

Cancer Network Newsletter

April - May 2018

Lung cancer drug resistance simulations

Scientists from UoB and Parma have used molecular simulations to understand resistance to anticancer drug osimertinib, used to treat types of lung cancer.

Osimertinib binds tightly to the epidermal growth factor receptor (EGFR), which is overexpressed in many tumours. EGFR is involved in a pathway that signals for cell proliferation, and so is a target for drugs. Blocking the action of EGFR can switch it off, and so is a good way to treat the disease.

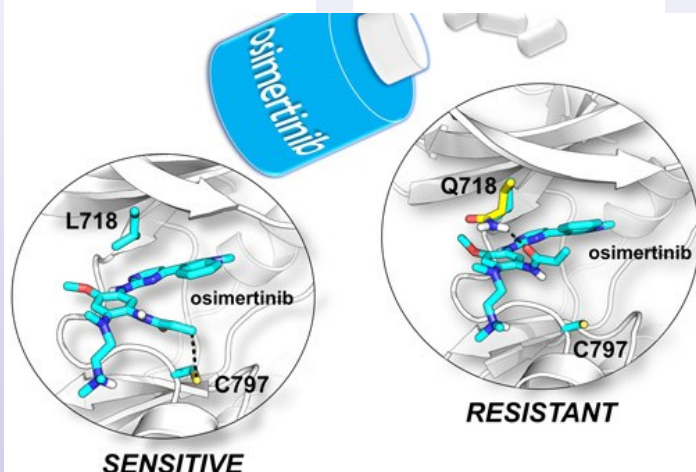
Osimertinib is an effective anticancer

drug that works in this way. It is used to treat non-small-cell lung cancer (NSCLC), in cases where the cancer cells have a particular (T790M) mutant form of EGFR. It is a covalent inhibitor which binds irreversibly to EGFR. Although patients generally respond well to osimertinib, most acquire drug resistance within one year of treatment due to EGFR protein mutation. Unlike other drug resistant mutants, it was not at all clear how this change stops the drug from binding effectively, information potentially crucial in developing new drugs to overcome resistance.

A collaboration between medicinal and computational chemists and clinical oncologists has revealed exactly how subtle changes in the protein target cause drug resistance.

By using combined quantum mechanics/molecular mechanics (QM/MM) methods the team was able to study chemical reactions in proteins; this is crucial in investigating covalent inhibitors, which react with their biological targets, and are the focus of growing interest in the pharmaceutical industry.

Callegari D et al. (2018). *L718Q mutant EGFR escapes covalent inhibition by stabilizing a non-reactive conformation of the lung cancer drug osimertinib*. *Chemical Science*. 9: 2740.




Inside this issue:

| | |
|--------------------------------------|-------|
| Events | 2-3 |
| News | 4-12 |
| EBI Funding | 13 |
| Funding Opps | 14-15 |
| Featured Publication | 16 |
| Contacts | 17 |

 cancer-research@bristol.ac.uk

 bristol.ac.uk/cancer

 0117 33 17610

EVENTS

Haematology Update - Teenage & Young Adults through to 30

11 May 2018, 9.30 - 17.00, Mary Ward House, London

Creative Reactions Bristol

11 - 22 May 2018, Hamilton House, 80 Stokes Croft, BS1 3QY

Open Presentation from Professor Duncan Wingham, Chief Executive NERC

11 May 2018, 11.30 - 12.30, Prof Duncan Wingham (Chief Executive of NERC), G1S Hepple Lecture Theatre, Geographical Sciences

International Clinical Trials Day

14 - 20 May 2018, University Hospital Bristol

Personalising Cancer Care with Genomic Medicine – Accelerated Design Event

16 May 2018, 9.30 - 16.00, DoubleTree by Hilton Bristol City Centre, Redcliffe Way, Bristol, BS1 6NJ

Statistics Clinic - 16 May 2018

16 May 2018, 14.00 - 15.30, SM2, Main Mathematics Building

Royal Society open presentation

17 May 2018, 11.00 - 13.00, G1S Hepple Lecture Theatre, Geographical Sciences

Mediation analysis with high-dimensional mediators

17 May 2018, 12.30 - 13.30, Rhian Daniel (Reader in Medical Statistics, Division of Population Health, Cardiff University), Room OS6, Oakfield House

A Town Hall Meeting – The Alan Turing Institute partnership

21 May 2018, 16.30 - 17.30, Sir Alan Wilson (CEO, Alan Turing Institute), Priory Road Complex 2D3 Lecture Theatre

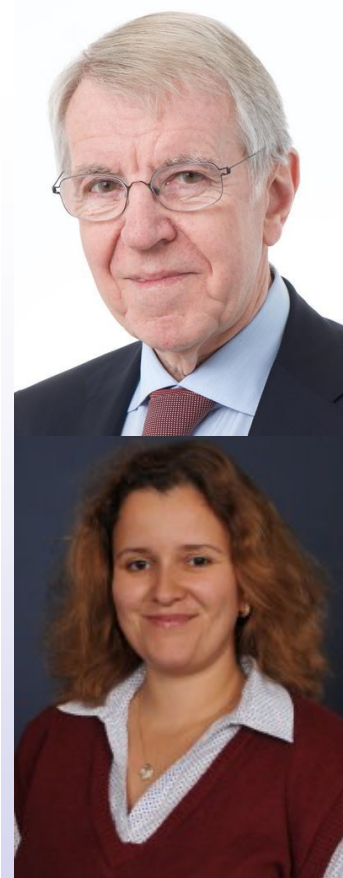
Sensing, New Materials, Micro- and Nanofabrication

23 May 2018, 12.30 - 13.30, Salzitsa Anastasova, PhD, MRSC, FHEA (Hamlyn Centre, Imperial College), Room OS6, Second Floor, Oakfield House

Decoding the Microbiome: Structural and Functional Analysis of an Elusive Genotoxin

23 May 2018, 13.00 - 14.00, Alan R Healy (University of Yale), G13/14 Life Sciences Building

Changing Minds about Changing Behaviour



From top: Duncan Wingham, Rhian Daniel, Sir Alan Wilson, Salzitsa Anastasova

EVENTS CON'T

23 May 2018, 14.30 - 16.00, Prof Dame Theresa Marteau (Director of Behaviour and Health Research Unit, University of Cambridge), Lecture Theatre 1, Chemistry Building

STFC Public Engagement Visit

24 May 2018, 12.00 - 15.30, Room 4.10, 35 Berkeley Square

Statistics Clinic - 30 May 2018

30 May 2018, 14.00 - 15.30, SM2, Main Mathematics Building

The public health record of the 2010-2018 UK Government

7 June 2018, 18.00 - 19.00, Prof Danny Dorling (University of Oxford), Bill Brown Design Suite, New Atrium, Queen's Building

Current trends in drug discovery: Young scientists and tomorrow's medicines

7 June 2018, 8.00 - 17.00, King's College London

Introduction to News Media

12 June 2018, 13.00 - 18.00, Priory Road Lecture Theatre

Statistics Clinic - 13 June 2018

13 June 2018, 14.00 - 15.30, SM3, Main Mathematics Building

Cancer Show and Tell event

21 June 2018, 14.00 - 17.00, Profs Anne Ridley (UoB) and Ann Ager (Cardiff University) + others TBC, C42 Biomedical Sciences Building

EACR25: From Fundamental Insight to Rational Cancer Treatment

30 June - 3 July 2018, RAI Amsterdam

Beatson International Cancer Conference: TALK TO THE NICHE - Understanding the Biology of the Metastatic Niche

1 - 4 July 2018, CRUK Beatson Centre, University of Glasgow

British Neuro-Oncology Society Annual Conference 2018

4 - 6 July 2018, University of Winchester

Infection and Immunity Early Career Researchers' Symposium

10 September 2018, 9.45 - 14.00, Life Sciences Building



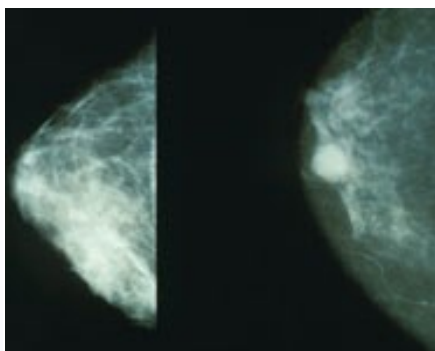
From top: Dame Theresa Marteau, Danny Dorling, Anne Ridley, Ann Ager

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

NEWS

Breast reconstruction after mastectomy

Having immediate reconstruction following a mastectomy does not delay the start of a patient's adjuvant breast cancer therapy but may increase the likelihood of complications requiring hospital readmission in the first six weeks after surgery, according to research led by UoB and the Royal Liverpool University Hospital presented at the UK Interdisciplinary Breast Cancer Symposium



(UKIBCS) held in Manchester in January 2018.

The option of immediate reconstruction is routinely offered to eligible breast cancer patients requiring a mastectomy, and can offer a number of potential benefits (fewer hospital visits, better cosmetic outcomes, psychological impact). While immediate reconstruction can help improve patients' body confidence, there have been concerns that their recovery from this more complex surgery could require them to delay the start of their chemotherapy or radiotherapy. Recent evidence has suggested that any delay in the start of adjuvant therapy of more than 7-12 weeks could be

enough to negatively impact a breast cancer patient's recurrence-free and overall survival.

In a new prospective multi-cohort study of 2,548 patients presented to delegates at the Symposium, immediate reconstruction was found not to have any significant impact on the time to delivery of patients' adjuvant therapy, compared to mastectomy alone.

The study was part of the iBRA-2 trial led by the Breast Reconstruction Research Collaborative which aims to generate the evidence to help women make more informed decisions about the type and timing of reconstructive surgery that is right for them.

Bristol Brain Tumour Research Centre

The Bristol Brain Tumour Research Centre, under Dr [Kathreena Kurian](#), put a bid together for recognition as a Centre of Excellence. A [short video](#) (4mins37secs) explains what the Centre does, who is collaborates with (including Molecular Biology and Engineering Mathematics) and which facilities the University benefits from.



Funding successes: Part 1

Dr Beth Coyle (PI, Nottingham) and Dr [Ali Bienemann](#) (co-applicant, BMS/THS, pictured) from **Children With Cancer UK** for *Convection enhanced delivery of N3-propargyl, a novel analogue of temozolomide*, £48,651 from 1 Apr 17 for 3 years. The aim of the project is to offer a better treatment to children with brain tumours in the future. TMZ is a DNA alkylating agent, activity of which depends on the absence of di-

rect repair by O6-methylguanine-DNA-methyltransferase (MGMT) and proficient mismatch repair (MMR). We have developed and demonstrated the ability of a novel temozolomide analogue (N3-propargyl) to circumvent MGMT in a non-mutagenic manner in vitro across a broad range of MGMT expressing adult (glioblastomas) and paediatric brain tumours (pHGG, diffuse intrinsic pon-

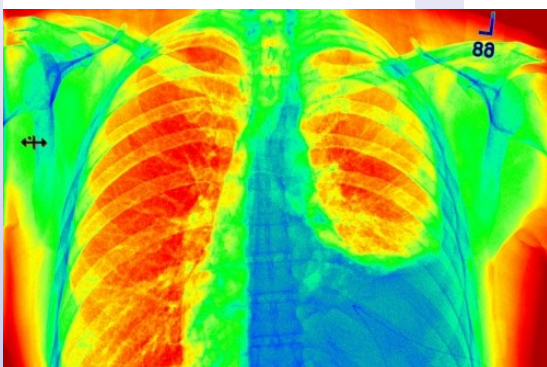
tine glioma (DIPG), ependymoma and medulloblastoma. This project gives a perfect opportunity to match a novel potent drug (N3-propargyl) to a delivery system ideally suited to its activation profile in children's high grade gliomas. By focussing our initial studies on pHGG and DIPG we will be targeting tumour types where there is the greatest need for effective chemotherapy.



Outpatient treatment for cancer condition

A problem in cancer patients is excess fluid build-up between the tissue lining the outside of the lung and the wall of the chest cavity (a malignant pleural effusion); it is particularly prevalent in lung and breast cancer patients and affects 50,000 people in the UK each year.

The commonest treatment for effusions involves inserting a temporary tube between the



ribs to drain the fluid; before its removal, medical talcum powder can be inserted to try to "glue" the lung to the inside of the chest wall to prevent further build-up. While relatively effective the process takes place in hospital over several days. The alternative "indwelling pleural catheter" (IPC method) has become increasingly popular; it involves only a few hours in hospital to have a long-term

drainage tube tunnelled under a short section of skin in the chest. The main downside is the tube may need to stay in place for many months as it doesn't prevent fluid

formation.

A 4-year study looked at a combined talc with an IPC method. 154 patients were randomly treated as outpatients with either an IPC alone, or with an IPC in combination with talc. The study showed that those patients given talc through their IPC were more than twice as likely to have their fluid dry up than those who were just treated as standard, with an IPC alone.

Bhatnagar R *et al.* (2018). [Outpatient Talc Administration by Indwelling Pleural Catheter for Malignant Effusion](#). *New England Journal of Medicine*. 378: pp1313-1322.

Funding boost for healthcare research centres

Three interdisciplinary research consortia, including the University of Bristol's SPHERE project, have been allocated more than £11 million to continue healthcare sensing systems research that is revolutionising how we identify and respond to outbreaks of infectious diseases, diagnose and manage lung diseases, and recognise and solve emerging health and wellbeing issues in the home environment.

The additional investment will enable vital collaborations to continue addressing many of the most pressing health and wellbeing issues, boosting the UK's status as an innovation

nation.

EPSRC's IRCs are centres of internationally acknowledged scientific and technological excellence, bringing together researchers, clinicians, industry and other professionals to make a real impact in areas of key future industrial relevance to the UK.

SPHERE (Sensor Platform for HEalthcare in a Residential Environment), led by the University of Bristol, is developing sensors for use in the home in order to spot health and wellbeing problems ranging from depression and obesity to cardiovascular and musculoskeletal diseases.



Funding successes: Part 2

Dr [Zuner Bortolotto](#) (PPN) a studentship from the **University of Exeter** for *Modulation of alternative splicing regulators during EMT in tumour progression*.

Prof [Ann Williams](#) (CMM) a studentship from **Bowel & Cancer Research** for *Combining cell biology with population based studies to investigate the role of BCL-3 in therapeutic resistance to improve the treatment of rectal cancer*, £72,145 starting 1 Sep 18 for 3 years.

Prof [Andres Lopez Bernal](#) (BMS/THS) from **Above and Beyond** for *Ovarian cancer and capillary density of the skin (OCCLUDES study)*, £14,415 from 1 Feb 18 for 1 year.

Prof [Jenny Donovan](#) (BMS/PHS) from **NIHR HTA** for *The ProtecT Trial - Evaluating the Effectiveness of Treatments for Clinically Localised Prostate Cancer (2018 - 2021)*, 1 Jan 18 for 3 years.

Dr [Maria Pufulete](#) (CTEU, pictured) has been awarded £1,854,558 from the **NIHR**

Technology Assessment Programme for the project *A multi-modal approach to prehabilitation in patients undergoing major surgery for cancer*. This project originated from a challenge proposed by Dr Sanjoy Shah (Consultant in Intensive Care Medicine, University Hospitals Bristol NHS Foundation Trust) as part of the Elizabeth Blackwell Institute's **Research for Health Challenge** scheme.



Professor Tavaré to lead new Faculty of Life Sciences

Prof Jeremy Tavaré will take up the role of Dean when UoB's new Faculty of Life Sciences is officially launched on 1 August this year.

Jeremy, a Biochemist and the current Director of Research



(Health & Life Sciences) is ideally placed to lead the new faculty which

will bring together the schools of Biochemistry, Biological Sciences, Cellular & Molecular Medicine, Experimental Psychology, and Physiology, Pharmacology & Neuroscience. His career began at UoB where he obtained a BSc and PhD in Biochemistry, before holding a succession of key roles including Director of Bristol's Wolfson BioImaging Facility, Chair of the Bristol Proteomics Facility, Faculty Research Director for the Faculty of Medical and Veterinary Sciences, Deputy Director of the EPSRC-funded [SPHERE Interdiscipli-](#)

[nary Research Centre](#) and Co-Director of the £5.2M Wellcome Trust-funded [GW4 Clinical Academic PhD Training Programme](#). He was also the inaugural Director of the [Elizabeth Blackwell Institute](#) for Health Research from 2012 - 2017.

The creation of the new Faculty of Life Sciences is part of the University's Vision and Strategy to become a life sciences destination for students, academics and research funding.

Elizabeth Blackwell Institute staffing updates

Dr **Richard Seabrook** MBA joined EBI in January 2018 as **Director of Business Development**. Richard will provide leadership to support the growth of partnerships and alliances with industry in the space across the health arena (ranging from pharmaceuticals, to devices, analytics and novel genomic and informatics methodologies) and assist with maximising opportunities to benefit from external funding streams to support these activities such as the government's new Industry Strategy Challenge Fund. He will also play a central role in identifying new opportunities to

translate fundamental research across UoB's entire health research portfolio into commercial impact.

Lauren Curtis started as the EBI **Diversity & Inclusion Champion** (Mon-Wed) in late 2017. Lauren's focus is on championing and challenging equality, diversity and inclusion within health and biomedical research communities at UoB.

Karen Wallace is now job-sharing the EBI **Executive Assistant** (Wed-Fri) role with **Jocelyn Egginton** (Mon-Wed).

Jo Barrell began her role as

EBI **Senior Communications Officer** (Tues and Thurs) role in February 2018. Jo has a lot of experience in communications in a range of contexts; her most recent role was Communications Manager at 'Together for Short Lives', the UK charity for children's palliative care.

Didier Laval is the EBI **Public Engagement Associate**, covering for Georgia Bladon who is currently on secondment to the Wellcome Trust. **Ellie Shipman** acts as the EBI **Public Engagement Officer/Fun Palaces Ambassador**. All EBI staff are based in Royal Fort House.

Observing the battle of the stem cells

Stem cells must compete with one another to remain among a smaller number of pluripotent, self-renewing cells rather than transform into a specialised cell. But how does this process play out, and with what effects? Dr [Marc Amoyel](#) (pictured), a developmental biologist, received an [EBI Early Career Fellowship](#) award to examine stem cell competition in *Drosophila*. The preliminary data from his

work at Bristol yielded a surprising result. It showed that when stem cell proliferation in fruit flies is impaired, the niche itself loses its quiescence and begins to proliferate and give rise to new stem cells. This shows that stem cells signal back to their niche to maintain the right balance of proliferating cells.

Dr Amoyel is submitting a paper on these findings, in

collaboration with Dr Erika Bach's laboratory at the New York School of Medicine, which is doing complementary research. He has also secured a five-year Career Development Award from the Medical Research Council.



Bristol Bladder Trial

A Phase II Trial of combination Cabazitaxel and Cisplatin Chemotherapy in the Neoadjuvant Treatment of Transitional Cell Carcinoma of the Urinary Bladder. The study has reached its primary endpoint and 2 of the 3 of its secondary endpoints:

Primary: To evaluate the overall response rate with this chemotherapy regimen in the neoadjuvant treatment of transitional cell carcinoma of the bladder and thus determine whether this approach warrants further research (randomised Phase II/ III trial).

Secondary: (i) to evaluate safety and tolerability; (2)

to assess progression-free and overall survival - patients in follow up; (3) to assess quality of life during treatment.

The study was presented on a poster at the American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium held in San Francisco, 8 - 10 February 2018. Entitled *The Bristol Bladder trial: A single-arm phase II trial of cisplatin and cabazitaxel for muscle invasive transitional cell carcinoma of the urinary bladder prior to radical cystectomy*, the poster was presented on 9 February 2018. The poster concluded that results demonstrate that CIS and CBZ

chemotherapy has an acceptable safety profile and is well tolerated in this setting. This combination shows promising efficacy (pCR 30.4%, ORR 56.5%) prior to definitive treatment for MI-TCC.

The study was led by Dr [Amit Bahl](#) (pictured).



ICEP news

The [Integrative Cancer Epidemiology Programme](#) (ICEP) has had much to celebrate recently:

Congratulations to Dr [Rebecca Richmond](#) who has been awarded the prestigious de Pass Vice Chancellor's Fellowship.

Rebecca will be funded for 4 years to investigate *From clustered behaviours to molecular mechanisms in cancer epidemiology*.

Claire Prince and Mark Gormley have both recently been awarded bursaries for their work with ICEP. [Claire Prince](#) is an UoB honorary staff member from the University of Exeter working with Rebecca Richmond on her CRUK funded e-cigarette study. Claire has been awarded £400 from the Deans' Individual Career

Development Fund at the University of Exeter.

[Mark Gormley](#) is an Academic Clinical Fellow working on head and neck cancer data in UK Biobank. Mark has been awarded £1500 from the Association of British Academic Oral and Maxillofacial Surgeons Bursary Prize 2017.

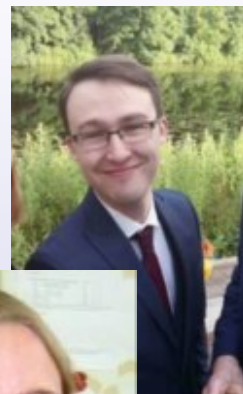
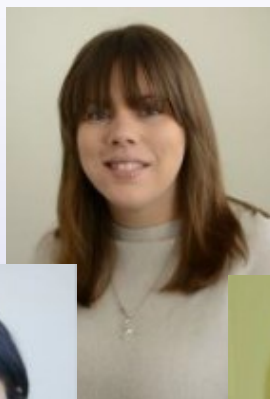
[Amy Howell](#) is a new PhD student under the supervision of Kathreena Kurian, Richard Martin and Caroline Relton. She is working on MR for risk factors for brain tumours.

[Nabila Kazmi](#) joined in Feb working within WP1. She will apply Mendelian randomization to investigate the causal role of a range of hypothesised and hypothesis-free risk factors for prostate and lung cancer.

[Kimberley Burrows](#) will also be working under WP1, exploring the causal associations between the essential micronutrient folate and a range of cancers.

[Alex McAleenan](#) has joined WP3 working alongside Julian Higgins. She will be aiming to perform systematic reviews of mechanisms of exposure–cancer associations. She is also working on two Cochrane reviews that aim to determine the best way of testing for two molecular markers in glioma.

[Jamie Robinson](#) is a new PhD student supervised by Kathreena Kurian, Richard Martin and Caroline Relton. Jamie will be using MR to look for new protein and drug targets in brain tumours.



From top left and clockwise: Rebecca Richmond, Kimberley Burrows, Jamie Robinson, Nabila Kazmi and Alex McAleenan

CAP Trial

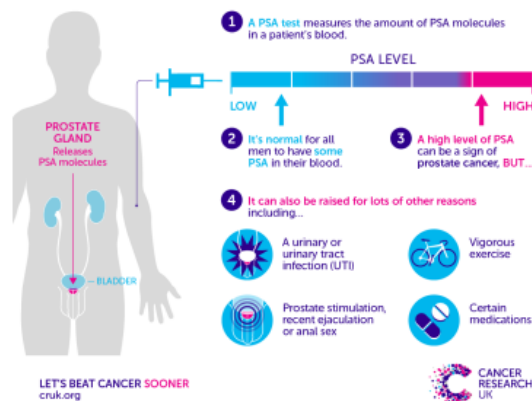
Inviting men with no symptoms to a one-off Prostate specific antigen (PSA) test for prostate cancer does not save lives. The research team at UoB and Oxford found that testing asymptomatic men with PSA detects some disease that would be unlikely to cause any harm, but also misses some aggressive and lethal prostate cancers. This highlights the flaws of a single PSA test as a way to screen for prostate cancer, and shows the need to find more accurate ways to diagnose cancers that need to be treated. Ideally, aggressive prostate cancers need to be identified and treated as early as possible. But finding a cancer that

would never have caused men harm during their lifetime can have a serious impact on quality of life, including the worry of a cancer diagnosis, the possibility of infection following a biopsy and impotence and incontinence following treatment.

CAP Trial: This was a randomised clinical trial during which 189,386 men aged 50-69 were invited for a single PSA-screen were compared with 219,439 men who were not actively invited for screening.

Martin RM *et al.* (2018). *Effect of a low-intensity PSA-based screening intervention on prostate cancer mortality: the CAP randomized clinical trial.* *Journal of the American Medical Association.* 319(9): 883-895.

THE PSA TEST AND WHY ITS RESULTS CAN BE CONFUSING



Funding successes: Part 3

Dr [Nobue Itasaki](#) (Centre for Applied Anatomy) from the **Medical Research Council** for Novel 3D liquid cell culture with low molecular weight agar applied to the study of cancer cell polarity and malignancy, £2,910 from 15 Feb 18 for 5 months.

Dr [Kathreena Kurian](#) (BMS/THS) from the **North Bristol NHS Trust** for a studentship in *Risk Factors in Glioma*, £120,000 from March 2018.

Dr [Barry Main](#) (BMS/PHS) from the **Academy of Medical Sciences** for *Exploring strategies for implementing core information sets for informed consent to surgery for head and neck cancer: operationalising Montgomery*, awarded 8 Feb 2018.

Dr [Caroline Wright](#) (BMS/PHS) from **Cancer Research UK** for *Longitudinal patterns and predictors of multiple cancer-risk behaviours among UK adolescents (Yr1)* from 1 July 2018 for 3 years.

Mr [Angus McNair](#) (BMS/PHS, pictured) an **NIHR Clinician Scientist Fellowship** for *Enhancing safe and transparent rectal cancer surgery innovation*.



Thangam Debonnaire visit to CMM

Ahead of World Cancer Day in February 2018, Bristol West MP Thangam Debonnaire, visited the School of Cellular and Molecular Medicine to meet researchers and explore the laboratories where cutting edge cancer research takes



place.

Thangam was welcomed by Head of School, cancer biologist [Prof Anne Ridley](#) and Grace Edmunds and comprised:

(i) Visiting the laboratory of [Prof Eugenia Piddini's](#) group,

where fruit fly tumour models are used to study the impact of cell competition in cancer. (ii) a demonstration of a high throughput fluorescence microscope in ac-

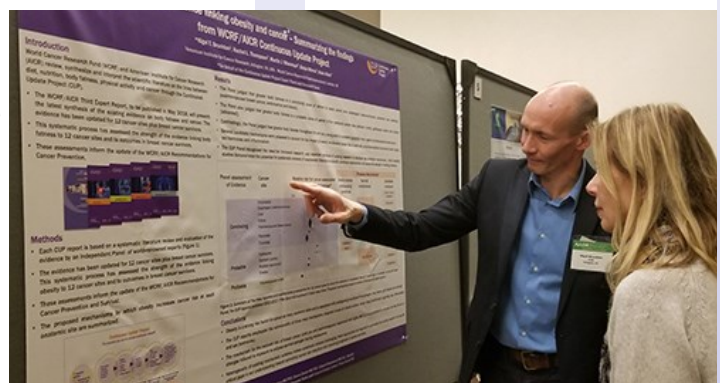
tion in [Prof Rafael Carazo Salas'](#) lab. The microscope allows researchers to image live cells over time, to investigate how human stem cells grow and develop *in vitro* and to improve tissue engineering techniques. (iii) A visit to the [Flow Cytometry Facility](#), to see how single immune cells are isolated from tumours to study the immune response to cancer. (iv) CMM's [bi-oprinting](#) facility for a demonstration of how 3D printing is used to print tumour spheroids (which mimic the structures of solid tumours).

Obesity and Cancer Conference

Dr Nigel Brockton (pictured) is Director of Research at American Institute for Cancer Research (AICR). On 29 January 2018 he presented at an American Association for Cancer Research Special Conference on Obesity and Cancer: Mechanisms Underlying Etiology and Outcomes which brought together researchers and clinicians from around the world and across the full spectrum of relevant disciplines to address the critical issue of how obesity causes cancer and its impact on outcomes after a cancer diagnosis. Body fatness is one of the core as-

pects of lifestyle on which AICR is focused. I will be presenting two posters. He presented two posters, the first a summary of the mechanisms that have been proposed in the 12 CUP reports for which the CUP Panel have judged the evidence to be strong ("convincing" or "probable") for obesity being a cause of cancer. The second he presented on behalf of Dr [Sarah Lewis](#)

(BMS/PHS), *Application of the WCRF International/University of Bristol methodology for systematically reviewing mechanistic evidence on the subject of obesity and cancer.* This presented a new method for reviewing the huge body of mainly laboratory-based research in a systematic way.



How cells rebuild after division

When cells divide, they need to rebuild their nucleus and organise their genome. New research demonstrates how cells achieve this through the unexpected deployment of filamentous actin (F-actin) to the nucleus. The study provides the first evidence that actin polymerisation in the nucleus helps in reshaping the nucleus and reorganising the genome after cell division (mitosis). In mammals the cell nucleus packages and protects the genome. When human cells divide, the nucleus is disassembled to allow segregation of the chromosomes. Once chromosome segregation is complete, new cells need to re-build their nucleus and organ-

ise their genome. This process, although essential for life, was poorly understood. [Alice Sherard](#) developed and implemented complementary and interdisciplinary methods to visualise nuclear structure and genome organisation after cells division. In so doing, she revealed that disruption of the formation of F-actin results in cells failing to expand their nuclear volume as well as their inability to de-compact their genome. Because of these defects, cells become inefficient in retrieving genetic information encoded in their DNA; thus, they divide slower. This discovery advances our fundamental knowledge of genome regulation in space and time,

and could have major implications in understanding cancer and degeneration.

Baarlink C *et al.* (2017). [A transient pool of nuclear F-actin at mitotic exit controls chromatin organization](#). *Nature Cell Biology*. 19(12): 1389- 1399.

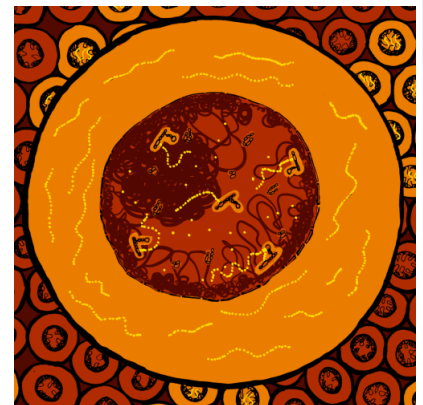


Illustration for nuclear F-actin working to reshape the nucleus and organise the genome © Claudia Stocker VividBiology.

Collaborative research to improve health and care

Scientists are collaborating with NHS and public health staff to ensure that research evidence is used effectively to improve public health and patient outcomes. Prof Jenny Donovan, NIHR CLAHRC West Director, and Lara Edwards, NIHR CLAHRC West Manager, explain why collaboration is so important and offer some examples of the benefits it brings.

Collaboration has increasingly become the watchword to guide research and health im-

provement. We are part of a complex landscape of research and healthcare organisations with an array of inscrutable acronyms: CRN, BHP, AHSN, CCG, PHWE, STP, BRC all of which are united in a commitment to improve the health of the population and the delivery of health and social care. CLAHRC West's particular focus is on encouraging the use of research evidence.

We work collaboratively with patients and members of the public, providers of NHS ser-

vices, NHS commissioners, universities, local authorities, charities and third sector organisations, to make research evidence more accessible so that it can be used to improve health and care. One example is *Developing skills in research evidence*; the development of skills in understanding, using and producing research evidence for the health, public health and commissioning workforce, and patients and members of the public.

[Read more](#)

ELIZABETH BLACKWELL FUNDING

[EBI Translational Acceleration and Knowledge Transfer \(TRACK\)](#)

This scheme provides funding to support health related translational projects.

Closing date: 25 June 2018

[EBI Identifying Candidates for Wellcome Trust Investigator Awards](#)

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

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

[EBI Workshops Funding](#)

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

[Returning Carers Scheme](#)

To support academic staff across all faculties in re-establishing their independent research careers on return from extended leave (16 weeks or more) for reasons connected to caring (e.g. maternity leave, adoption leave, additional paternity leave, leave to care for a dependant.).

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

[EBI Bridging Funds for Senior Fellows](#)

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

FUNDING OPPORTUNITIES

Would you like to receive timely, tailored funding opps information?

Do you want to know what funding opportunities come up in your research area?

Get tailored funding alerts?

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

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

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

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

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

Cancer Research UK

[Early phase and feasibility study awards](#)

Closing date: 14-Jun-18

Award amount: £200,000

These support studies that test the viability of larger trials, including the ability to recruit or to explore tolerability or efficacy of treatments. Grants are usually worth up to £200,000 each over four years.

Cancer Research UK

[Biomarker project awards](#)

Closing date: 14-Jun-18

Award amount: £500,000

These provide funding for biomarker assay development, validation and qualification for use in the clinical setting. Grants are worth up to £500,000 each for up to five years.

Cancer Research UK

[Brain Tumour Awards - call details and internal process](#)

Internal closing date: 02-Jul-18

Award amount: up to £10m

There will be a community event for the call to facilitate collaboration and bid team formation, particularly across discipline areas **30 May 2018 12:00, Senate House room 3.15**. If interested but unable to attend send zoe.holland@bristol.ac.uk a short summary of your expertise and what you would like to contribute to a potential bid. Short expressions of interest (EOIs) from bid teams to be sent to zoe.holland@bristol.ac.uk by midday **2nd July** for initial internal review. [DOWNLOAD THE TEMPLATE](#).

Cancer Research UK

[Population research postdoctoral fellowship](#)

Closing date: 22-Nov-18

Maximum award: unspecified

This enables postdoctoral researchers to develop their careers in the field of population research. The fellowship is awarded for three years and covers salary for the fellow and research expenses.

H2020-SC1-DTH-2019 digital transformation in health and care, single stage

[SC1-DTH-01-2019: Big data and Artificial Intelligence for monitoring health status and quality of life after the cancer treatment](#)

Closing date: 24 Apr 19

Max award: €8m

This supports projects that manage health and wellbeing while empowering the participation of citizens and facilitating the transformation of health and care services to more digitised, person-centred and community-based care models, thereby enabling better access to healthcare and the sustainability of health and care systems.

H2020-SC1-DTH-2019 digital transformation in health and care, single stage

[Exploiting the full potential of in-silico medicine research for personalised diagnostics and therapies in cloud-based environments](#)

Closing date: 24 Apr 19

Max award: €8m

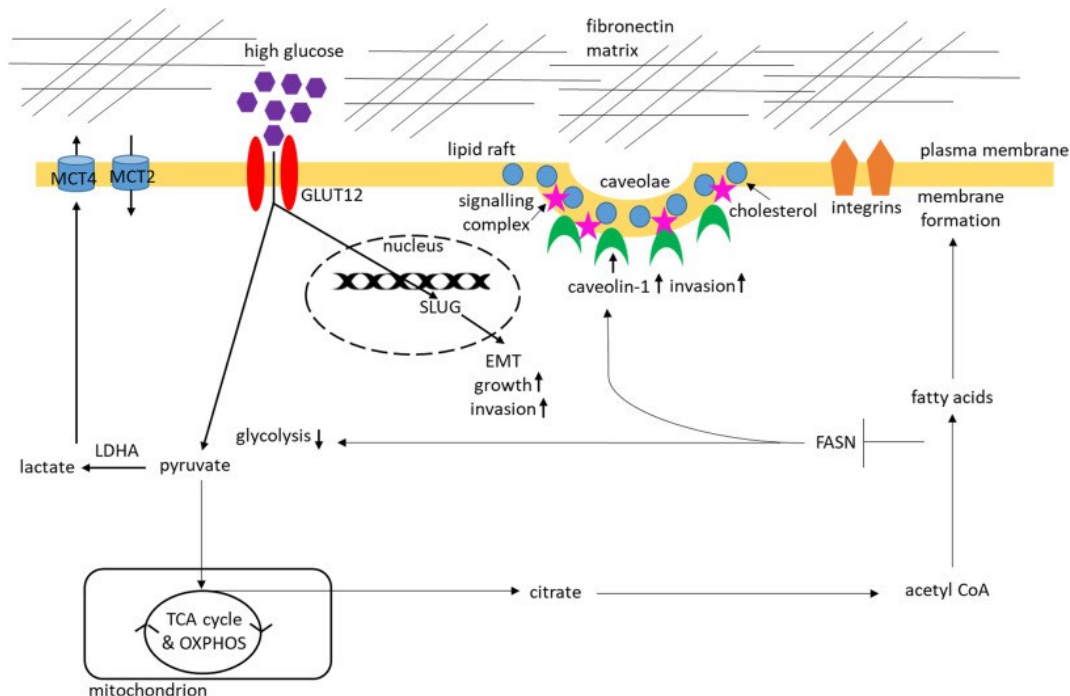
This supports projects that manage health and wellbeing while empowering the participation of citizens and facilitating the transformation of health and care services to more digitised, person-centred and community-based care models, thereby enabling better access to healthcare and the sustainability of health and care systems.

FEATURED PUBLICATION

Inhibition of FASN and ER α signalling during hyperglycaemia-induced matrix-specific EMT promotes breast cancer cell invasion via a caveolin-1-dependent mechanism

Zielinska HA, Holly JMP, Bahl A and Perks CM

Since disturbed metabolic conditions such as obesity and diabetes can be critical determinants of breast cancer progression and therapeutic failure, we aimed to determine the mechanism responsible for their pro-oncogenic effects. Using non-invasive, epithelial-like ER α -positive MCF-7 and T47D human breast cancer cells we found that hyperglycaemia-induced epithelial to mesenchymal transition (EMT), a key programme responsible for the development of metastatic disease. This was demonstrated by loss of the epithelial marker E-cadherin together with increases in mesenchymal markers such as vimentin, fibronectin and the transcription factor SLUG, together with an enhancement of cell growth and invasion. These phenotypic changes were only observed with cells grown on fibronectin and not with those plated on collagen. Analyzing metabolic parameters, we found that hyperglycaemia-induced, matrix-specific EMT promoted the Warburg effect by upregulating glucose uptake, lactate release and specific glycolytic enzymes and transporters. We showed that silencing of fatty acid synthase (FASN) and the downstream ER α , which we showed previously to mediate hyperglycaemia-induced chemoresistance in these cells, resulted in suppression of cell growth: however, this also resulted in a dramatic enhancement of cell invasion and SLUG mRNA levels via a novel caveolin-1-dependent mechanism.



A schematic diagram illustrating the proposed mechanism of caveolin-1-mediated increase in invasion observed upon silencing FASN/ER α during hyperglycaemia-induced, matrix-specific EMT. Exposure to hyperglycaemia and fibronectin induces EMT and further enhances the Warburg effect by upregulating glucose uptake, lactate release and specific glycolytic enzymes and transporters. Inhibiting FASN/ER α signalling suppresses the glycolytic phenotype and promotes invasion via upregulation of caveolin-1 in lipid rafts also enriched in cholesterol and various signalling proteins and receptors. Considering the direct involvement of caveolin-1 in mediating cellular cholesterol homeostasis this pro-invasive phenotype is potentially associated with a metabolic shift from glycolysis to cholesterol biosynthetic pathway.

CONTACTS



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

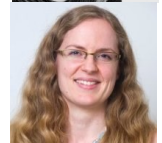


[Catherine Brown](#), *Network Administrator*

• 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 Theme is led by a Steering Group:

 cancer-research@bristol.ac.uk

 bristol.ac.uk/cancer

 0117 33 17610