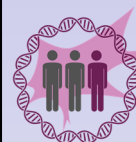


Cancer Network Newsletter

2023: Issue 2



Bristol
Cancer Research
Network

New Cancer Network co-Lead

The Bristol Cancer Research Network is delighted to announce that Dr [Emma Vincent](#), Senior Lecturer in Molecular Metabolism based in Bristol Medical School: Translational Health Sciences, has taken up the role of Network co-Lead representing the cancer biology community. She follows Head of School for Cellular and Molecular Medicine Prof [Anne Ridley](#) who stepped down following the completion of her three-year term of office as co-Lead.

Emma has been a member of the Network's steering group since March 2018 when she joined as an Early Career Researcher interdisciplinary representative working across cancer biology and population health. She became a Senior Lecturer in October 2021 and continues to work across disciplines.

During this time she co-lead the Elizabeth Blackwell Institute's [Mechanisms to Populations Research Strand](#) and built up her own research laboratory which studies metabolism in health and disease with a particular focus on the very earliest changes to metabo-



lism that precede cancer development in the context of obesity and diabetes.

Understanding these changes will reveal more relevant approaches for their prevention and treatment. Normal approaches to cancer prevention and thera-

py may not be appropriate or optimal for people with type 2 diabetes (T2D). To enable effective ways to screen for and to prevent and treat the cancers that develop in people with T2D, we need to understand what is it about the characteristics of T2D that causes specific cancers to develop.

The Network is currently recruiting for representatives in Population Health Science and Cancer Biology, and, following the departure of long-term member Prof [Richard Martin](#),

we are also looking for a co-Lead to represent Population Health Sciences. If you are University of Bristol-based and are interested in submitting an expression of interest for any of these roles, please contact [Catherine Brown](#) in the first instance.

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University of
BRISTOL

Elizabeth Blackwell Institute
for Health Research

EVENTS

Lives in Sciences - A Celebration of Marginalised Voices

25 July 2023, 14.00 - 19.00, Life Sciences Building

Reassessing the causal role of obesity in breast cancer susceptibility: a comprehensive multivariable Mendelian randomization investigating the distribution and timing of exposure

26 July 2023, 10.30 - 11.30, Luke Mahoney (University of Bristol), online

Cancer Data Driven Detection Workshop

11 September 2023, 10.00 - 16.00, London

EDI conference 'Redefining the status quo in academia'

13 - 14 September 2023, Queen's Building, Cardiff University, CF24 3AA

Immunomodulation Update Day

20 September 2023, 9.00 - 16.30, Derby and Chester Conference Suite, The Midland Hotel, Peter Street, Manchester M60 2DS

Research, the NHS and You - NIHR Conference for people new to research

21 September 2023, 9.00 - 17.00, ExCel London

CAR-T Study Day for Nursing & Allied Healthcare Professionals

22 September 2023, 9.00 - 16.50, Cavendish Conference Centre, Duchess Mews, London W1G 9DT

UK CLL Forum Clinical Sciences Day

22 September 2023, 9.30 - 16.45, hybrid Event from the Hallam Conference Centre, 44 Hallam Street, London W1W 6JJ

World Congress of Epidemiology (WCE): Epidemiology and complexity: challenges and responses

24 - 26 September 2023, Cape Town, South Africa

South West Lymphoma Group

27 September 2023, 15.30 - 19.30, The Castle Hotel, Castle Green, Taunton, Somerset TA1 1NF

How to harness the immune system to target cancer

27 September 2023, 16.00 - 17.30, online

South West Haemostasis and Thrombosis Meeting

28 September 2023, 9.00 - 16.40, The Castle Hotel, Castle Green, Taunton, Somerset, TA1 1NF

6th South West Blood and Marrow Transplant Training Day

28 September 2023, 9.00 - 16.50, Mercure Exeter Rougemont Hotel, Queen Street, Exeter EX4 3SP

Molecular Analysis for Precision Oncology Congress

4 - 6 October 2023, Maison de la Chimie, 28 Rue Saint-Dominique, 75007 Paris, France

NEWS

Participating in everyday life while dying

The adaptations people of working age with advanced cancer make so they can continue participating in everyday life was a PhD project undertaken by the National Institute for Health and Care Research (NIHR) [Applied Research Collaboration](#) (ARC) West's Dr Julie Brose at the [Research Centre for Palliative Care, Death and Dying](#).

Julie talked to eight adults with advanced cancer living in the Rocky Mountains, Canada. The 33 in-depth interviews took place over a 19 month period. They explored how the

people had adapted their daily activities so they could continue participating in everyday life, such as working or spend-



ing time with family. She found that people living with advanced cancer try to continue doing what is important to them, albeit in a modified form. This is despite

the challenge of unrelenting change and loss as death approaches.

Adapting to functional decline is an active, ongoing process. It occurs through continued engagement in activities. Palliative rehabilitation has a part to play in enabling participation in everyday life.

Brose JM, Willis E and Morgan DD (2023). [The intentional pursuit of everyday life while dying: A longitudinal qualitative study of working-aged adults living with advanced cancer](#). *Palliative Medicine*.

Bristol Cancer Early Career Researchers' event

The Bristol Cancer Research Network hosted its second annual Early Career Researchers' (ECRs) symposium on 28 June 2023.

With over 90 registered participants, the day saw eight ECRs and two keynote speakers, Marc Gunter from Imperial and Rob Jones from Cardiff/Velindre, deliver oral presentations, and 16 researchers revealing their work via posters.

[Read a summary of the day](#)
We are delighted to have

awarded a number of prizes to our presenters:

- 1st place oral presentation: Katy Pinnell (MSc student, Bristol), a £50 Amazon voucher supported by Qiagen
- 2nd place oral presentation: Daniel Turnham (Research Associate, Cardiff), a £30 cash prize
- 1st place poster presentation: Jules Lavalou (Research Associate, Bristol), a £50 cash prize
- 2nd place poster presentation: Elmira Ebrahimi (PhD

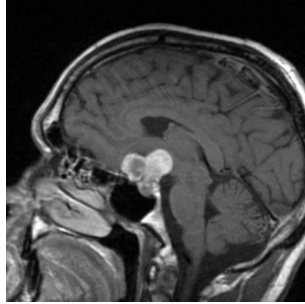
student, International Agency for Research on Cancer), a £30 cash prize

- 3rd place poster presentation: joint awards to Alexandra Creavin ST2 Academic Clinical Fellow in Public Health) and Ashley Hoskin PhD student, Bristol), a £20 cash prize each

Thanks to the [Elizabeth Blackwell Institute](#), [Population Health Science Institute](#) and [Qiagen](#) for supporting the event.

Eating behaviour and childhood onset craniopharyngioma

Researchers have confirmed a link between hyperphagia – an abnormally strong desire for food – and body mass index (BMI) in patients affected by childhood onset craniopharyngioma. The study demonstrates that eating behaviour research would be both feasible and acceptable in this patient group.



Craniopharyngiomas are rare brain tumours. They are non-malignant and have high survival rates but can affect a pa-

tient's vision and their endocrine system (a system responsible for hormone regulation and release). This includes causing hypothalamic obesity, a type of obesity caused when a part of the patient's brain called the hypothalamus doesn't function normally. Because hypothalamic obesity is such a common feature of childhood craniopharyngioma, the study team wanted to assess whether this young patient

group would tolerate and accept work around food-related behaviours. They also wanted to explore whether it would even be possible to recruit patients to carry out this type of research.

[Read the NIHR Biomedical Research Centre news item](#)

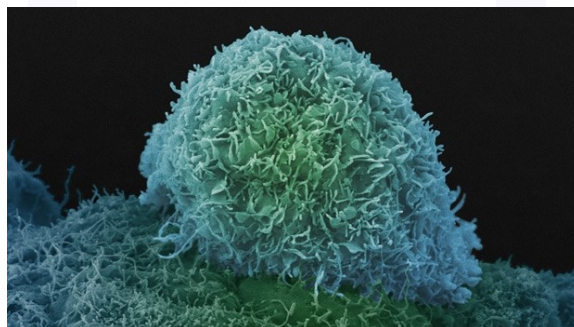
Hinton EC *et al.* (2023). [Evaluating Eating Behaviour, Energy Homeostasis, and Obesity in Childhood-Onset Craniopharyngioma: A Feasibility Study](#). *Hormone Research in Paediatrics*.

ARV7 and protein interaction in prostate cancer

Interactions between androgen receptor variant 7 (ARV7), the forkhead box protein A1 (FOXA1) and insulin-like growth factor-2 (IGFBP-2) could potentially contribute to a more aggressive form of prostate cancer developing. Researchers found positive associations between ARV7 and the two proteins in tissue from patients with prostate cancer.

Prostate cancer is one of the leading causes of cancer-related deaths in men. Localised prostate cancer – cancer that is limited to the prostate – can be treated effectively, but most patients go on to de-

velop a more aggressive form of the disease. Male sex hormones such as testosterone play an important role in the growth and function of the



prostate. These hormones are also called androgens and they form links with androgen receptors. In turn, androgen receptors are involved in prostate cancer development and progression.

The study team wanted to explore the role of ARV7 – an androgen receptor variant – in prostate cancer progression.

ARV7 is created during a process called alternative splicing, where different proteins with distinct structures and functions can be produced from a single gene.

[Read the full NIHR Biomedical Research Centre news item](#)

Biernacka KM *et al.* (2023). [A role for androgen receptor variant 7 in sensitivity to therapy: Involvement of IGFBP-2 and FOXA1](#). *Translational Oncology*.

The Mediterranean diet and breast cancer

It is possible that following a Mediterranean diet could have long-term health benefits for patients with breast cancer, according to a paper published recently in *Nutrients*. Researchers at the NIHR Bristol BRC and the University of Bristol found that the association between following a Mediterranean diet and quality of life parameters wasn't consistent, but their results highlighted its potential to reduce mortality in this group of people.



Female breast cancer is the most frequently diagnosed

type of cancer. Survivors commonly experience weight gain, menopausal symptoms and have an increased risk of de-

veloping cardiovascular disease and osteoporosis because of the treatments they undergo.

This means they might not engage with long-term therapy, which increases their risk of the cancer recurring and can reduce their quality of life.

Although long-term survival rates have increased, women's needs for high-quality

healthcare are still not being met. Previous studies have reported that following a Mediterranean diet has a positive effect on the health of the general population because it focuses on olive oil, fruits, vegetables, legumes, and whole grains. Compared to a typical Western diet, it includes fewer ultra-processed foods and meat and is associated with reducing the risk of breast cancer and other health benefits.

[Read more via the NIHR BRC](#)

Chen G, Leary S *et al.* (2023). [The Role of the Mediterranean Diet in Breast Cancer Survivorship... *Nutrients*](#).

University Cancer Research Fund awards 2023

The Bristol [University Cancer Research Fund \(UCRF\)](#), runs an annual seedcorn funding call which awards Bristol researchers up to £5,000 to support innovative early-stage projects.

Overseen by the Bristol Cancer Research Network, the UCRF is delighted to announce the following awards for the first round of the UCRF:

- Dr [Alexandria Andrayas](#) (Research Associate, School of Psychological Science): "Patient and public involvement (PPI) to inform future

research on risk factors for smoking or e-cigarette use and tailoring public health policy" - £260.82



- Dr Pau Erola (Research Systems Technical Manager,

Bristol Medical School: Population Health Sciences): "Pilot Identification of Early Cancer Biomarkers Using ALSPAC Data" - £5,000

- [Tracey Collard](#) (Senior Research Associate in Population to Mechanism Studies, Bristol Medical School: Translational Health Sciences): "The impact of Aspirin and 5-aminosalicylic Acid (5-ASA) on Cell Signalling and Metabolism." - £5,000

The second UCRF round is now open with a closing date of 8 September 2023

Quality of life in PIPAC

A new project being undertaken by the [Surgical and orthopaedic innovation theme](#) of the National Institute for Health and Care Research (NIHR) Biomedical Research Centre (BRC) Bristol aims to explore the views and experiences of patients with peritoneal metastases (cancer that has spread to the lining of the abdomen), who are undergoing pressurised intraperitoneal aerosol chemotherapy (PIPAC).

PIPAC is a new chemotherapy

delivery method. It allows a surgeon to spray chemotherapy directly onto the cancer



that has spread into the lining of the abdomen, which they

do during keyhole surgery. During the study the research team will speak with healthcare professionals and patients who are taking part in the [PICCOS](#) (PIPAC in Cancers of the Colon, Ovaries and Stomach) trial to:

- Explore and understand their views of PIPAC treatment
- Understand how treatment with PIPAC affects patients' symptoms and quality of life

[Read more](#)

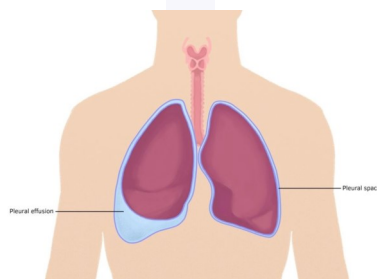
Predicting if pleural effusions are caused by cancer

Can DNA methylation biomarkers predict whether pleural effusion is caused by cancer? Is new project being undertaken by the [Translational data science theme](#) of the NIHR BRC Bristol.

Pleural effusion, where fluid builds up in the cavity around the lungs, can develop in a range of conditions, from mild heart problems to severe infections or cancer. Malignant pleural effusions, where cancerous tissue is present in the cavity, affect around 50,000 people in the UK every year.

So far, no biomarker can accurately

tell whether the fluid build-up is caused by cancer, which is the cause that clinicians are most concerned with identifying. Invasive and costly biopsies are the only way to find out.



The best existing method for checking whether a biopsy is needed is looking at protein or cells from the pleural

area by microscope. This fluid is collected via a minimally invasive 'tap' when patients arrive at hospital. However, this is only accurate in about 60% of cases, leading to delays in diagnosis and patients undergoing treatment they might

not need.

DNA methylation (DNAm) is a chemical process that regulates how genes are expressed. It is often disrupted when cancer is developing, where it is a hallmark of tumour development and cancer progression.

DNAm-based methods for detecting cancer are starting to see some success. DNAm measured in pleural fluid is likely to be particularly useful in indicating pleural malignancy early. This work could help to develop a point-of-care test to rapidly and cost-effectively tell whether a pleural effusion is cancerous or not.

[Read more](#)

The effect of metabolism on oral cancer risk

A recent World Health Organization report states that at least 40% of all cancer cases may be preventable, with smoking, alcohol consumption and obesity identified as three of the most important modifiable lifestyle factors. Given the significant decline in smoking rates, particularly within developed countries, other potentially modifiable risk factors for head and neck cancer warrant investigation. Obesity and related metabolic disorders such as type 2 diabetes and hyper-

tension have been associated with head and neck cancer risk in multiple observational studies. However, adiposity has also been correlated with smoking, with bias, confounding or reverse causality possibly explaining these findings.

To overcome the challenges of observational studies, we conducted two-sample Mendelian randomization using genetic variants which were robustly associated with adiposity, glycaemic and blood pressure

traits in genome-wide association studies (GWAS). We found limited evidence of a causal effect of genetically proxied body mass index on oral and oropharyngeal cancer risk. Similarly, there was limited evidence for related traits including type 2 diabetes and hypertension.

Gormley M *et al.* (2023). [Evaluating the effect of metabolic traits on oral and oropharyngeal cancer risk using Mendelian randomization.](#) *eLife*.

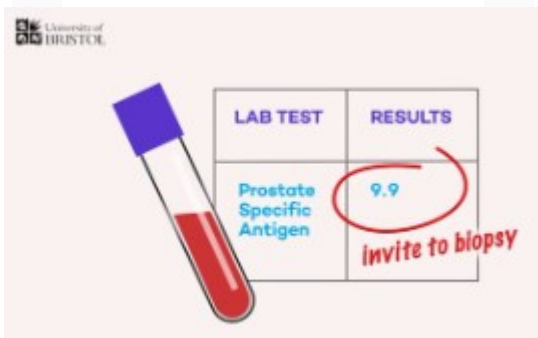
Impact of PSA testing on secondary care costs

Screening men for prostate cancer using prostate-specific antigen (PSA) testing remains controversial. We aimed to estimate the likely budgetary impact on secondary care in England and Wales to inform screening decision makers.

The Cluster randomised triAl of PSA testing for Prostate cancer study (CAP) compared a single invitation to men aged 50–69 for a PSA test with usual care (no screening). Routinely collected hospital care data were obtained and NHS reference costs were mapped to each event via Healthcare Resource Group (HRG) codes. Secondary-care costs per man per year were calculated, and

cost differences (and population-level estimates) between arms were derived annually for the first five years following randomisation.

tion level, the introduction of a single PSA screening invitation could lead to additional secondary care costs of £314 million.



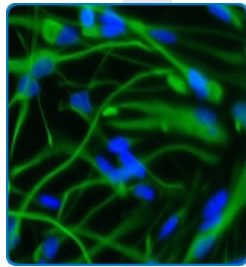
In the first year post-randomisation, secondary-care costs averaged across all men (irrespective of a prostate cancer diagnosis) in the intervention arm were £44.80 higher than for men in the control arm. Extrapolated to a popula-

The team concluded that introducing a single PSA screening test for men aged 50–69 across England and Wales could lead to very high initial secondary-care costs.

Thorn JC *et al.* (2023). [Impact of PSA testing on secondary care costs in England and Wales: estimates from the Cluster randomised triAl of PSA testing for Prostate cancer \(CAP\).](#) *BMC Health Services Research*.

DNA methylation and glioma risk

Genetic evidence suggests glioma risk is altered by leukocyte telomere length, allergic disease (asthma, hay fever or eczema), alcohol consumption, childhood obesity, low-density lipoprotein cholesterol (LDLc) and triglyceride levels. DNA methylation (DNAm) variation influences many of these glioma-related traits and is an established feature of glioma. Yet the causal relationship between DNAm variation with both glioma incidence and glioma risk factors



is unknown. We applied a two-step Mendelian randomization (MR) approach and several sensitivity analyses to assess the association of DNAm with glioma risk factors and glioma incidence. MR evidence indicated that DNAm at 3 CpG sites in one genomic region (HEATR3) had a putative association with glioma and glioblastoma risk. Colocalization presented evidence against genetic confounding and suggested that differential DNAm at the 3 CpG sites and glioma were

driven by the same genetic variant. MR provided little evidence to suggest that DNAm acts as a mediator on the causal pathway between risk factors previously examined and glioma onset. Subsequent analyses are required to improve the robustness of our results and rule out horizontal pleiotropy.

Howell AE *et al.* (2023). [Role of DNA methylation in the relationship between glioma risk factors and glioma incidence: a two-step Mendelian randomization study](#). *Scientific Reports*.

New AI in Biosciences Network

Bristol BioDesign Institute co-Director Dr Lucia Marucci, a new member of the Bristol Cancer Research Network steering group, is part of a team that has been awarded £1.6 million by the Biotechnology and Biological Sciences Research Council (BBSRC) to establish an Artificial Intelligence (AI) in Biosciences Network (AiBio-UK) that will run over a five-year period. The network will run several training activities and networking events as



well as fund pilot/feasibility projects, which will aim at accelerating progress and bringing the two communities closer together.

The network is led by Andrew French (University of Nottingham); with Lucia, Robert Knight (King's College London),

Reyer Zwiggelaar (Aberystwyth University), Yizhi [Patrick] Cai (University of Manchester), Dipali Singh (Quadram Institute) as co-Investigators. Several partners including NVIDIA, Syngenta, ONE Life Sciences (Biohub), The Data Lab - Innovation Centre, CENSIS, The Alan Turing Institute, Biomathematics and Statistics Scotland, and others supported the proposal.

Roles of posttranslational modifications

The extracellular matrix (ECM) is central to the physiology of animal tissues, through its multifaceted roles and cell interactions, and by its cell-signalling activities that regulate cell phenotype and behaviour. The secretion of ECM proteins typically involves multiple transport and processing steps within the endoplasmic reticulum and the subsequent compartments of the secretory pathway. Many ECM proteins are substituted with various posttranslational modifications (PTMs) and there is in-

creasing evidence of how PTM additions are required for ECM protein secretion or functionality within the extracellular milieu. This review discusses selected examples of PTMs of ECM proteins for which the PTM has known importance for anterograde trafficking and secretion of the core protein, and/or loss-of-function of the respectively modifying enzyme leads to alterations of ECM structure or function with pathophysiological consequences in humans. Protein disulfide isomerases (PDI) are

discussed in relation to emerging knowledge of the roles of certain PDIs in ECM production in the pathophysiological context of breast cancer. Cumulative data suggest the possible applicability of inhibition of PDIA3 activity to modulate ECM composition and functionality within the tumour microenvironment.

Adams J (2023). [Passing the post: roles of posttranslational modifications in the form and function of extracellular matrix](#). *Cell Physiology*.

Impact of procedure type after breast reconstruction

This study aimed to explore the impact of reconstruction type on the number of revisions and secondary reconstructions performed 3, 5, and 8 years after immediate breast reconstruction in a large population-based cohort.



Women undergoing unilateral mastectomy and immediate breast reconstruction for breast cancer or ductal carcinoma in situ in England between 1 Apr '09 - 31 Mar '15 were identified. Numbers of revisions and secondary reconstructions in women undergoing primary definitive immedi-

ate breast reconstruction were compared by procedure type at 3, 5, and 8 years after index surgery.

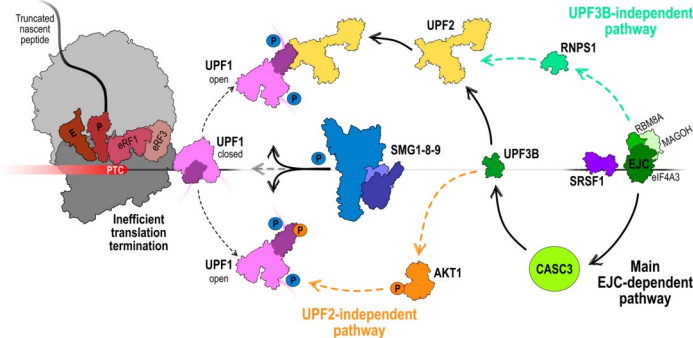
Of 16,897 women who underwent immediate breast reconstruction, 14,069 had a definitive reconstruction with an implant only, latissimus dorsi flap with or without an implant, or abdominal free flap. Women undergoing implant-only reconstruction were more likely to require revision, with 69.5% undergoing at least one revision by 8 years compared with 49.3% in other reconstruction groups. They were also more likely to

undergo secondary reconstruction, with the proportion of women having further reconstructive procedures increasing over time. Long-term rates of revisions and secondary reconstructions were considerably higher after primary implant-based reconstruction than autologous procedures. These results should be shared with patients to support informed decision-making.

Johnson L *et al.* (2023). [Impact of procedure type on revisional surgery and secondary reconstruction after immediate breast reconstruction in a population-based cohort](#). *British Journal of Surgery*.

mRNA Decay Factor Functions in Human Health and

Nonsense-mediated mRNA decay (NMD) is a cellular surveillance mechanism that degrades mRNAs with a premature stop codon, avoiding the synthesis of C-terminally truncated proteins. In addition to faulty mRNAs, NMD recognises ~10% of endogenous transcripts in human cells and downregulates their expression. The up-frameshift proteins are core NMD factors and are conserved from yeast to human in structure and function. In mammals, NMD



diversified into different path-

ways that target different mRNAs employing additional NMD factors. Here, we review our current understanding of molecular mechanisms and cellular roles of NMD pathways and the involvement of

more specialised NMD factors.

We describe the consequences of mutations in NMD factors leading to neurodevelopmental diseases, and the role of NMD in cancer. We highlight strategies of RNA viruses to evade recognition and decay by the NMD machinery.

Sun L, Mailliot J & Schaffitzel C (2023). [Nonsense-Mediated mRNA Decay Factor Functions in Human Health and Disease](#). *Biomedicines*.

Public health gaps in the “levelling up” agenda

The UK government's levelling up agenda is set to fail in its mission to address inequalities unless it tackles the root causes of poor health, according to a new study.

The research, led by the Universities of Bristol and Bath, presents policy recommendations to tackle the root causes of poor health which hold the key to overcome inequalities. The study used data from interviews with 132 key government and industry professionals to assess if the 12 ‘missions’ published in the



[Levelling Up White Paper](#) will achieve better quality of urban living to improve public health.

The study is part of [TRUUD](#), a transdisciplinary research project led by the University of Bristol, which aims to reduce non-communicable disease (such as cancers, diabetes, obesity, mental ill-health and respiratory illness) and health inequalities linked to the quality of urban planning and development.

Using seven principles that could underpin a successful ‘levelling up’ strategy for

healthy urban developments, researchers recommend how the Government might address the wider determinants of health in the implementation of its ambitions. These include establishing a cross-government commitment for health, led by the Prime Minister's office, further local devolution of powers, simplified means of funding, and increased use of evidence from local communities and health sources for decision-making.

Ayres S *et al.* (2023). [What needs to happen to 'level up' public health?](#) *Contemporary Social Science*.

Five-year funding award for epidemiology research

The Medical Research Council Integrative Epidemiology Unit (MRC IEU) at the University of Bristol has been awarded funding to enable a further five years of world-leading research.

MRC IEU, which was established in 2013, is a leading centre for research into methods for causal inference, and evidence triangulation. It is also a leading centre for the application of causal methods to answer important

questions about diseases in populations. Research from IEU enables valuable insight into many key challenges for population health, with important impact for further re-



MRC Integrative Epidemiology Unit

search, policy and practice. The new funding totals £11,637,000. It covers work spanning six key programme themes:

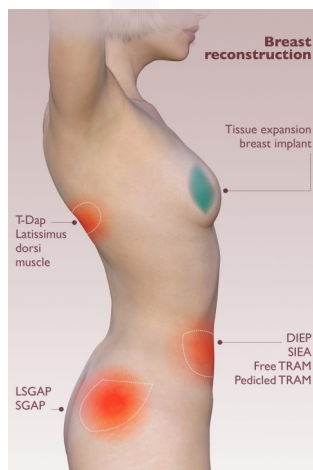
- Mendelian randomization
- Statistical methods for causal inference
- Data mining epidemiological relationships
- Molecular drivers and predictors of pregnancy complications and future health
- Immunopsychiatry
- Behavioural, social and environmental determinants of physical and mental health

[Read the full University of Bristol news item](#)

Secondary healthcare costs following breast surgery

Immediate breast reconstruction (IBR) following mastectomy can improve quality-of-life for women with breast cancer and rates are increasing. Long-term inpatient costs of care were estimated to understand the impact of different IBR procedures on healthcare expenditure.

Hospital Episode Statistics Admitted Patient Care (HES-APC) data were used to identify women undergoing unilateral mastectomy and IBR in English NHS hospitals (01/04/2009-31/03/2015) and any subsequent procedures performed to revise, replace,



or complete the BR. 16,890 women underwent mastectomy and IBR: implant, expander, autologous LD flap (ALD), LD flap with implant (LDI), and abdominal free flap (AFF).

Mean cumulative cost was lowest for LDI (€20,103) over three years and highest for AFF (€27,560). Over eight years, expander (€29,140) and LDI reconstructions (€29,312) were least expensive, while AFF (€34,536) remained most expensive despite having lower costs for revisions and secondary reconstructions. This was driven primarily by

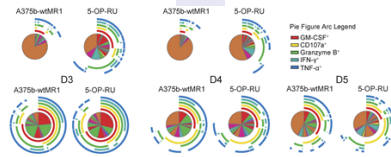
the cost of index procedure.

HES-APC-HRG data provided a comprehensive longitudinal cost assessment of secondary care. Although AFF was the most expensive option, higher costs of the index procedure need to be balanced against ongoing long-term costs of revisions/secondary reconstructions which are higher after prosthesis-based procedures.

Mohiuddin SG *et al.* (2023). [Secondary healthcare costs following mastectomy and immediate breast reconstruction for women with breast cancer in England: a population-based cohort study](#). *British Journal of Surgery*.

MR1 drives mucosal-associated T-cell response

Mucosal-associated invariant T (MAIT) cells use canonical semi-invariant T cell receptors (TCR) to recognize microbial riboflavin precursors displayed by the antigen-presenting molecule MR1. The extent of MAIT



TCR cross-reactivity toward physiological, microbially unrelated antigens remains underexplored. We describe MAIT TCRs endowed with MR1-dependent reactivity to tumour and healthy cells in the absence of microbial metabolites. MAIT cells bearing

TCRs cross-reactive toward self are rare but commonly found within healthy donors and display T-helper-like functions in vitro. Experiments with MR1-tetramers loaded with distinct ligands revealed significant cross-reactivity among MAIT TCRs both ex vivo and upon in vitro expansion. A canonical MAIT TCR was selected on the basis of extremely promiscuous MR1 recognition. Structural and molecular dynamic analyses associated promiscuity to unique TCR β -chain features

that were enriched within self-reactive MAIT cells of healthy individuals. Thus, self-reactive recognition of MR1 represents a functionally relevant indication of MAIT TCR cross-reactivity, suggesting a potentially broader role of MAIT cells in immune homeostasis and diseases, beyond microbial immunosurveillance.

Chancellor A *et al.* (2023). [Promiscuous recognition of MR1 drives self-reactive mucosal-associated invariant T cell responses](#). *Journal of Experimental Medicine*.

Professorial Research Fellow in Cell Biology [Eugenia Piddini](#) (pictured) based in the School of Cellular and Molecular Medicine has been elected as a European Molecular Biology Organization (EMBO) Member, in recognition of her outstanding contributions to research.

The new members and associate members join a community of more than 2,000 leading life science experts. They take their place alongside 91 Nobel laureates who have been elected to EMBO Membership. Members provide guidance and support for EMBO activities, for example by evaluating

funding applications and serving on EMBO Council and Committees.



Eugenia's research group aims to understand how cell competition impacts on tissue colonization. We use *Drosophila*, mammalian cells in culture, genetics, omics and cell biology to investigate the mechanism of action of cell competition in health and disease. We aim to

New EMBO member

control tissue colonization outcomes for therapeutic applications, specifically to inhibit tissue colonisation of cancer

cells and to promote tissue repopulation in regenerative medicine.



[Read more about Eugenia's research](#) on the Bristol Cancer Research webpages

FUNDING OPPORTUNITIES

Research Professional provides access to an extensive database of funding opportunities. You can set up individualised funding alerts based on keywords or areas of research. UoB staff and students have **FREE** online access to the database.

You can search for funding information by discipline, sponsor, database searches, by recent calls or by upcoming deadlines. 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 School Research Directors, and **are available** on the [Research Development website](#).

*Research Professional

British Gynaecological Cancer Society

[Allied Health Professional Travelling Fellowship](#)

Closing date: 31 August 2023

Award amount: £1,000

This fellowship is awarded to an established Gynaecological Oncology Allied Health Professional in NHS practice to increase their knowledge and experience in the management of the late effects of cancer treatment.

Gateway for Cancer Research

[GFCR Integrative Program](#)

Closing date: 31 August 2023

Award amount: USD \$200,000-1.5 million

Gateway funds Phase I and II patient-centered cancer clinical trials that have the potential to shift the paradigm for standard of care. We strive to fund treatment-based studies at the bedside, including all types of cancers.

We advance our mission by funding Phase I and II patient-centered clinical trials focusing on the following priority research areas: Biomarkers/Molecular Markers (genomic or proteomic); Gene Therapy; Histology Agnostic/Basket Trial; Immunotherapy; Targeted Therapies.

Our focus is on the following therapeutic areas: New Investigational Therapies; Novel Use or Approach; Precision Medicine; Integrative Medicine.

Cancer Research Institute

[Postdoctoral Fellowship](#)

Closing date: 1 September 2023

Award amount: USD \$240,000

Supports qualified young scientists at leading universities and research centres around the world who wish to receive training in fundamental immunology or cancer immunology. CRI seeks hypothesis-driven, mechanistic studies in both immunology and tumour immunology. The applicant and sponsor should make every effort to demonstrate the potential of the proposed studies to directly impact our understanding of the immune system's role in cancer.

Cancer Research UK[Clinical trial fellowship award](#)

Closing date: 6 September 2023

Award amount: £150,000

This supports clinicians with an interest in clinical trials and who would benefit from further training within a clinical trial unit setting. This aims to enable fellows to gain cancer related clinical trial experience, with the ultimate objective of leading high impact, practice changing cancer clinical trials in the future as a chief investigator. Applications must be a collaboration between a fellow and an experienced clinical trial unit, and must demonstrate the collaborative development of a training programme exposing the fellow to all aspects and stages of trials, and must not limit the fellow to a one study.

Medical Research Foundation[Cancer Pain Clinical Fellowships](#)

Closing date: 6 September 2023

Award amount: unspecified

Applications from clinicians who have the potential to be the research leaders of the future, to support research that will increase understanding of the disease mechanisms underlying Cancer Pain, are invited. Researchers whose work may lead to better understanding of prevention, treatment or management of cancer pain are welcome to apply.

American Association for Cancer Research[AACR-American Cancer Society Award for Research Excellence in Cancer Epidemiology and Prevention](#)

Closing date: 15 September 2023

Award amount: unspecified

Cancer researchers affiliated with any institution involved in cancer research, cancer medicine, or cancer-related biomedical science anywhere in the world may be nominated.

Cancer Research UK[Early detection and diagnosis programme awards](#)

Closing date: 21 September 2023

Award amount: £2.5 million

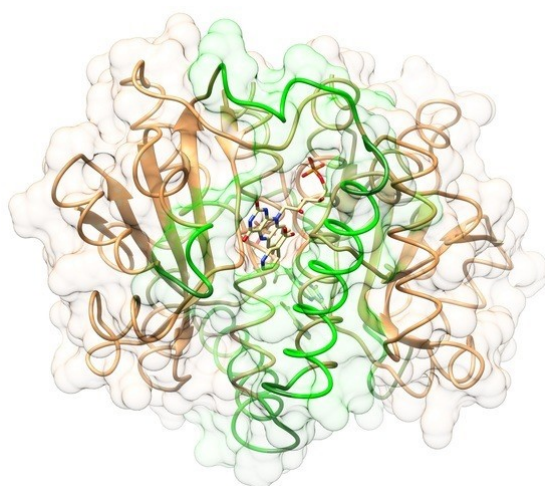
These support long-term, integrated and renewable programmes of exceptional science to transform how and when early cancers and pre-cancerous states are diagnosed. The remit of the awards includes: identification and validation of early detection and diagnosis markers and understanding of disease trajectory; identification of high-risk groups for early detection and diagnosis research and implementation; data and computation-driven approaches to ED&D; development and use of appropriate preclinical model systems; ED&D technology development; etc.

FEATURED PUBLICATION

Structure and Dynamics of Three *Escherichia coli* NfsB Nitro-Reductase Mutants Selected for Enhanced Activity with the Cancer Prodrug CB1954

Day MA, Christofferseon AJ, Anderson JLR, Vass SO, Evans A, Searle PF, White SA & Hyde EI. (2023). *International Journal of Molecular Sciences*.

Escherichia coli NfsB has been studied extensively for its potential for cancer gene therapy by reducing the prodrug CB1954 to a cytotoxic derivative. We have previously made several mutants with enhanced activity for the prodrug and characterised their activity in vitro and in vivo. Here, we determine the X-ray structure of our most active triple and double mutants to date, T41Q/N71S/F124T and T41L/N71S. The two mutant proteins have lower redox potentials than wild-type NfsB, and the mutations have lowered activity with NADH so that, in contrast to the wild-

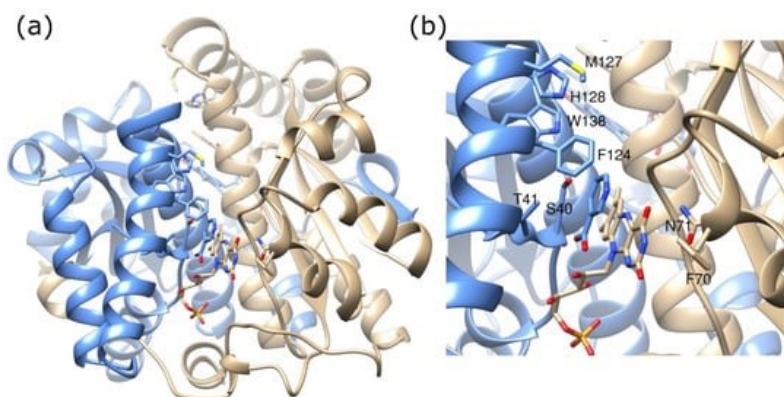


type enzyme, the reduction of the enzyme by NADH, rather than the reaction with CB1954, has a slower maximum rate. The structure of the triple mutant shows the interaction between Q41 and T124, explaining the synergy between these two mutations. Based on these structures, we selected mutants with even higher activity. The most active one contains T41Q/N71S/F124T/M127V, in which the additional M127V mutation enlarges a small channel to the active site. Molecular dynamics simulations show that the mutations or reduction of the FMN cofactors of the protein has little effect on its dynamics and that the largest backbone fluctuations occur at residues that flank the active site, contributing towards its broad substrate range.

Images:

Left image shows the graphical abstract.

Right image shows a ribbon diagram of wild-type protein showing positions mutated. (a) Structure of full protein with one subunit in blue and the other in tan, from 1ICR [30]. The side chains of mutated residues are shown in full and coloured in CPK colours, as are the FMN and bound nicotinate. (b) Close-up of the active site, in the same orientation as in Figure (a), with the mutated residues labelled.



CONTACTS



Network Co-Leads:

- [Emma Vincent](#), Senior Lecturer in Molecular Metabolism (Cancer Biology)
- [Helen Winter](#), Medical Oncologist and Clinical Director, SWAG Cancer Alliance (Clinical)
- Population Health co-Lead under recruitment

Steering Group members:

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- [Laura Ballisat](#), PhD student
- [Johanna Blee](#), Research Associate
- [Anya Burton](#), Senior Research Associate
- [Adam Chambers](#), Clinical Lecturer
- [Grace Edmunds](#), Clinical Research Fellow
- [Kathreena Kurian](#), Professor of Neuropathology and Consultant Clinical Neuropathologist
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