - 13.30, Elinor Griffiths (Research Grants Manager) and Margie Berrow [Study Support Service Manager, CRN West of England, NIHR Clinical Research Network (CRN)], Tutorial Room 4, Education and Research Centre, Upper Maudlin Street

#### **Education Research Tutorials**

19 February 2020, 12.00 - 14.00, Dr Ellayne Fowler, TLHP Seminar Room, Top Floor, 39-41 St Michaels Hill

**T3 Technical Talk Time Seminar series** 19 February 2020, 14.00 - 15.00, venue TBC

'Miss' Suzanne Doyle - Why I hate being called Miss!20 February 2020, 12.30 - 13.30, The Wodehouse Lecture Theatre, HelenWodehouse Building, 35 Berkeley Square

Childhood Obesity; 'they' should do something about that 20 February 2020, 17.00 - 18.00, Ashley Adamson (Professor of Public Health Nutrition, Newcastle University), Room 2D1, Priory Road Complex

**EBI workshop on Interdisciplinarity in Health Research** 24 February 2020, 10.30 - 13.00, The Enderby Room, HH Wills Physics Laboratory, BS8 1TL

Faculties of Health and Life Sciences: Introduction to Research Grant Applications

25 February 2020, 10.00 - 12.30, room 2.26, 35 Berkeley Square

From top: Aneurin Wright, Elinor Griffiths, Margie Berrow, Ellayne Fowler, Ashley Adamson













#### SEE ALL EVENTS ON THE CANCER RESEARCH NETWORK WEBSITE

#### January - March 2020

## **EVENTS** CON'T

#### UK-Japan Symposium on Data-Driven Health: Data strategies to predict risk, prevent and manage disease in individuals and populations

26 February 2020, 9.00 - 16.45, 41 Portland Place, London W1B 1QH

Famous for 3 minutes 26 February 2020, 12.30 - 14.00, The Library Room, Royal Fort House

Children's Brain Tumour Drug Delivery Consortium: accelerating progress in drug discovery workshop

27 February 2020, 9.00 - 17.00, Fellow's Library, Playfair Building, Surgeons Quarter, Edinburgh

**National GP ACF Annual Conference** 4 - 5 March 2020, Bristol

South West Lymphoma Group spring meeting: Hodgkin Lymphoma and **HLH Review** 

4 March 2020, 17.00 - 20.45, The Castle Hotel, Castle Green, Taunton, Somerset TA1 1NF

#### South West regional meeting of the Society for Academic Primary Care 2020: 20:20 vision for primary care

5 - 6 March 2020, The Bristol Hotel, Prince Street, Bristol BS1 4QF

Crowd-sourcing Machine Learning in NMR 5 March 2020, 10.00 - 17.00, Lecture Theatre 2.41, Fry Building

**Active Outreach staff training** 6 March 2020, 13.30 - 16.30, venue TBC after registration

**RED Research Development International Drop in Session** 10 March 2020, 9.00 - 12.00, Verdon Smith Room, Royal Fort House

**Faculty of Life Sciences film club** 10 March 2020, 17.30 - 20.30, E29 Biomedical Sciences Building

#### **W** University of BRISTÓL

**Cardiff-Bristol joint symposium** 31 March 2020, 14.00 - 17.00

Senate House room 5.22, Tyndall Avenue, Bristol BS8 1TH

The Universities of Cardiff and Bristol are holding their next joint symposium on stem cells, metastasis and DNA repair. Presentations will precede break-out sessions on each area. A fund of £5,000 is available to apply for on a competitive basis to support collaborative projects. **REGISTER NOW** 

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#### SAPC iety for Academic Primary Care





CARDIFF

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**AERDY** 

# NEWS

### **MRI** assisted biopsies in cancer detection

Using MRI scans to target biopsies is more effective at detecting prostate cancers that are likely to need treatment than standard ultrasound guided biopsies alone. The research combined the results from seven studies covering 2,582 patients. The team, based across the Universities of Bristol, Ottawa, Exeter and Oxford, found that the use of pre-biopsy MRI combined with targeted prostate biopsy was better than a biopsy alone in detecting prostate cancers that are likely to need treatment, despite the differences between the seven individual studies. Using prebiopsy MRI led to fewer biopsy cores being taken per procedure, which in turn reduced side effects, and may potentially lead to avoiding biopsies for some men. Taken together, this new evidence supports the use of pre-biopsy MRI in diagnostic pathways for suspected prostate cancer. Prostate biopsies can cause side effects, and do not always identify the severity



of a cancer when it is present. MRI scans are increasingly being used before undertaking a prostate biopsy as part of the clinical pathway to diagnose prostate cancer, but their use isn't yet widespread in many countries. In the UK, pre-biopsy MRI has recently been recommended by the National Institute for Health and Care Excellence (NICE).

Elwenspoek MMC *et al.* (2019). Comparison of multiparametric magnet resonance imaging and targeted biopsy with systematic biopsy alone for the diagnosis of prostate cancer: a systematic review and meta-analysis. *JAMA Network Open.* 2(8):e198427.

### **Obesity and cancer risk**

A team of researchers conducted genetic analyses on eight common obesity-related cancer types and compared the genetic Mendelian randomization estimates of the association between body mass index (BMI) and cancer risk with the estimates from classical cohort studies. Excess body fatness is already recognised as an important cause of cancer and has



been estimated to account for 6% of all cancers in high-income countries. According to the results of this new analysis, the proportion of cancers attributable to overweight and obesity is, in fact, substantially higher.

Mariosa D, Carreras-Torres R, Martin RM, Johansson M & Brennan P (2019). What can Mendelian randomization tell us about causes of cancer?. International Journal of Epidemiology. 48(3), pp 816–821.

#### Funding successes: Part 1

To Dr David Coe (Cellular & Molecular Medicine), a Translational Acceleration and Knowledge Transfer (TRACK) award for *A novel system for the manufacture of tumour targeting T cells*. Funded by the Wellcome Trust, the £15,498 award will support a pilot study to demonstrate the concept of a proposed solution to a health, clinical or product development need.

#### Dr Alex Greenhough

(University of the West of England) was awarded £25,000 from **Bowel Cancer UK** in collaboration with Dr Adam Chambers and Prof Ann Williams (both UoB). They will be studying proteins that are found in bowel cancer cells to find out if they affect how patients respond to chemotherapy and radiotherapy. Read more

Dr Melanie Griffin (University Hospitals Bristol NHS Foundation Trust) received an Action Medical Research grant for Identifying risks and improving pregnancy care in childhood cancer survivors. The project will look at the long-term impact of cancer treatment involving bone marrow transplantation on women's reproductive health. She hopes to identify new ways to improve care for these childhood cancer survivors before and during their pregnancy, reducing the chances of their babies being born too soon. Read more

To Drs Kathreena Kurian (Bristol Medical School) and Sabine Hauert (Engineering Mathematics), a £500,000 Early Detection Project award from Cancer Research UK. This interdisciplinary project, Development of a cheap sensitive blood test for early detection of new and proven biomarkers of glioblastoma using fluorescent carbon dots and nanophotonics, came about as a result of the funder giving an open presentation and hosting a Q&A session here at UoB.

### Gut bacteria and bowel cancer

People who have a certain type of bacteria in their guts may be at greater risk of developing bowel cancer. The findings were presented by Elizabeth Blackwell Institute Early Career Fellow, Dr Kaitlin Wade (Bristol Medical School) at the 2019 National Cancer Research Institute (NCRI) conference in Glasgow, 4 Nov 219.

The study is the first to use Mendelian randomisation to investigate the causal role played by bacteria in the development of bowel cancer. The technique uses complex statistical analysis of data from large populations to provide evidence for cause and effect, rather than just the existence of an association. The researchers used data from the Flemish Gut Flora Project, the German Food Chain Plus study and the PopGen study, and the international Genetics and Epidemiology of Col-



orectal Cancer Consortium. They searched for small variations in the genomes of participants that occur more frequently in people with a particular disease or characteristic than in people without that disease or characteristic. They found that genetic variation in the population in particular parts of the genome were linked to the presence or varying amounts of 13 types of gut bacteria, and that people with an unclassified type of bacteria from the Bacteroidales group had a higher risk of bowel cancer compared to people who did not have these bacteria. Read more

### **External engagements: Part 1**

Dr Rebecca Richmond

(Bristol Medical School) was awarded a poster prize for her presentation on *Investi*gating DNA methylation signatures of e-cigarette use at the Society for Research on Nicotine and Tobacco (SRNT)-Europe conference held in Oslo, Sept 2019.

Dr Pau Erola (Bristol Medical School) presented a poster (a portion of which is reproduced here) on data-driven identification of molecular mechanisms in cardiooncology which was highly



#### Figure 2. This is a plot vow to explore the potential of EpiCospCO to inform us about proteins that are triaded to the pathogshopping of concer and cardiovancular disease (CVO). For each carcer type (plot diseased), we seenbed for carear ended proteins (light late clinics) that interact with other proteins identified as protein questificate trial laci (pOTLs) for CVO (red diamond), we seenbed for carear ended proteins (light late clinics) that interact with other proteins identified as protein questificate trial laci (pOTLs) for CVO (red diamonds for pathologies, orange triangles for risk factors). These pOTLs can be acting in citi (solid lives) or trans-acting (lotted fines), Proteins can interact other directly, a protein-protein interaction (dathed blue edges), or through the participation in the same pathway (red parallel lives). Shared pathways are represented with blue hexagons. We also queried which of these proteins are targeted by existing drugs. We found that the cancer drug centarized pathways are represented with blue hexagons. We also queried which of these proteins are targeted by existing drugs. We found that the cancer drug centarized plates (crist) inhibits DOPS. Other potential stage are degraded in light hows threagand meta-codes that are detailed tarlow.

commended at the Cardio-Oncology Symposium (ECOS) held in Barcelona, Oct 2019.

Dr Bernadette Carroll (Vice Chancellor's Fellow, Biochemistry) was awarded a Royal Society and Wellcome Trust Sir Henry Dale Fellowship. The award of just under £820,000, entitled Dysregulation of mTORC in senescence, covers Berni's time and a postdoc for 5 years. They will study jhow rewiring cellular equilibrium contributes to cellular senescence (a tumour suppressor mechanism of cell cycle arrest).

Dr Emma Vincent (Bristol Medical School / Cellular and Molecular Medicine) was awarded £300,000 from the World Cancer Research Fund for Are metabolites associated with obesity causing colorectal cancer? Read more

Dr Rebecca Richmond (Bristol Medical School) has been awarded £90,332 from the **Above & Beyond** charity for *Assessing the role of sleep in reducing risk and improving outcomes for breast cancer,* starting Jan 2020 for 2 ½ years.

Prof Dudley Shallcross (Chemistry) received £349,833 from **Children with Cancer UK** from Nov 2019 for two years. An atmospheric chemist, Dudley will help measure the toxi-

cology of aerosols in Thailand.

### Funding successes: Part 2

To Prof Ann Williams (Cellular and Molecular Medicine) from **Bowel & Cancer Research**, an award for Understanding Aspirin's mechanism of action in the clinical response of rectal cancer patients to chemoradiotherapy, Starting Oct 2019 until Apr 2021.

To Dr Avon Huxor (Policy Studies), Dr Emma Turner, Ms Eleanor Walsh (both Bristol Medical School) & Dr Raul Santos-Rodriguez (Engineering) a Jean Golding Institute seed corn fund for Elements of free text used in decision making: an exemplar from death reviews in prostate cancer and learning disabilities.

### Being active reduces risk of prostate cancer

Prostate cancer is the most common cancer in men in the UK, yet we still don't know all of its causes. The largest ever study to use genetics as a measurement for physical activity to look at its effect on prostate cancer, reveals that being more active reduces the risk of prostate cancer. Over 140,000 men were included in the study, of which 80,000 had prostate cancer. It found that people with the variation in their DNA sequence that makes them more likely to be active had a 51% reduced risk

of prostate cancer than people who did not have this particular variation. Importantly, the findings relate to overall physical activity, not just intense exercise.

The study looked at the effect of 22 risk factors on prostate cancer, but the results for physical activity were the most striking. This will pave the way for even more research, where similar methods could be applied to other lifestyle factors, to help identify ways men can reduce their risk of prostate

cancer.

Kazmi N et al (2019). Appraising causal relationships of dietary, nutritional and physicalactivity exposures with overall and aggressive prostate cancer: two-sample Mendelian randomisation study based on 79,148 prostate cancer cases and 61,106 controls. International Journal of Epidemiology.



#### **External engagements: Part 2**

Integrative Epidemiology Cancer Programme (ICEP) researcher Dr Aayah Nounu attended the 4th European Association for Cancer Research (EACR) Cancer Genomics meeting in Cambridge, June 2019. An important focus of the conference was tumour immunotherapy, and using genomics or whole exome sequencing to predict epitopes presented by cancer cells that can then be exploited for tumour immunotherapy:

An important benefit (of attending) was to discover current research focuses in cancer genomics. It has definitely given me ideas of potential areas where we might be able to apply epidemiological methods.

PhD student Meda Sandu presented at the Mendelian Randomization Conference hosted by the Medical Research Council's Integrative Epidemiology Unit (MRC-IEU) in Bristol in July 2019. Her work explored a new application of two-step Mendelian Randomization to assess long term outcomes in feasibility RCTs.

Two Bristol Cancer researchers



were invited speakers on the **Richard Doll seminar series** hosted by the Nuffield Department of Population Health at the University of Oxford. On 21 May 2019 Prof Caroline Relton (Bristol Medical School) presented *Embracing epigenetics* in epidemiological studies: Uses in prediction and understanding disease mechanisms. Prof Athene Lane (Bristol Medical School) presented on 29 Oct 2019 with *Prostate cancer* screening and treatment: what is the trial evidence and linked epidemiology?

Like minded professionals making a difference to teachers and kids #mrconf2019

### Breast screening film for women with learning difficulties

A film made by and for women with learning disabilities to take the fear out of going for breast screenings launched and premiered at North Bristol NHS Trust in November. The biggerhouse film production for Avon Breast Screening tells the story of a woman with learning difficulties being asked to go for a mammogram and follows her through the process.

It has been well documented that women with learning disabilities are not well informed about breast cancer and that the uptake of breast screening in this group is very low. The team are hoping this video, which was filmed at North Bristol NHS Trust, will help change perceptions for people with learning difficulties and encourage them to look after their health by going for the test.

More than 40 people attended the launch at North Bristol NHS Trust where the film

was premiered.

WATCH THE FILM: Do The Test - GO FOR IT!



### Brain tumour research and precision medicine

New research on brain tumours could improve patient diagnosis and treatment options as part of a precision medicine approach. Brain tumours are the leading cause of cancer deaths in children and adults under the age of 40, with 16,000 people in the UK diagnosed with a brain tumour each year. The study, led by the Brain Tumour Research Centre at the University of Bristol in collaboration with the Cancer Research and Cell Biology (CCRCB) at Queen's University Belfast, investigated the genetics of brain tumours.

The research outlines the mutations that are particular to different tumour types. This information is important to enable precision medicine, where a patient would receive therapies tailored to the specific DNA mutations in their tumour. These findings could pave the way for developing new targeted treatments that are more effective. The research also followed the mutations that develop during brain cancer, which could identify new therapy options to be given as the cancer progresses and help to extend patient



survival.

With only 5% of the national spend on cancer research allocated to brain cancer, there is a pressing need to build capacity and develop research programs for brain tumour research throughout the UK particularly to advance precision medicine, which promises more individualised treatments and better outcomes for brain tumour patients.

Ellis HP *et al.* (2019). Clinically actionable insights into initial and matched recurrent glioblastomas to inform novel treatment approaches. *Journal of Oncology.* 

### VR documentary shown at Venice Film Festival

The 76th Venice International Film Festival, the oldest film festival in the world, hosted a viewing of The Waiting Room, written by BAFTA winning documentary filmmaker Victoria Mapplebeck. The film documents her breast cancer journey from diagnosis through to treatment and recovery, and is one of three which makes up the multi-disciplinary research project, Virtual Realities: Documentary Encounters project, a collaboration between the University of Bristol, University of Bath and the University of West

of England and funded by the Engineering and Physical Sciences Research Council [EPSRC].

When Victoria was diagnosed with breast cancer, she decided to create a film and VR project which would explore each step of her journey from diagnosis to recovery. Shot entirely



on an iPhone X, she filmed her time in waiting rooms, surgery, consultations, CT scans and chemotherapy. The result is an unflinching portrait of the blood, sweat and tears of cancer treatment. Victoria makes visible the often invisible parts of cancer treatment, the sickness, the fatigue, the tears and

the hair loss, and how family life was transformed by a year of living with cancer.

The film was shortlisted to win a prize in its section (linear).

### 'Supercharged' cell therapies to treat solid tumours

A University of Bristol spin-out company has raised £1.1 million in funding to develop next generation cell therapies that could open new ways to treat solid tumours. Treatments for solid tumours are limited by the inability of immune cells to penetrate the tumour microenvironment. CytoSeek's pioneering cell membrane augmentation technology is being used to create the first effective cell therapy for solid tumours; the process involves modifying a patient's own immune cells to "supercharge" them against cancer cells.

At the moment cell therapies of this kind are only used in

the treatment of cancers in the blood. CytoSeek are looking at ways that cell therapy can also be used for solid tumours, which are responsible for 85% of cancer-related deaths. To do this, They have developed a protein-based cellular paint that can be put on cells to improve their cancer-killing performance.

The company, founded by Adam Perriman, Professor of Bio-





engineering (Cellular and Molecular Medicine), is based at Bristol's Unit DX incubator. It secured funding from ten entrepreneurs who are all members of the Bristol Private Equity Club; the Venture Capitalist fund UKI2S and the University of Bristol Enterprise Fund managed by Parkwalk.

Below: the surface of a tumour © CytoSeek ; above, Prof Adam Perriman

Po

### Key risk factors for epithelial ovarian cancer

Recent work led by Integrative Cancer Epidemiology Programme (ICEP) researcher James Yarmolinksy (Bristol Medical School) found that only two of twelve previouslyreported risk factors – a genetic tendency to endometriosis and smoking - actually increase the risk of invasive epithelial ovarian cancer. Little evidence was found to support roles for most other previously-reported risk factors for this cancer. However, some of these risk factors were associated with specific types of ovarian cancer, including height with clear cell

carcinoma and menopause age with endometrioid carcinoma.

The team carried out the research because it was not clear whether previously reported risk factors for epithelial ovarian cancer, including reproductive and lifestyle factors, actually caused the disease or whether they were observed as a result of bias



inherent in some research techniques. They used Mendelian randomisation (MR) to provide more reliable evidence of the causal effects of factors on disease outcomes. The team hope that their findings will lead to the development of strategies for the future prevention of epithelial ovarian cancer.

Yarmolinsky J et al. (2019). Appraising the role of previously reported risk factors in epithelial ovarian cancer risk: A Mendelian randomization analysis. *PLoS Med*. 16(8), e1002893.

#### Cytarabine remains the backbone of therapy in acute myeloid leukemia (AML). The ability to assess intracellular cytarabine triphosphate (ara-CTP) levels in patients receiving cytarabine represents a major goal in the prediction of treatment response. This study, conducted within a clinical setting, aimed to assess ara-

CTP levels in circulating peripheral blasts from non-M3 AML patients receiving cytarabine at one of three dosing levels, using a novel biosensor assay. Results from the initial 72 hours postcommencement were

### Predicting remission in acute myeloid leukaemia

correlated with day 28 remission status, with feasibility parameters concurrently assessed. Intracellular ara-CTP was detectable in *ex vivo* blasts post-treatment for standard-dose (SD) and highdose (HD) patients, and quantification revealed a 27-fold increase in intracellular steady-state concentration

AML blas

ara-CTP

eripheral bloc

between the two dosing levels. Concurrent assessment of peripheral leukemiaassociated immunophenotype (LAIP)-positive cells revealed a decline in burden (0–72 hours), which correlated with remission status.

Anderson E *et al.* (2019). Intracellular cytarabine triphos-

Deel intracellular (ara CTP) in circulating AVR, blants outputs at day 387

phate in circulating blasts post-

treatment predicts remission status in patients with acute myeloid leukemia. *Experimental Hematology*. 74, pp. 13-18.

### **£10M for postgraduate biomedical sciences research**

The Wellcome Trust has awarded the University of Bristol over £10 million in funding for two PhD programmes in the faculties of Health Sciences and Life Sciences. The programmes will provide fouryear PhD studentships to support promising students to undertake in-depth postgraduate training in genetics and population health, and in molecular and cellular biology. The Molecular, Genetic and Lifecourse **Epidemiology** Programme will train a new generation of researchers in the integration of genetic and molecular data in epidemiological studies (which focus on the incidence, distribution and control of disease in populations). The Dynamic Molecular Cell Biology Programme will train the next generation of cell biologists to examine the dynamics of living cells, tissues and organisms, and their role in human health and disease. Each programme application was assessed for both scientific excellence and the culture of the research environment that students would be trained in, including supporting wellbeing, diversity, good research practice, strong supervisory and mentorship arrangements, and support for students to consider a range of onwards career destinations.



### **UK Reproducibility Network**

UK universities will collaborate to improve the quality of UK academic research output. Whilst the UK is at the leading edge of research globally, there is a need to constantly strive to improve in order to retain that positions. Crucially, institutions must produce research that is rigorous, robust and of high-quality, to ensure that the UK retains its reputation for producing worldleading research. The UK Reproducibility Network UKRN is currently an informal network of over 40 research institutions across the UK that works with researchers, universities, and a range of stakeholders to promote the adoption of initiatives in order to further improve research rigour, robustness and quality. Advances in science depend on research that is replicable, and this is underpinned by high-quality training and appropriate incentives for researchers. UKRN initiatives will include developing common training across career stages, aligning promotion and hiring criteria to support open and reproducible



research practices, and sharing best practices. Academic leads will liaise with grassroots networks of researchers at their institutions and with UKRN stakeholders, including funders and publishers. Prof Marcus Munafò (Experimental Psychology) is Chair of the UK Reproducibility Network steering group.

### Adult fly could help understand intestinal regeneration

Intestinal epithelial cells (IECs) are exposed to diverse types of environmental stresses such as bacteria and toxins, but the mechanisms by which epithelial cells sense stress are not well understood. New research by the Universities of Bristol, Heidelberg and the German Cancer Research Center (DKFZ) have found that Nox-ROS-ASK1-MKK3-p38 signalling in IECs integrates various stresses to facilitate intestinal regeneration. They used the adult fly intestine to understand how IECs sense stress or damage, defend themselves and promote epithelial regeneration. The team found that NADPH Oxidase (Nox) in IECs produce reactive oxygen species (ROS) upon stress, but it wasn't fully understood how ROS promote intestinal regeneration. Their research showed that it is partly effected by Ask1-MKK3p38 signalling in IECs, stimulating their production of intestinal stem cell (ISC) mito-



gens and ISC-mediated regeneration. Inflammatory bowel diseases (IBDs, e.g., ulcerative colitis, Crohn's disease) are characterised by chronic gastrointestinal inflammation due to damage, and have been linked to an increased risk for colorectal cancer. The cause of IBDs and how they develop is not well understood.

Patel PH *et al.* (2019). Damage sensing by a Nox-Ask1-MKK3p38 signaling pathway mediates regeneration in the adult *Drosophila* midgut. *Nature Communications*.

PhD training across the biosciences has received a massive boost thanks to a £18.5 million funding award from the Biotechnology and Biological Sciences Research Council to the University of Bristol-led South West Biosciences Doctoral Training Partnership (SWBio DTP).

The SWBio DTP will offer fouryear PhD studentships over five cohorts starting in October 2020, during which students will undertake interdisciplinary training in statistics, bioinformatics, coding, experimental design, innovation and understanding the impact of research. Students will also

#### £18.5 million boost for South West biosciences

undertake three-month Professional Internship for PhD Students (PIPS) placement to develop their skills further and to explore possible future career directions. The partnership, which is led by Bristol together with the Universities of Bath, Cardiff and Exeter (the GW4 Alliance), alongside Rothamsted Research, has recently expanded to include six new regional associate partners that will provide access to expertise and facilities across the South West and Wales.



These encompass, the Marine Biological Association (MBA), Plymouth Marine Laboratory (PML), Swansea University, SetSquared Bristol, UCB Pharma and the University of the West of England (UWE).

### **External engagements and funding successes: Part 3**

Men who are larks (morning preference) are at lower risk of prostate cancer according to findings by Dr Rebecca Richmond (Bristol Medical School) presented at the Mendelian Randomization Conference hosted by the Medical Re-

| Replication in  | UK Biobank<br>Chronotype and prostate cancer risk |
|---|---|
| One-sample MR analysis<br>Octo remove related<br>dividuals and restricted to<br>vinite British <sup>*</sup><br>towelfact allele score<br>number of morning<br>preference alleles for each<br>dividual<br>skil prostate cancer cases<br>and 19/4 37 made controls<br>pre category increase |   |
|   | 0.7 Odds ratio                                    |

search Council's Integrative Epidemiology Unit (MRC-IEU) in Bristol in July 2019. The meeting was very well attended (see image right) and included talks from researchers in cancer, cardiovascular disease, mathematics, education and women's health.

Vice Chancellor's Fellow Dr Bethan Lloyd-Lewis (Cellular and Molecular Medicine) was awarded £99,929 from the Academy of Medical Sciences to pursue a project entitled



Deciphering the contribution of development and age to breast cancer aetiology. The project will begin in February 2020 and continue for two years.

### Mendelian randomization study of pancreatic cancer

The 5-year mortality rate for pancreatic cancer is amongst the highest of all cancers; greater understanding of underlying causes could inform population-wide intervention strategies for prevention. Genetic data from genome-wide association studies (GWAS) have become available for thousands of phenotypes; data can be exploited in Mendelian randomization (MR) phenomewide association studies (PheWAS) to efficiently screen the phenome for potential determinants of disease risk. The team conducted an MR-PheWAS of pancreatic cancer using 486 phenotypes and summary genetic data from a GWAS of pancreatic cancer

(7,110 cancer cases; 7,264 controls). They found evidence that previously reported risk factors of body mass index and hip circumference were associated with pancreatic cancer. They also found evidence of novel associations with metabolites that have not previously been implicated in pancreatic cancer: fibrinogen-cleavage peptide and O-sulfo-L-tyrosine. An inverse association was also observed with lung adenocarcinoma. This implies that markers of adiposity (BMI and



hip circumference) are potential intervention targets for pancreatic cancer prevention. Further clarification of the causal relevance of fibrinogen cleavage peptides and O-sulfo-L-tyrosine in pancreatic cancer aetiology is required, as is the basis of observed association with lung adenocarcinoma. For pancreatic cancer, MR-PheWAS can augment existing risk factor knowledge and generate novel hypotheses to investigate.

Langdon RJ, Richmond RC *et al.* (2019). A phenome-wide Mendelian randomization study of pancreatic cancer using summary genetic data. *Cancer Epidemiology, Biomarkers and Prevention.* 

## Phase II trial of penile cancer treatment

A Phase II single-arm trial was designed to recruit 17 patients with relapsed penile cancer to gauge at which stage the cancer shrank or disappeared after treatment (the objective response rate, or ORR). Treatment comprised six 21-day cycles of cabazitaxel; 9 patients were recruited from four UK centres with a median age of 61 (range, 27– 73.6) years, and 7 patients had metastases. Patients received a median of two chemotherapy cycles. None of the nine patients achieved ORR and the trial was stopped. Cabazitaxel was well tolerated with no dose reductions or delays. Three patients had grade 3/4 adverse events (anaemia, vomiting, or neutropenic sepsis). The median progression-free and overall survival were 1.3 and 5.6 months, respectively. The trial did not reach the threshold for further continuation of single-agent cabazitaxel. However, the observed tolerability profile supports its further investigation in combination with other agents to improve patient outcomes.

Challapalli A *et al*. (2019). A phase II trial of cabazitaxel as second line chemotherapy in relapsed locally advanced and/or metastatic carcinoma of the penis. *Journal of International Research*.

The University of Bristol has committed £800,000 from its Quality Related (QR) Global Challenges Research Fund (GCRF) allocation to support research activities with partners in low and middle income countries. These QR GCRF Investment Grant awards will develop research capacity and conduct research that will provide real impact in Ethiopia, Zimbabwe, South Africa, Peru, India, Pakistan and Nepal. Research activities span from de-

veloping a glacial flour from sediments released from melting glaciers to understanding the impact of HIV infections and its treatment on the effect menopause has on the musculoskeletal health of African women.

### Funding to research global challenges

One of the funded projects, Functional interplay of ciliary trafficking complexes and motor proteins, was awarded UK Research and Innovation funding of £460,000, and will be led by Prof David Stephens (Biochemistry), in collaboration with Professor Kazuhisa Nakayama at Kyoto University.

Cilia – microscopic, hair-like structures that extend from the surface of cells – are essential for human and animal development and are important in the formation and maintenance of bone, kidney function, signalling in the brain and many more body functions. This fundamental bioscience project aims to provide a fuller understanding of their structure and function, which is relevant in a wide range of fields such as the development of medicines to target common cancers.

> The Fund for International Collaboration will ensure that UK researchers and innovators are at the forefront of global efforts to tackle these challenges, delivering benefits that will be felt here in the UK and throughout the world.



#### **Swarming Across Scales**

If complex systems science had a mascot, it might be the murmuration. These enormous flocks of starlings darken skies across the northern hemisphere, performing intricate airborne manoeuvres with no central leadership or plan. Each bird behaves according to a simple set of rules about

how closely it tracks neighbours, resulting in one of the world's most awesome natural spectacles. This notion of self-organising



flocks of relatively simple agents has inspired a new paradigm of engineering, building simple, flexible, adaptive swarms that stand to revolutionise the way we practice medicine, map ecosystems, and extend our public infrastructure. We're living at the dawn of the age of the robot

> swarm – and these metal murmurations help us create communications networks, fight cancer, and evolve to solve new problems

for an age that challenges the isolated strategies of individuals.

Dr Sabine Hauert (Engineering) was a guest on the Complexity show, hosted by the Sante Fe Institute on 16 October 2019. In the episode, they talk about how swarms have changed the way we think about intelligence, and how we build technologies for everything from drug delivery to home construction.

Listen to the podcast

### Risk of bias in approval of new cancer drugs

The European Medicines Agency (EMA) is responsible for evaluating the clinical effectiveness and safety of new medicines. In 2017, more than a quarter (24 of 92) of EMA approvals were for cancer drugs, most of which were based on evidence from randomised controlled trials, considered to be the "gold standard" for evaluating treatment effectiveness.

However, flaws in the design, conduct, analysis, or reporting of randomised controlled trials can distort estimates of treatment effect. To evaluate these flaws in more detail, researchers led by the London School of Economics, with methodological input from the National

Institute for Health Research (NIHR) Bristol Biomedical Research Centre (BRC) and NIHR Collaboration for Leadership in Applied Health Research and Care West (CLAHRC West), examined the design, risk of bias, and reporting of randomised controlled trials that supported European approvals of cancer drugs from 2014 to 2016. The risk of bias was assessed using the new Risk of Bias tool for randomised trials (RoB 2) developed by researchers from CLAHRC West and BRC, which assesses several domains of trial design, conduct, analysis and reporting.

During this period, the EMA approved 32 new cancer drugs on the basis of 54 studies.

Overall, 19 trials (49%) were judged to be at high risk of bias because of deficits in their design, conduct, or analysis. Trials that evaluated overall survival were at lower risk of bias than those that evaluated surrogate measures of clinical benefit. Policymakers and regulators should carefully consider risk of bias in trials that support regulatory decisions.

Naci H et al. (2019). Design characteristics, risk of bias, and reporting of randomised controlled trials supporting approvals of cancer drugs by European Medicines Agency, 2014-16: cross sectional analysis. BMJ. 366, I5221.

#### January - March 2020

The Bristol City Fellows Programme, funded by a £118,000 Impact Acceleration Account grant from the Economic and Social Research Council, is led by the University of Bristol with Bristol City Council's City Office and the Social Justice Project. The new fellows, announced at the Mayor's City Gathering on 10 January 2020, will work with charities and community groups over 18

**Richard Martin**, Professor of Clinical Epidemiology (Bristol Medical School) led the Cancer Research UK (CRUK)-funded **Cluster Randomised Trial of PSA Testing for Prostate Cancer** 

(CAP) trial. The trial attracted national recognition for providing definitive answers about the value of Prostate-Specific Antigen (PSA) testing in prostate cancer screening. In an interview with CRUK, Richard spoke about the impact of the study and the advice he'd give researchers seeking funding for population research.

"There have been exciting developments in the last couple of years that mean we will be able to consider options for prostate cancer screening other than PSA testing. Advances in the use of multiparametric magnetic resonance imaging (MRI)

months to ensure marginalised voices have a say in decision-making and in turn tackle systemic inequalities across Bristol. One of the fellows, Lucie Martin-Jones, Head of Community Services at The West of England Centre for Inclusive Living, will look at



#### **Bristol City Fellows**

improving healthcare and support for disabled people, ultimately creating new systems which are person-centred and allow disabled people more independence and control:

We will be looking at existing healthcare systems to establish how effectively they are delivering what matters to our citizens and how they can be improved. This works towards Bristol's One City Plan aspirations for health and wellbeing.

### Insights into population health research

to select people with aggressive prostate cancer who need a biopsy could reduce some of the overdetection and harms that can result from the PSA test. However, costs of imaging all men aged 50-69 would be prohibitive; we'd need tests for triage. The genetic basis of prostate cancer is becoming increasingly well-defined. Samples from our trial have contributed to understanding which germline genetic variants are associated with increased risk of prostate cancer; genetics may help in identifying men who are at greater risk of prostate cancer and targeting them for MRI. Other tests, such as Stockholm3, that combine protein and genetic analyses have shown promise in identifying men who need further imaging and biopsy. In terms of treatment, active surveillance compared very favourably with radical treatment (surgery or radiotherapy) in our ProtecT trial, the treatment trial nested within the CAP study, particularly in men with low risk disease. The increasing use of active surveillance in low-risk disease would reduce the overtreatment of less aggressive prostate cancer.

Applications require a lot of time and effort to put together. You need to explain the objectives clearly and describe your methods in a careful and robust way; for example, people often forget to include sample size calculations. Funders are increasingly interested in understanding the potential impact of any findings, and working with a patient and public involvement group can be invaluable." **Read the full interview** 

#### **Graphic Medicine on the wall**

A mural in Stokes Croft is providing an accessible and inclusive way of representing and communicating issues surrounding healthcare. Graphic Medicine 'resists the notion of the universal patient and vividly represents multiple subjects with valid and conflicting points of view' and is intended to stand alongside more academic discourses and to enrich them, as new images and stories of illness and health emerge. The mural, titled *Wall* #1, is by physician, comics artist and writer, Ian Williams. He wanted to see how a comic strip would work on a wall and chose a series of wordless pan-

els to give a sense of the passing of time and the kind of things a doctor might see during a surgery. It was commissioned by the Centre for Health, Humanities and Science, which promotes work at the intersection of humanities, medicine, health and science, is opening the door to new





### Bristol's Children of the 90s project renewed

Bristol's Children of the 90s study will be supported for the next five years through an established collaboration between the University of Bristol, the Medical Research Council and The Wellcome Trust. A new commitment of up to £8.2 million will enable international research to continue into health, well-being and social science using data and samples from thousands of families.

Set up in 1991, Children of the 90s recruited 14,500 pregnant women from the Bristol area and has been charting their health, plus that of their children, ever since. Almost thirty years later the study is now recognised as the premier multigenerational birth cohort internationally with an outstanding reputation for enabling research.

The study's future plans include using face-to-face data and sample collection along with a growing collection of remote data collection technologies. This will ensure that



as many participants as possible can take part and help the study thrive and that over the next five years Children of the 90s will continue to lead the way in safe data storage and access for exciting new science. There are also plans to increase data collection from under-represented groups in health research such as fathers, continue recruiting the

new generation (children of the Children of the 90s) and to find ways to make it easier for participants to stay involved with more flexible clinics, remote data collection and by making better use of existing official records.

#### January - March 2020

### **Tractionless motion is possible**

Understanding how cells move autonomously is a fundamental question for both biologists and physicists. A team have identified a different propulsion mechanism particularly suited for cell motion in tissues: self-propulsion without traction (=local force on the surrounding environment) is possible if you are made of "active" matter, as cells are. They describe how a drop of active matter can move itself forward in a narrow channel without exerting any force on the walls around it.

The mechanism...provides a possible explanation to the open



question of how cells move in those environments. Such motility is crucial to a multitude of physiological processes in living organisms, including immune response and wound healing, and its deregulation is key to cancer dissemination (metastasis). Dr Aurore Loisy (Mathematics)

Loisy A *et al.* (2019). Tractionless Self-Propulsion of Active Drops. *Physical Review Letters.* 123, 248006.

#### Life Sciences growth in the south west

For the first time Life Sciences has been properly recognised locally as an enabler of growth. This could mean more opportunities for employment plus increased potential for research collaborations with partners. Richard Seabrook, Elizabeth Blackwell Institute's Advisor for Business Development, explained in a GW4 opinion piece what's next for the strategy to deliver

long-term growth for the Life Sciences sector in the area. GW4 achieved recognition for life and health sciences innovation in Bristol and the South West of England for the relaunched UK Industrial Strategy Life Science Sector Deal. The University of Bristol have been working alongside partners such as Invest Bristol and Bath, Bristol Health Partners, University of Bath and UWE, on the West of England Combined Authority local Industrial Strategy (WECA), launched Jul 19. WECA's first ever Local Industrial Strategy sets out how the area will contribute towards delivering the national Industrial Strategy's aim to raise productivity levels and create high-quality, well paid jobs across the country. The strategy mentions Life Sciences as a sector growing at pace and draws on the unique strengths of the region, underlining their ambition to be a driving force for clean and inclusive growth. It focuses on four key priorities: crosssectoral innovation; inclusive growth; the productivity chal-

lenge; innovation in in infrastructure.

**Read more** 



### **Collaboration for data science and digital technologies**

A formal partnership has been agreed between the University of Bristol and analytical instrumentation provider Malvern Panalytical. The Memorandum of Understanding formalises the organisations' relationship and focuses on mutual areas of interest and collaboration, including data analytics, machine learning, artificial intelligence, and the science underlying the structure and properties of materials. A key aim of this collaboration is to establish a pipeline of talented graduates, equipped with skills and expertise in the fields of data science and digital technologies. The partnership follows the opening of



Malvern Panalytical's new Data Science Hub at Engine Shed, the University-run innovation space next to Bristol Temple Meads, in 2019. The company, which employs more than 2,000 people worldwide, is also working with academics across the University - from Chemistry to Law - to test some of its new technologies while exploring issues around the ownership of data. **Read more** 

### The National Institute for Health Research (NIHR) in Bristol

The NIHR is the nation's largest funder of health research and Bristol does well in terms of NIHR funding. The city, through its universities and hospitals, hosts key NIHR infrastructure. The University of Bristol is the only university to host centres for all three NIHR schools; it also hosts one of only a handful of NIHR Blood and Transplant Research Units (BTRUs) – the BTRU in Red **Blood Cell Products**, which is growing red blood cells in the laboratory to treat rare diseases.

Bristol Health Partners has given a brief overview of the NIHR in Bristol:

•NIHR South West Research Design Service (RDS), a bespoke service to help you design studies and successfully apply for grants

 Bristol Trials Centre (BTC), collaborating with you to set up and manage studies, from grant application to publishing results

## National Institute for Health Research

- •NIHR Clinical Research Network (CRN) West of England, helping you run clinical research in the NHS, public health and social care settings
- NIHR Bristol Biomedical Research Centre (BRC), bridging the gap between fundamental research and new treatments
- •NIHR Applied Research Col-

laboration West (ARC West), applied health research to address the issues facing the health and social care system

- NIHR School for Primary Care Research (SPCR), driving forward primary care research to influence policy and practice
- NIHR School for Public Health Research (SPHR), driving forward public health research to influence policy and practice
- NIHR School for Social Care Research (SSCR), driving forward adult social care research to influence policy and practice

## ELIZABETH BLACKWELL FUNDING

Nurturing Research. Improving Health.



#### 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.

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?

**Research Professional** provides access to an extensive database of funding opportunities, and can send out tailored alerts based on keywords that <u>you</u> 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 Clinical trial award

Closing date: 19-Mar-20

Award amount: £1.5 million

This supports investigator-led interventional clinical trials of cancer treatment, including systemic treatment, radiotherapy and surgery, with the aim of improving outcome.

Cancer Research UK Experimental Medicine award Closing date: 19-Mar-20

Award amount: £5 million

This support investigator-led studies for translational research conducted in association with a clinical trial or clinical study, with the objective of optimising treatment and maximising patient benefit. Proposals must be for interventional studies of cancer treatment developed with the involvement of an experienced clinical trials unit.

#### Dr Josef Steiner Cancer Foundation Cancer research award

Closing date: 15-Apr-20

Award amount: CHF 1,050,000

This supports young investigators involved in projects related to the translation of new basic or theoretical insights into clinical applications, within basic or clinical cancer research.

Applicants should typically be 40 years or less, and able to provide the infrastructure needed to carry out the proposed project. Priority is given to applications from scientists based within European institutions.

#### Medical Research Council

Primary and secondary prevention of cancer funding call

Closing date: 30-Apr-20

Award amount: CHF 1,050,000

This seeks to generate new knowledge on interventions and their implementation for the prevention of cancer in low- and middle-income countries. The aim is to adapt and scale-up the implementation of interventions in accessible, affordable and equitable ways in order to improve the prevention and early diagnosis of cancer in real-life settings. Interventions should meet conditions and requirements of the local health and social system context and address any other contextual factors identified as possible barriers.

#### Koninklijke Nederlandse Akademie van Wetenschappen, NL

Bob Pinedo cancer care award

Closing date: 01-May-20

Award amount: €100,000

This recognises an internationally acclaimed researcher or research team currently active in the field of translational cancer research and compassionate cancer patient care. The award is expected to be used to finance a research project in the area of specialisation of the award winner.

#### National Cancer Institute (US)

Innovative research in cancer nanotechnology

Closing date: 21-May-20

Award amount: USD \$2,250,000

Support projects addressing major barriers in cancer biology or oncology using nanotechnology and should emphasise fundamental understanding of nanomaterial or nanodevice interactions with biological systems.



## FEATURED PUBLICATION

#### **Outcompeting cancer**

Vishwakarma M & Piddini E (2020). Nature Reviews Cancer. Published 13 January 2020.

The tumour microenvironment plays a critical role in determining tumour fate. Within that environment, and indeed throughout epithelial tissues, cells experience competition with their neighbours, with those less fit being eliminated by fitter adjacent cells. Herein we discuss evidence suggesting that mutations in cancer cells may be selected for their ability to exploit cell competition to kill neighbouring host cells, thereby facilitating tumour expansion. In some instances, cell competition may help host tissues to defend against cancer, by removing neoplastic and aneuploid cells. Cancer risk factors, such as high-sugar or high-fat diet and inflammation, impact cell competition-based host defences, suggesting that their effect on tumour risk may in part be accounted for by their influence on cell competition. We propose that interventions aimed at modifying the strength and direction of cell competition could induce cancer cell killing and form the basis for novel anticancer therapies.



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Cell competition is a form of cell-to-cell communication that selectively eliminates less fit or misspecified cells ('loser cells'), when they interact with fitter or correctly specified cells ('winner cells'). A defining feature of cell competition is that loser cells are viable on their own, in the absence of cell competition. As loser cells are removed, through mechanisms such as apoptosis or extrusion, winner cells replace them and take over the tissue.

Cell competition as a putative driver of colorectal cancer. APC-/--driven tumours grow by inducing host cell death via apoptosis. Blocking apoptosis or reducing Hippo signalling inhibits cell competition and the growth of APCmutant tumours.



APC-/- cell

Normal cells

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