Cancer Network Newsletter
2023: Issue 2

Bristol Cancer Research Network

Screening reduces bowel cancer incidence

The incidence of bowel cancer in the lowermost portion of the large bowel has decreased by approximately 15% following the introduction of the English Bowel Cancer Screening Programme (BCSP) in 2006.

Researchers from the University of Bristol and University Hospitals Bristol and Weston NHS Foundation Trust wanted to investigate the impact of the BCSP on incidence rates of bowel cancer among adults in England. After its introduction, the BCSP was expanded in 2010 to offer screening to all adults aged 60 to 74 years registered with a GP. As part of the programme, adults in this age group are automatically sent an NHS bowel cancer screening kit every two years.

While the incidence rate of bowel cancer initially peaked in the years following the introduction of the BCSP, it subsequently decreased with the greatest reduction in incidence being observed in tumours of the lowermost portion of the large bowel. In 2001, the incidence of tumours of the lowermost portion of bowel

was 11% higher in patients from the most deprived compared to the least deprived areas, reducing to 4% by 2017. Furthermore, men were also noted to have experienced a greater reduction than women over time-period of the study for tumours of both the uppermost and lowermost portions of the large bowel.

Results show that one of the benefits of screening is a significant lowering of colorectal cancer incidence rates that is primarily driven by detecting and removing pre-cancerous polyps at colonoscopy. Future work should be focused on reducing the incidence of tumours of the uppermost portion of the large bowel by increasing screening uptake through use of the new faecal immunohistochemical test (FIT), and improving the quality of colonoscopy.

Chambers A *et al*. (2023). Colorectal cancer incidence trends by tumour location among adults of screening-age in England: a population-based study. *Colorectal Disease*.

Listen to an interview with Adam on BBC Radio Bristol (starts 2:08:50)

Inside this issue:

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University of BRISTOL
Elizabeth Blackwell Institute for Health Research

EVENTS

An Introduction to Co-produced Research
10 January 2024, 12.00 - 16.00, Room G.16, Victoria Rooms, 88 Queens Road, Bristol, Bs8 1SA

AI in the Biosciences UK Network Kick-off event
11 January 2024, 9.00 - 16.00, Conference Aston, Birmingham and online

Convergence Science Centre Annual Symposium - Engineering Cancer Research
17 January 2024, 13.00 - 18.30, Keynote: Professor Mehmet Toner (Medical School and Massachusetts General Hospital), Royal Geographical Society, London SW7 2AR

Shaping Tomorrow's Research: Commitment to Equality, Diversity, and Inclusion (EDI)
22 January 2024, 13.00 - 14.30, online

Elizabeth Blackwell Institute Annual Public Lecture 2023: Facts, fakes, society and health
22 January 2024, 18.30 - 20.00, Patricia Kingori (Professor of Global Health Ethics, Nuffield Department of Population Health, Wellcome Senior Investigator, and Senior Research Fellow at Somerville College, University of Oxford), Conference Hall, City Hall, College Green, Bristol BS1 5TR

Post ASH Significant Highlights
23 - 24 January 2024, Cavendish Conference Centre, 22 Duchess Mews, London W1G 9DT

Night work and breast cancer risk: from the beginnings to what we know today
29 January 2024, 16.00 - 17.00, Eva Schernhammer (Medical University of Vienna, Austria & Harvard Medical School, USA), online

EACR-EMBO Commercialising Your Research: What's Involved?
30 - 31 January 2024, online

Tackling drug resistance in cancer: An interdisciplinary workshop
31 January 2024, 9.30 - 18.15, Hilton York, 1 Tower Street, York YO1 9WD

Marie Curie Improving End of Life for All Research Conference 2024
5 - 9 February 2024, online

Post ISTH & ASH Headlines 2024
6 February 2024, 9.00 - 17.00, Austin Court, IET Birmingham, 80 Cambridge Street, B1 2NP

UK Haemato-Oncology Clinical Study Group Update
7 February 2024, 8.30 - 17.00, Cavendish Conference Centre, 22 Duchess Mews, London W1G 9DT

Signaling Circuits in Cancer
13 - 14 February 2024, online

Data-driven cancer research conference 2024
27 - 28 February 2024, etc.venues Manchester

SEE ALL EVENTS ON THE CANCER RESEARCH NETWORK WEBSITE

NEWS

Robot could help diagnose breast cancer early

A device has been created that could carry out Clinical Breast Examinations (CBE). The manipulator, designed by a team at the University of Bristol and based at the Bristol Robotics Laboratory, is able to apply very specific forces over a range similar to forces used by human examiners and can detect lumps using sensor technology at larger depths than before. This could revolutionise how women monitor their breast health by giving them access to safe electronic CBEs, located in easily accessible places such as pharmacies and health centres, which provide accurate results.

Precision, repeatability and accuracy are of paramount importance in these tactile medical examinations to ensure favourable patient outcomes. A range of automatic and semi-automatic devices have been proposed to aid with optimising this task, particularly for difficult to detect and hard to reach situations such as during minimally invasive surgery. The simulations allowed the team to perform thousands of palpations and test lots of hypothetical scenarios such as calculating the difference in efficiency when using two, three, or four sensors at the same time. In the lab, they were able to carry out the experiments on a silicone breast to demonstrate the simulations were accurate and to experimentally discover the forces for the real equipment.

Jenkinson G *et al*. A robotIc Radial palpatIon mechaniSm for breast examination (IRIS). Presented at the RO-MAN conference.

New Population Health Cancer Network co-Lead

The Bristol Cancer Research Network is delighted to announce that Dr Rebecca Richmond (pictured) based in Bristol Medical School: Population Health Sciences has taken over the role of Population Health co-Lead.

Becky is a Vice-Chancellor's Research Fellow in Molecular Epidemiology whose research aims to:

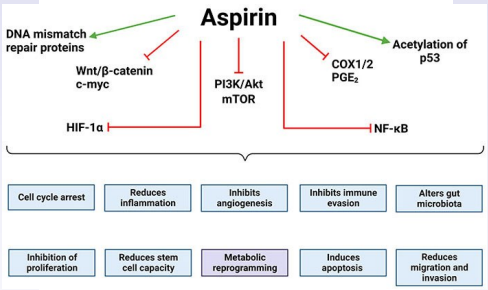
- highlight the relative importance and inter-relationships of several health behaviours (including smoking, e-cigarette use, alcohol, sleep, physical activity) for prioritisation in disease prevention strategies
- identify molecular pathways (e.g. epigenetic and metabolomic) which could serve as therapeutic targets for intervention.

Her major areas of focus are on the large-scale integration of molecular data in population-based and clinical health science as well as the development and application of causal inference methods, including Mendelian randomization. She hase specific interests in cancer, women's health and lifecourse epidemiology.

She will be working alongside our other co-Leads, Helen Winter (clinical) and Emma Vincent (cancer biology) and our steering group members (to provide strategic oversight of the University's work in cancer. Welcome, Becky!

Aspirin and the metabolic hallmark of cancer

Aspirin is a well-known non-steroidal anti-inflammatory drug (NSAID) that has a recognised role in cancer prevention as well as evidence to support its use as an adjuvant for cancer treatment. Importantly, there has been an increasing number of studies contributing to the mechanistic understanding of aspirins' anti-tumour effects and these studies continue to inform the potential clinical use of aspirin for both the prevention and treatment of cancer. This review focuses on the emerging role of aspirin as a regulator of metabolic reprogramming, an essential "hallmark of cancer" required to support the increased demand for biosynthetic intermediates needed for sustained proliferation.



The increasing evidence that aspirin impacts metabolism in cancer cells suggests that aspirin could provide a simple, relatively safe, and cost-effective way to target this important hallmark of cancer. Excitingly, this review highlights a potential new role for aspirin in improving the efficacy of a new generation of metabolic inhibitors currently undergoing clinical investigation.

Hoskin AJ *et al*. (2023). Aspirin and the metabolic hallmark of cancer: novel therapeutic opportunities for colorectal cancer. *Exploration of Targeted Anti-tumor Therapy*.

Ultra-processed foods and risks of oral cancers

Eating more ultra-processed foods (UPFs) may be associated with a higher risk of developing cancers of upper aerodigestive tract (including the mouth, throat and oesophagus), according to a new study led by researchers from the University of Bristol and the International Agency for Research on Cancer (IARC).

The authors of this international study, which analysed diet and lifestyle data on 450,111 adults who were followed for approximately 14 years, say obesity associated with the consumption of UPFs may not be the only factor to blame.

Since many UPFs have an unhealthy nutritional profile, the team sought to establish whether the association between UPF consumption and head and neck cancer and oesophageal adenocarcinoma (a cancer of the oesophagus) in EPIC could be explained by an increase in body fat.

Results from the team's analyses showed that eating 10% more UPFs is associated with a 23% higher risk of head and neck cancer and a 24% higher risk of oesophageal adenocarcinoma in EPIC. Increased body fat only explained a small proportion of the statistical association between UPF consumption and the risk of these upper-aerodigestive tract cancers.

Morales-Berstein F *et al*. (2023). Ultra-processed foods, adiposity and risk of head and neck cancer and oesophageal adenocarcinoma in the European Prospective Investigation into Cancer and Nutrition study: a mediation analysis. *European Journal of Nutrition*.

Mistletoe Therapy in Cancer

Dr Lorna Duncan, Research Fellow at the University of Bristol's Centre for Academic Primary Care, is part of a team who recently completed the first randomised controlled trial of Mistletoe Therapy for cancer patients receiving NHS chemotherapy treatment in the UK.

Mistletoe contains a variety of unusual substances which may be beneficial when integrated into conventional oncology treatment programmes. Mistletoe Therapy has been shown to affect biological processes, for example stimulating the immune system, as well as improving patients' quality of life.

However, there has been little investigation into mistletoe therapy in the UK where it is relatively unknown; and patients' experiences of this treatment have also been less studied. Lorna undertook qualitative interviews with patients for the Mistletoe And Breast cancer trial, which was part-funded by Camphill Wellbeing Trust and the Swiss Association for Cancer Research (VfK). She found patients were enthusiastic about mistletoe therapy, despite having to self-administer it sub-cutaneously. They liked the idea of having a 'natural', if surprising, treatment alongside their chemotherapy and also that it was an accepted therapy in countries such as Germany and Switzerland.

Read the full news item on the Elizabeth Blackwell Institute news pages

Mascher A *et al*. (2023). The Introspective Patient Experience of Mistletoe Therapy in Cancer: A Qualitative Study. *Integrative Cancer Therapies*.

Latest University Cancer Research Fund awards

The University Cancer Research Fund (UCRF) is an endowment which supports the wide range of exceptional cancer research taking place in the University. It is recognised that there remain significant challenges in securing funding when first establishing an independent research programme. To support these future leaders in the field, the UCRF launched a support fund for Early to Mid-Career Researchers that will provide up to £30,000 (over two years) to help launch their research careers.

We are delighted to announce that we were able to support two applications this year:

- Dr Siang Boon Koh (Cellular and Molecular Medicine). Siang's research focuses on discovering cancer features that are clinically relevant, with the goal to translate his work into tangible outputs such as predictive tumour biomarkers and personalised medicine strategies. Currently, he is interested in identifying therapeutic ways to reverse therapy resistance in tumours.
- Dr Rebecca Richmond (Bristol Medical School). The project being proposed under this award will further Becky's investigation into the role of sleep in breast cancer by exploring a new resource: the All of Us Research Programme, a large and diverse health database which comprising 1 million people across the United States. The award will support access to this resource, which includes genetic, sleep and cancer data on its participants. The award will also support Becky's first post-doctoral researcher.

Pioneering projects announced by The Little Princess Trust

The Little Princess Trust announced funding of three groundbreaking childhood cancer research projects including a new University of Bristol-led study that will investigate how protein production is changed in childhood cancer cells.

Karim Malik, Professor of Molecular Oncology in the School of Cellular and Molecular Medicine at Bristol, will study a new way that cancer cells can alter the production of proteins in order to help them grow unchecked. While researchers know that cancer cells can have more of the messenger molecules that read the genetic code, which contains instructions for proteins which control cell behaviour. Professor Malik proposes that they also have changes to how these instructions are translated into proteins.

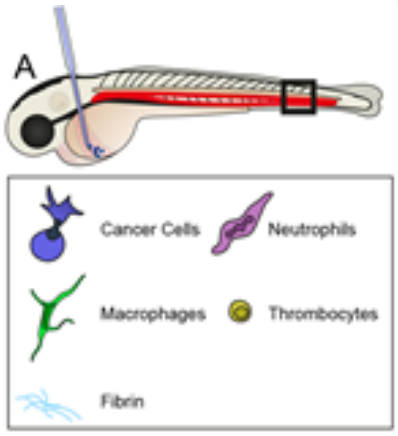
His project will focus on understanding how the translation of the genetic code into proteins is altered by molecules called tRNAs. These are a vital part of the translation process, bringing together the components needed to build each protein. Inhibition of cancer cell tRNAs may provide new cancer treatments in the future. The project, *The tRNA epitranscriptome: the missing link in MYCN-driven childhood tumours,* received £49,915 and will run January 2024 to July 2026.

Read more

Inflammatory response enhances cancer cell 'leakage'

Clinical observations for more than a century have indicated that thrombosis is associated with cancer progression and metastatic spread. More recent experimental studies have revealed that this link is, in part, because many cancers release pro-thrombotic factors, but platelets and fibrin might also act to protect blood-borne cancer cells from shear forces and immune attack. Furthermore, microclots might function as a favoured pre-metastatic niche for immune cell recruitment and the unintentional leakage of vesicant fluids from the cancer cell into the surrounding tissue (extravasation).

Given this evidence linking clotting and cancer metastasis, the study team used the translucency of zebrafish larvae to live image the dynamic relationship between cancer cells,



endothelial cells, platelets and immune cells, and investigated spontaneous cancer cell extravasation episodes and those at sites of microclots, in standard conditions and after pharmacological or genetic inhibition of clot formation.

Data show a clear indication of how microclots might lead to extravasation of blood-borne cancer cells through their interactions with fibrin, platelets and innate immune cells, thereby hinting at potential targets for therapeutic inhibition of clot-mediated cancer cell extravasation.

Ward J and Martin P (2023). Live-imaging studies reveal how microclots and the associated inflammatory response enhance cancer cell extravasation. *Journal of Cell Science*.

Saluting Our Sisters – Black History Month October 2023

PhD student in the School of Engineering Mathematics and Technology and Centre for Ethics in Medicine, and Bristol Cancer Research Network steering group member Matimba Swana (pictured), was recently highlighted in a Government Science and Engineering blog published on 23 October 2023.

Matimba recently completed an internship in the Futures team in the UK Government Office for Science; her experience in the role allowed her realise that future thinking is not about dystopias and utopias but understanding long-term issues or challenges shaping future development in policy. There are many future possibilities that can happen, but we can also influence things based on what we do today. Her research involves cancer nanomedicine, swarm medicine, bioethics, and the use of virtual tumours and patient twin models in clinical trials.

Matimba is also one of the co-founders of the University's Black and Brown in Bioethics network, which aims to achieve racial equity with the UK bioethics community.

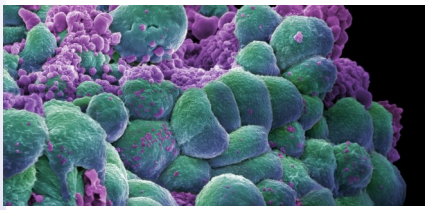
Read the full blog

Funding successes

Prof Karim Malik (Cellular and Molecular Medicine) received £218,364 from the **Children's Cancer and Leukaemia Group** for *Synergistic and selective combination methyltranferase therapy for poor prognosis Wilms' tumour*, starting January 2024 for 18 months.

Prof Linda Wooldridge (Bristol Veterinary School) received £5,600 from **Instil Bio** for *Genetic Engineering Tumour Infiltrating Lymphocytes (TILs) to achieve enhanced tumour killing*, starting October 2023 for four years.

Novel Treatment for Prostate Cancer by repurposing Alzheimer Drugs: determining the role of amyloid precursor protein was supported by a £245,410 award from **Prostate Cancer UK**. Dr Rachel Barker (Bristol Medical School) started the project in October 2023; it will run until September 2026.



Dr Bernadette Carroll (Biochemistry) was awarded £113,067 from the **Biotechnology and Biological Sciences Research Council** for *Senescence in skin ageing*, October 2023 to September 2027.

Prof Richard Martin (Bristol Medical School) received £332,924 from **Cancer Research UK** (CRUK) for *Answering key questions needed to inform prostate cancer screening policy: long-term follow-up of the ProtecT (15-year) and CAP (18-year) randomised controlled trials*; this extends the work of these trials until June 2026.

CRUK also awarded Dr James Yarmolinsky (Bristol Medical School) £71,314 for *Using reverse Mendelian randomization to discover novel circulating biomarkers for early detection of cancer*, starting November 2023 for one year.

External engagements

Prof Anne Ridley (Cellular and Molecular Medicine, pictured below) presented at the Mechanobiology Conference, 26-29 September 2023 in Singapore. Her presentation, *Mechanosignalling in endothelial cells*, revealed how endothelial overlapping cell-cell junctions maintain their resilience to flow and permeability depending on stress fibres, endothelial loops and YAP activity. Anne studies how cells migrate through their environment, using cell surface receptors to change their internal cytoskeleton dynamically to move faster or more slowly. I currently work on cancer progression and cancer spreading.

Prof Nick Maskell (Bristol Medical School, pictured right), respiratory disease theme and workstream lead at the Bristol Biomedical Research Centre, has been elected president of the British Thoracic Society. His appointment began following the Society's Annual General Meeting on 22-24 November 2023 in London.

British Thoracic Society

Interdisciplinary research awards

In April 2023 the Elizabeth Blackwell Institute at the University of Bristol launched a funding call to support health-related interdisciplinary research. Amongst the awards were:

- James Armstrong (Bristol Medical School): *Developing a framework for AI-guided chemotherapy*

Cancer is a major healthcare challenge, and although there are many different drugs that can be used, we do not always select the right combination. With this funding from the Elizabeth Blackwell Institute, we will explore how artificial intelligence can be used to guide the selection of drugs for treating cancer. Co-Investigators: Alessandro Masullo (School of Computer Science, Electrical & Electronic Engineering and Engineering Maths) & Emma Vincent (Bristol Medical School: Translational Health Sciences)

- Chiara De Sio (School of Physics, pictured): *TIDE: Temporal Impact on DNA Effects - Exploring Cell Survival in Radiation Experiments*

This project is about measuring short-time effects and radiation damage to cells at DNA level. We irradiate cell cultures with two types of radiation (protons and photons) at different doses, to better understand the DNA damage and DNA repair mechanisms. This will improve our current simulations and, hopefully, treatment planning for localised cancer treatments such as brachytherapy and targeted alpha treatments. Co-Investigators: Adam Chambers (School of Cellular and Molecular Medicine), Anna Chambers (School of Biochemistry), Jaap Velthuis (School of Physics)

Read about the other awards

Morphometric analysis of intestinal organoids

Organoids offer a powerful biological model to study cellular self-organisation, the growth of specific tissue formation, and to assess potential medical therapies. However, many different organoid shapes can be observed in practice, and the mechanisms underlying their generation are not yet fully understood. This means that it is still a challenge to standardise organoid cultures for experimental manipulation, and hence to derive the maximum benefit for understanding human health and disease.

Mathematical models offer a potential solution to this problem, although the question remains of how to use data of lab-grown organoids to properly calibrate and test the models, given the number and complexity of the images generated by both in-vitro and in-silico experiments. Here, the study team developed methods that can automatically extract the key morphological features from collections of intestinal organoids images; specifically, to count budding structures generated from both new *in-vitro* experiments and *in-silico* simulations. Experimental results are compared to simulations of a multiscale mathematical model which describes the system physiology and can replicate the budding structures that are seen experimentally.

Montes-Olivas S *et al*. (2023). *In-silico* and *in-vitro* morphometric analysis of intestinal organoids. *PLOS Computational Biology*.

Aspirin reprogrammes colorectal cancer cells

To support proliferation and survival within a challenging microenvironment, cancer cells must reprogramme their metabolism. As such, targeting cancer cell metabolism is a promising therapeutic avenue. However, identifying tractable nodes of metabolic vulnerability in cancer cells is challenging due to their metabolic plasticity. Aspirin has a well-established role in cancer prevention, particularly in colorectal cancer (CRC), although the mechanisms are not fully understood.

The research team generated a model to investigate the impact of long-term (52 weeks) aspirin exposure on CRC cells, which has allowed them to comprehensively characterise the metabolic impact of long-term aspirin exposure. Using this information, the team were able to identify nodes of metabolic vulnerability for further targeting, investigating the impact of combining aspirin with metabolic inhibitors *in vitro* and *in vivo*.

They showed that aspirin regulates several enzymes and transporters of central carbon metabolism and results in a reduction in glutaminolysis and a concomitant increase in glucose metabolism, demonstrating reprogramming of nutrient utilisation. Treatment with glutaminase 1 inhibitor CB-839 alone had little effect on CRC cell growth or survival. However, in combination with aspirin, CB-839 inhibited CRC cell proliferation and induced apoptosis *in vitro* and, importantly, reduced crypt proliferation in Apcfl/fl mice *in vivo*.

Holt A *et al*. (2023). Aspirin reprogrammes colorectal cancer cell metabolism and sensitises to glutaminase inhibition. *Cancer & Metabolism*.

Extreme heat and disease in urban areas

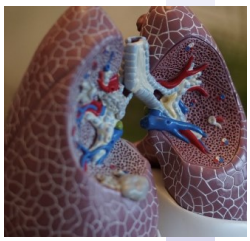
Advanced tools and more experimental studies are needed to urgently understand the impact of extreme heat events on urban health and wellbeing in the UK. A study under the TRUUD project aims to reduce non-communicable disease (NCD - such as cancers, diabetes, obesity, mental ill-health and respiratory illness) and health inequalities linked to the quality of urban planning and development.

The team looked at gaps in our knowledge between the urban environment and heatwaves, indoor heat, and non-communicable diseases and examined what we already know about the effects of extreme heat, NCDs and related risk factors to help urban planners factor health considerations in the decision-making process. Findings consistently demonstrated that higher temperatures above defined heat thresholds were significantly associated with increased mortality rates. The studies included in the review reported that for every 1°C rise above the heat threshold, mortality increased by up to 2.5%, emphasising the urgent need for mitigation strategies. Furthermore, the projected impact of temperature rise on heat-related mortality showed alarming figures, with estimates suggesting a potential 90% increase in heat-related deaths between the 2020s and 2050s under medium-emission scenario.

Ige J *et al*. (2023). A systematic review of the impacts of extreme heat on health and wellbeing in the United Kingdom. *Cities and Health*.

Clinical academic funding for Academic Respiratory Unit

Three clinicians based in the Academic Respiratory Unit (ARU) have been successful in gaining prestigious and highly competitive clinical academic funding from the National Institute for Health and Care Research (NIHR) and the Medical Research Council (MRC).
The ARU, led by Prof Nick Maskell, is part of Bristol Medical School.



Dr Anna Bibby, Consultant Respiratory Physician and Honorary Lecturer, and Dr Steven Walker, Senior Respiratory Registrar and Academic Clinical Lecturer, were both awarded NIHR Advanced Fellowships (AF).
Dr Rahul Bhatnagar, Consultant Respiratory Physician and Honorary Senior Lecturer, was awarded an MRC/NIHR Clinical Academic Research Partnership (CARP).

The funding awarded will provide each individual with dedicated research and training time to deliver their respective projects.

Dr Bhatnagar will undertake a multicentre clinical study to collect pleural fluid samples from lung cancer patients, before applying epigenetic analyses (in conjunction with the MRC Integrative Epidemiology Unit) to identify predictive biomarkers for key outcomes such as survival and treatment response.

Dr Bibby will undertake a programme of work (*Increasing informed participation in lung cancer screening (IMPALA): a mixed methods study and feasibility trial*) aiming to increase participation in lung cancer screening. Her work will build on the recent announcement of a national lung cancer screening programme, aiming to increase the overall impact of the programme and reduce health inequalities. She was awarded £1,144,168 and her fellowship will run from October 2023 to September 2028.

Small Intestinal Neuroendocrine Tumours

Small intestinal neuroendocrine tumours (siNETs) are rare neoplasms which present with low mutational burden and can be subtyped based on copy number variation (CNV). Currently, siNETs can be molecularly classified as having chromosome 18 loss of heterozygosity (18LOH), multiple CNVs (MultiCNV), or no CNVs. 18LOH tumours have better progression-free survival when compared to MultiCNV and NoCNV tumours, however, the mechanism underlying this is unknown. Here, the research team used genome-wide tumour DNA methylation and gene expression to better understand how gene regulation varies by 18LOH status.

They identified 27,464 differentially methylated CpG sites and 12 differentially expressed genes between 18LOH and non-18LOH. These genes were highly enriched with the differentially methylated CpG sites compared to the rest of the genome. They identified differences in tumour microenvironment between 18LOH and non-18LOH tumours, including CD14+ infiltration in a subset of non-18LOH tumours which had the poorest clinical outcomes.

Waterfield S *et al*. (2023). Chromosome 18 Loss of Heterozygosity in Small Intestinal Neuroendocrine Tumours: Multi-Omic and Tumour Composition Analyses. *Neuroendocrinology*.

Maintaining activity in advanced cancer

The motivation behind the doing – what motivates people to do certain things while living with advanced cancer – is more important to them than their sense of competence in daily life. A project found that motivation and environment played a central role in how people living with advanced cancer adapt to keep engaging with activities they see as valuable.

People living with cancer often experience a steady decline in their ability to function in their final year of life. This means they may find it increasingly more difficult to engage with various activities they may have enjoyed or that may have been part of their routine in the past, such as work or hobbies.

Researchers wanted to understand the experiences of working-age adults living with advanced cancer in terms of occupational engagement and adaptation. To do this, they interviewed eight adults (40–64 years old) over a period of 19 months. Throughout the study they used the term 'occupation' to mean everything that occupies a person's time. They used the term 'occupational adaptation' to describe how people adapt how they carry out daily activities after experiencing something challenging.

Study findings showed that volition, what motivates people to keep doing things as their life is coming to an end, among their interviewees was closely related to their valued roles of parent, spouse, friend, or worker. Volition, alongside the environment a person found themselves in, played a more central role in occupational adaptation than feelings of occupational competency.

Brose JM *et al*. (2023). Occupational adaptation for adults living with advanced cancer: A phenomenological longitudinal study. *Australian Occupational Therapy Journal*.

New Bristol Evidence Synthesis Group awarded £2.5m

The Bristol Evidence Synthesis Group is one of nine new specialist research groups in the UK, set up to provide sound evidence to health and social care policymakers. The National Institute for Health and Care Research (NIHR) Evidence Synthesis Groups, part of NIHR's Evidence Synthesis Programme, will investigate what evidence is available to answer important questions spanning healthcare, public health and social care. Each group has been granted £2.5 million over five years. Together, the groups could work on up to 45 research projects per year.

NIHR | National Institute for Health and Care Research

These groups will carry out projects requested by stakeholders such as NHS trusts, local authorities, patient communities and members of the public. Other projects will be identified through NIHR processes and working closely with policymakers to make sure they address policy and practice needs. Research topics will be allocated without the need for a lengthy commissioning process.

Evidence synthesis is an approach that allows researchers to identify, appraise and analyse all the information on a particular research question. It is a powerful way of combining data across many different studies to find more definitive answers.

Genomics project will provide insight in global diversity

A collaboration aims to improve global health by uncovering the effects of genomic and environmental diversity on differences in disease risk observed across the globe, thanks to a new partnership of 20 research groups.

The groundbreaking five-year project, led by researchers in the University of Bristol, the MRC Unit The Gambia at London School of Hygiene & Tropical Medicine and the CSIR Centre for Cellular and Molecular Biology in India, will explore key population health questions using datasets from across African, Asian, and North and South American continents.

The Diverse Epigenetic Epidemiology Partnership (DEEP) study, funded by the Medical Research Council, will generate genomic datasets in underrepresented populations. It will develop software and infrastructure and conduct advanced statistical analyses to build new resources. These resources will sit alongside international health and genetics databases to look at trends in variation in DNA methylation (a process where chemical groups attach to DNA in order to help to turn genes on and off).

There is huge variation in disease onset and symptoms for people living in different global regions; however, much of the population health research conducted draws heavily on data collected from people of white European origins. The study aims to bridge this gap by studying individuals representing diverse genetic and environmental contexts and learn which DNA methylation patterns contribute to their disease risk in each context. This will enable identification of disease-causing mechanisms that are common worldwide and those which are unique to particular groups or regions.

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**.

Alex's Lemonade Stand Foundation for Childhood Cancer
Crazy 8 Initiative

Closing date: 08 January 2024 Award amount: USD 5 million

This ALSF Crazy 8 RFA focuses on understanding childhood cancer predisposition and prevention. The focus must be on pediatric/adolescent cancer predisposition and should be a consortium of two or more institutions with different areas of research collaborating to integrate their expertise. It is strongly encouraged to have a patient advocate on the team. The proposal should address a topic that is responsive to at least one of the five areas of focus listed below. The proposals will be judged on innovation, scientific soundness, significance, and the potential for impact on improving the lives of children with cancer.

Five major areas of focus have been identified for this Crazy 8 RFA:

- New Gene Discovery
- Genotype-phenotype correlations
- Surveillance optimization
- Predisposition Models
- Cancer Prevention

Medical Research Foundation
Cancer Pain Clinical Fellowships

Closing date: 11 January 2024 Award amount: unspecified

Invites 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. Researchers whose work may lead to better understanding of prevention, treatment or management of cancer pain are welcome to apply.

Cancer Research UK

Multidisciplinary project award

Closing date: 11 January 2024 Award amount: £500,000

This supports collaborations between cancer researchers and scientists from engineering and physical science disciplines. The aim is to generate creative research ideas and explore their applicability in cancer research. Proposals across all engineering and physical science disciplines including physics, engineering, mathematical and computational modelling, chemical and molecular sciences, materials science, molecular and tissue engineering and regenerative medicine are welcomed. The research themes for this award include:

- direct application of physics, engineering, chemical or mathematical concepts to address the underlying physical processes of cancer, including tumour initiation, growth and metastasis;
- development of new transformational approaches or the translation of technologies for direct applications in, or a clear path to, a direct application in the prevention, diagnosis or treatment of cancer.

National Cancer Institute

Modulating Human Microbiome Function to Enhance Immune Responses Against Cancer (R01 Clinical Trial Not Allowed)

Closing date: 5 February 2024 Award amount: unspecified

Support basic research that elucidates mechanisms by which the human microbiome inhibits or enhances anti-tumor immune responses, and to identify potential novel molecular targets for cancer prevention strategies.

Applications should be focused on delineating how host interactions with specific microbes (or consortia) or their metabolites target immune responses that enhance or prevent inflammation-associated or sporadic tumor formation. Concentration, timing, and duration of administered beneficial microbes may alter its effectiveness and thus those parameters should be rigorously addressed in the application.

Cancer Research UK

Early detection and diagnosis primer award

Closing date: 21 March 2024 Award amount: £100,000

The award aims to encourage scientists at all career stages to engage with the early detection and diagnosis of cancer field. It will support new and exploratory research ideas and/or pilot studies of high scientific risk and potential reward. It supports the development of new partnerships and exploration of highly novel concepts, involving researchers from any research area, including from non-traditional cancer fields.

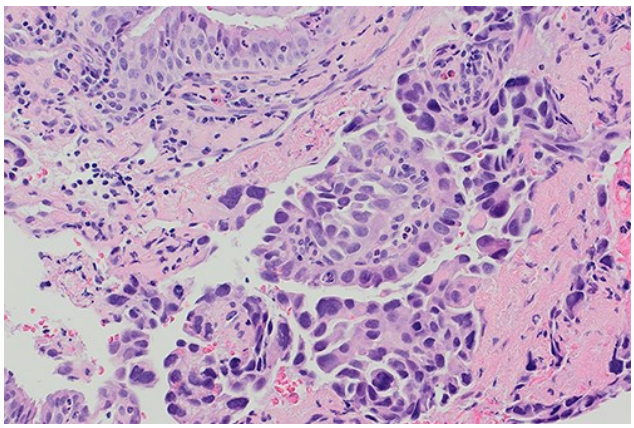
FEATURED PUBLICATION

Genomic Landscape and Actionable Mutations of Brain Metastases derived from Non-Small Cell Lung Cancer: a systematic review

Andrews LJ, Thornton ZA, Saleh R, Dawson S, Short SC, Daly R, Higgins JPT, Davies P, Kurian KM. *Neuro-Oncology Advances*.

The largest review of papers for brain cancer that has spread from the lungs has found abnormalities in the brain cancer and for which licensed drugs could be clinically trialled to find out if they could treat the disease. The research led by the University of Bristol also found genetic differences between smokers and non-smokers.

Around 25,000 patients in the UK suffer from cancer that has spread to the brain -known as metastases - most commonly from lung and breast cancer, and causes death in the majority of these patients.



The genetic mutations in primary lung cancers have been widely studied, but less is known about the changes in the cancer once it has spread to the brain. The research team wanted to find out the genetic changes in brain metastasis from non-small cell lung cancer (NSCLC) and whether there are drugs already available that could potentially be offered to these patients.

The researchers carried out a review from 72 papers of genetic mutations in brain metastasis of NSCLC from 2,346 patients' data on patient demographics, smoking status, genomic data, matched primary NSCLC, and PD-L1, which is a protein found on cancer cells.

The study found the most commonly mutated genes were EGFR, TP53, KRAS, CDKN2A, and STK11. Common missense mutations —mutations that lead to a single amino acid change in the protein coded by the gene— included EGFR L858R and KRAS G12C.

In certain cases the genetic mutations were different in the brain metastasis from the primary lung cancer. There were also differences in the genetic mutations in smokers versus patients who had never smoked. Brain metastases of smokers versus non-smokers had different missense mutations in TP53 and EGFR, except for L858R and T790M in EGFR, which were seen in both subgroups.

The research team found from the top ten commonly mutated genes which had primary NSCLC data, 37% of the specific mutations assessed were different between primary NSCLC and brain metastases. The researchers suggest Medicines and Healthcare products Regulatory Agency-approved drugs already licensed could potentially be tested to treat the disease in clinical trials.

Image shows non-small cell lung cancer (NSCLC) invading bronchial epithelium © Kathreena Kurian

Cancer Network

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The Cancer Research Network is led by a Steering Group:

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- Helen Winter, Medical Oncologist and Clinical Director, SWAG Cancer Alliance (Clinical)
- Rebecca Richmond, Senior Research Fellow (Population Health)

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