Launch of SRIs and Networks

In Dec 2016 UoB announced the formation of Specialist Research Institutes (SRIs) following a competitive application process. Under the University’s new strategy plan, an SRI represents a field in which Bristol is acknowledged to be a world leader and where there is significant alignment with regional, national and international ambitions. SRIs will complement existing disciplinary strengths in Schools and Faculties and will be limited in number to have an effective role in institutional branding. An external launch of the SRIs took place in March 2017.

There are three Institutes which will sit in the biomedical / health space:
- Bristol BioDesign Institute (Dir: Dek Woolfson)
- Bristol Heart Institute (Dir: Gianni Angelini)
- Bristol Population Health Science Institute (Dir: Caroline Relton)

From 2017 University Research Themes will cease to be formally endorsed and presented at an institutional level. This means that the Cancer Research Theme has been transformed into the Cancer Research Network. Networks, which also include Infection and Immunity, Neuroscience and Fundamental Biosciences, have migrated from the University’s Research pages and now sit under the Elizabeth Blackwell Institute. (This also applies to the external face of PURE, Explore Bristol).

There are guidance notes further explaining the roles of SRIs and Neworks online (Single Sign-on required).

Despite the shift it is still very much business as usual for Cancer. The steering group is continuing to meet, Newsletters and digests are still being produced and the website is being regularly updated with news and events.

**NB:** With the gradual demise of People Profiler, PURE will act as an interim profiling tool. As such, the People listing on the Cancer website now points to PURE. Membership on PURE has been recently updated; if you know of people within your research groups who should/would like to be added to the mailing list and the PURE group, please contact me.
GW4 data intensive research workshops: Challenges and opportunities for the Alliance
22 May 2017, 10.00 - 17.00, University of Exeter

Information Event: MSCA Individual Fellowships
23 May 2017, 10.30 - 15.30, Physics Building

Skeletal systems mechanobiology and personalized medicine
23 May 2017, 13.00 - 14.00. Ralph Müller (ETH Zürich), Seminar rooms A&B, Level 1 Learning & Research building, Southmead Hospital

GW4 Early Career Neuroscientist Day
5 June 2017, 9.30 - 18.00, Cardiff University

CRICBristol Research Showcase 2017
5 June 2017, 10.00 - 16.00. Paul Matthews, OBE, MD, DPhil, FRCP, FMedSci (Imperial College), Watershed

GW4 data intensive research workshops: Challenges and opportunities for the Alliance
5 June 2017, 10.00 - 17.00. WX3.07 West Extension Building, Queens Buildings, 5 The Parade, Cardiff CF24 3AA

How to prepare a good research bid (Medical Faculties)
8 June 2017, 10.00 - 16.30. Pamela Johnstone, Brunel Room, The Hawthorns

Bristol Population Health Science Institute launch
9 June 2017, 9.30 - 16.30. Nancy Krieger (Harvard University), Arnolfini Contemporary Arts Centre

GW4 data intensive research workshops: Challenges and opportunities for the Alliance
15 June 2017, 10.00 - 17.00, Engineers House

Introduction to research grant applications: Medical Faculties
19 June 2017, 14.00 - 17.00, Senate House room 3.16

NIHR Statistics Group Annual Conference: Challenges and Opportunities for Applied Statisticians
22 - 23 June 2017, The Edge, Sheffield

From top: Ralph Müller, Paul Matthews, Nancy Krieger
Metabolic Dysfunction and Cancer: Molecular Epidemiologic Approaches
23 June 2017, 12.00 - 13.00. Marc Gunter (Head of Section of Nutrition and Metabolism, International Agency for Research on Cancer), Room OS6, Oakfield House

CRUK Lab Tours
28 June 2017, 10.00 - 16.00, Southmead

Immunotherapy for Haematological Malignancies - The Future
4 July 2017, 9.30 - 17.15. Doubletree by Hilton Hotel, Redcliffe Way, Bristol

Big Bang Bristol
6 - 7 July 2017, Trinity Centre

13th World Congress on Inflammation
8 - 12 July 2017. Plenaries: Janet Lord (Birmingham University) & Michal Schwartz (Weizman Institute of Science), Hilton London Metropole Hotel

NIHR Public Health Research Information Event
14 July 2017, 9.30 - 16.00.

Symposium and Launch: GW4 Cryo-EM Facility
1 September 2017, 9.30 - 17.00, Life Sciences Building

Integrating Inherited Cancer Syndromes into Cancer Care

South West Lymphoma Group meeting
27 September 2017, 17.00 - 19.30. Steve Robinson (Bristol) & Simon Rule (Plymouth), The Castle Hotel, Taunton

Elizabeth Blackwell Annual Public Lecture
2 November 2017, 16.00 - 19.30. Prof Helen Stokes-Lampard FRCGP.
New classification proposal for meningiomas

A new paper published co-authored by Hayley Ellis and Prof Kathreena Kurian in Lancet Oncology proposes a new classification for meningiomas.

Background
The WHO classification of brain tumours describes 15 subtypes of meningioma. Nine of these subtypes are allotted to WHO grade I, and three each to grade II and grade III. Grading is based solely on histology, with an absence of molecular markers. Although the existing classification and grading approach is of prognostic value, it harbours shortcomings such as ill-defined parameters for subtypes and grading criteria prone to arbitrary judgment. In this study, we aimed for a comprehensive characterisation of the entire molecular genetic landscape of meningioma to identify biologically and clinically relevant subgroups.

Methods
In this multicentre, retrospective analysis, we investigated genome-wide DNA methylation patterns of meningiomas from ten European academic neuro-oncology centres to identify distinct methylation classes of meningiomas. The methylation classes were further characterised by DNA copy number analysis, mutational profiling, and RNA sequencing. Methylation classes were analysed for progression-free survival outcomes by the Kaplan-Meier method.

Findings
We retrospectively collected 497 meningiomas along with 309 samples of other extra-axial skull tumours that might histologically mimic meningioma variants. Unsupervised clustering of DNA methylation data clearly segregated all meningiomas from other skull tumours. We generated genome-wide DNA methylation profiles from all 497 meningioma samples. DNA methylation profiling distinguished six distinct clinically relevant methylation classes associated with typical mutational, cytogenetic, and gene expression patterns. Compared with WHO grading, classification by individual and combined methylation classes more accurately identifies patients at high risk of disease progression in tumours with WHO grade I histology, and patients at lower risk of recurrence among WHO grade II tumours (p=0.0096) from the Brier prediction test. We validated this finding in our independent cohort of 140 patients with meningioma.

Interpretation
DNA methylation-based meningioma classification captures clinically more homogenous groups and has a higher power for predicting tumour recurrence and prognosis than the WHO classification. The approach presented here is potentially very useful for stratifying meningioma patients to observation-only or adjuvant treatment groups. We consider methylation-based tumour classification highly relevant for the future diagnosis and treatment of meningioma.

View the full article online
New EBI Director from 1 August 2017

Following an open, internal, competitive appointment process, Prof Rachael Gooberman-Hill has been appointed to the role of Director of the Elizabeth Blackwell Institute, which she will commence on 1 August 2017.

Rachael is Professor of Health and Anthropology in the School of Clinical Sciences and currently leads the STAR Programme of Research to improve treatment for long-term pain after knee replacement as well as numerous other research projects. She also works on the Engaged University Steering Group, the Ethics of Research Committee, the Digital Health Steering Group, and the School of Clinical Sciences Equalities Committee.

Thanks have been extended to Prof Jeremy Tavaré as he has led the Institute since its inception in 2011. During his tenure EBI has established itself as an asset to this institution in building collaborative research activities, providing seed-corn funding for early career and established staff and secured significant external funding particularly through the Welcome Trust ISSF funds. Jeremy will now take up the position of Director of Health Research in the University.

Telomere length and cancer

Whilst shorter telomeres are hypothesized biological markers of older age and have been linked to many diseases, including cancer and cardiovascular diseases, whether these associations are causal is unknown.

A team investigated the effect of longer telomeres on the risk of 83 diseases, including cancer, cardiovascular diseases, diabetes, psychiatric diseases and autoimmune diseases in 420,081 cases and 1,093,105 controls, using Mendelian randomization. They found that longer telomeres appeared to increase the risk for several cancers, including glioma, serous low-malignant-potential ovarian cancer, lung adenocarcinoma, neuroblastoma, bladder cancer, melanoma, testicular cancer, kidney cancer and endometrial cancer but to decrease the risk for coronary heart disease, abdominal aortic aneurysm, coeliac disease and interstitial lung disease.

These findings suggest that potential clinical applications based on telomere length may have to consider a trade-off in risk between cancer and other diseases. For example, a number of companies offer telomere length measurement services to the public, claiming that shorter telomeres are a general indicator of poorer health status and older biological age and that such information can be used to motivate healthy lifestyle choices in individuals. However, the conflicting direction of association between telomere length and risk of cancer and other diseases suggests that such services to the general public may be premature. More info...
Targeting high grade brain tumours

A recent study has shown for the first time that the drug Panobinostat can be encapsulated in a water soluble molecule and delivered to a brain tumour to destroy high grade glioma cells. Dr Will Singleton, who is co-funded by the Brain Tumour Charity, tested the delivery of the drug Panobinostat using convection enhanced delivery (CED). CED is a technique that allows the infusion of drugs directly to the brain through surgically implanted micro-catheters. This overcomes the major challenge of having to get drugs across the blood brain barrier (BBB),

Panobinostat is a new anticancer drug that is known to manipulate the body’s immune system to cause tumour cell death in other cancers, but as it is water insoluble it is not suitable for delivery via CED. Will, however, has shown that through chemical modification the drug can be administered in nanoparticle form by CED and is associated with a prolonged survival in glioma-bearing animal models. This technology has the potential to be applied to any water insoluble drug that is unable to cross over the BBB, opening up the possible exploration of drugs that have never been considered for the treatment of brain tumours.

Read the full article published in the International Journal of Nanomedicine.

Early career training and support

The Faculties of Biomedical Sciences and Health Sciences have a dynamic postgraduate community enrolled in taught or research-based programmes. Postgrads receive their training in internationally renowned research groups which span the biomedical science disciplines of Biochemistry, Cellular and Molecular Medicine and Physiology, Pharmacology and Neuroscience through to the disciplines associated with population health which include life course epidemiology, genomics, primary care and public health with a particular emphasis on methodology. Research takes place in laboratories within the University and in clinical settings across Bristol, including the University Hospitals Bristol Trust, North Bristol Trust, as well as general practices and other community health services. For further details visit the Elizabeth Blackwell Institute (EBI).
Support for Data Science

The University's youngest research institute, the Jean Golding Institute for Data-intensive Research, runs a data science support service dubbed 'Ask JGI'. Which is available to all staff (and PhD students through their supervisors). It provides advice, support and guidance on all data science queries, including statistical, computing, data management, visualisation, and storage questions. Support is available via email and 1:1 meetings. The Institute works closely with 'data champions' throughout the University and can triage questions to experts and foster collaboration if they are unable to help directly. Staff can also signpost to other data intensive research facilities in the University such as on Advanced Computing (ACRC) and data storage (RDSF).

Get in touch via ask-jgi@bristol.ac.uk.

“Wearable” robotic tools for surgery

A collaborative team is to develop a wearable robotic system for minimally invasive surgery that will offer surgeons natural and dexterous movement as well as the ability to ‘sense’, ‘see’, control and safely navigate through the surgical environment. The €4m project, funded by the ERC, will be led by Prof Sanja Dogramadzi from the Bristol Robotics Laboratory, alongside 9 other partners. Minimally invasive surgery for some clinical applications is replacing the traditional ‘open access’ approach, and has been associated with patient benefits such as reduced blood loss, fewer infections and faster recovery. More advanced robotic systems have the potential to replace laparoscopic tools for keyhole surgery in several clinical areas if developed with integrated better vision, precision and ergonomic systems. Researchers will develop modern biomedical tools based on clinical feedback that mimic complex human dexterity and senses. These can be worn by the surgeon and transmit the surgeon’s own movements to the closed surgical interface without restrictions. This will reduce the overall cognitive, manipulation and training demand.

*Image: Exoskeleton prototype, © UWE Bristol*
Funding successes

Dr Rhys Morgan, £10,000 from the British Society for Haematology to perform pilot studies in Acute Myeloid Leukaemia.

Dr Karim Malik (PI), Dr Abdelkader Essafi and Dr Keith Brown (co-applicants), £84,940 from the Children’s Cancer and Leukaemia Group for In vitro modelling of MYCN-driven poor prognosis Wilms’ tumour for assessment of novel therapies, 1 Apr 2017 - 1 Aug 2018.

Dr Karim Malik (PI), Dr Abdelkader Essafi and Dr Abderrahmane Kaidi, £372,107 from the Biotechnology and Biological Sciences Research Council for Arginine methylation and its influence on transcription and genotoxic stress.

Miss Shelley Potter has been awarded an NIHR Clinician Scientist Award and will be returning to Bristol in July 2017. The award is a post-doctoral research training fellowship to support clinical academics to undertake training and develop specific skills relevant to their career in clinical and applied health research. Shelley has been granted funding for 5 years and as part of the fellowship her proposed projects include:

determining a core measurement set for reconstructive breast surgery; developing a microcosting framework for use in surgical trials and undertaking a pilot RCT in implant-based breast reconstruction.

Dr Emma Vincent has been awarded an RD Lawrence Fellowship from Diabetes UK for a project entitled The impact of cancer on people living with type 2 diabetes, £587,237.

Centre for Cancer Epidemiology

Profs Caroline Relton and George Davey Smith visited Mumbai to attend the Scientific Symposium Frontiers in Epidemiology. The event commemorated the inauguration of the Centre for Cancer Epidemiology (CCE), a new centre established by the Tata Memorial Centre. At the symposium, Caroline presented Whole epigenome and its role in understanding disease mechanisms, and George presented Mendelian randomization. As guest speakers, Caroline and George were invited to the opening of the new building where they each had a tree planted in their name.
Integrative Cancer Epidemiology Programme update

On 23 Nov 2016 the Integrative Cancer Epidemiology Programme (ICEP) hosted their first Annual Scientific Meeting showcasing some of their research. Session 1 dealt with Mendelian Randomization; Session 2 with Epigenetics and Metabolomics; Session 3 on Mechanistic Insights. Further details on the day are available on the event’s website.

This was followed by the second meeting of the Scientific Advisory and Review Board (SARB) where they reviewed the group’s progress against last year’s recommendations and discussed potential future scientific directions.

Overall the SARB said “progress has been outstanding across all work packages with a significant volume of work produced”. The SARB set out recommendations to be focussed on.

On 13 Jan 2017 the team working in the labs at Southmead Hospital hosted a second round of lab tours. Various supporters and fundraisers for Cancer Research UK visited the Learning and Research building to get an insight into how cancer is investigated. Jeff Holly and Claire Perks gave talks to the public.

Immunotherapy Clinical Primer

When the body detects cancer it sends CD8+ Tumour Infiltrating Lymphocytes (TILs) into the tumour to destroy it. However, once inside the tumour, TILs are suppressed often by molecules in the tumour that engage inhibitory receptors on the TILs – so that they fail to kill cancer cells. Targeting these inhibitory pathways so that the TILs can function again may lead to the design of new anti-cancer drugs.

Drugs that block two known co-inhibitory receptors, PD-1 and CTLA-4, show great promise in clinical trials. However, they only produce anti-tumour responses in a sub-group of patients and can be associated with severe side effects. Nonetheless, these trials suggest that immunotherapies can give better responses than some chemotherapy and radiotherapy treatments.

Thanks to an EBI Clinical Primer, Bristol graduate Grace Edmunds won a Wellcome Trust Fellowship to take such research forward. Grace is now 6 months into her PhD and has already contributed data for a paper produced by the Morgan lab, and produced a documentary on tumour immunology in her spare time which won a joint first prize at the Bristol Science Film Festival.

Grace Edmunds
ELIZABETH BLACKWELL FUNDING

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

**EBI Catalyst Fund**
Pump priming awards support the most promising and ambitious ideas across the widest interdisciplinary boundaries. They will be identified largely through the running of workshops to explore new possibilities and identify the big questions. 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 Research for Health challenge**
This scheme aims to encourage healthcare practitioners and University of Bristol researchers to work together to develop innovative thinking around clinical problems.

Closing date: 24 May 2017

**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

A calendar of potential funding opportunities for Cancer has been set up via Research Professional. Subscribing to a calendar will place the entries in your own calendar, which will update automatically according to pre-specified search criteria. Staff and students have FREE access to Research Professional online from all computers on the University network. You can create your own personalised funding opportunity e-mail alerts by registering with RP. Find out all about it on the RED website.

The listing below represents 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. Note that some calls may be subject to a major bids process; all details are on the website.

NIHR CLAHRC West
Training bursary scheme

Closing date: 1 Feb, 1 Jun & 1 Sep (annual)  
Award amount: £600

Gives staff from the local NHS, health and social care sector the opportunity to attend high quality research and evaluation training at half the price. Bursaries are available for 50 per cent of the course fees; the applicant or their employer is expected to fund the remaining 50 per cent. The bursary aims to promote wider engagement and improve skills in research and evidence in the CLAHRC West patch, particularly for those who have not previously had opportunities for this type of training.

You can apply for bursary support towards any course relevant to research and evaluation in health and social care. This includes study days, workshops and short courses (including individual modules) but not MSc or PhD tuition fees.

Laura Crane Youth Cancer Trust
Research funding

Closing date: none  
Award amount: unspecified

Supports research projects on cancer affecting teenagers and young people between the age of 13 and 24, which aim to bring increased understanding of cancer in this age group, improved treatments and save more lives. The funding amount is not fixed and is dependent on the research project.

Union for International Cancer Control
Rapid international transfer of cancer research knowledge and clinical technology fellowships
Facilitate rapid international transfer of cancer research and clinical technology by supporting investigators to visit another research centre for a month. Between 120 and 150 fellowships are available, which on average are worth USD 3,400 to cover travel and living costs.

**National Cancer Research Institute, GB**

**Conference prizes**

Closing date: 04-Jun-17  
Award amount: £1,000

For poster presentations at the National Cancer Research Institute Conference, 5 - November 2017 in Liverpool.

**Children with Cancer UK**

**Clinical PhD and training studentships**

Closing date: 20-Jun-17  
Award amount: not specified

Enable clinicians to study towards a PhD or MRes research foundation qualification in the field of childhood cancers, as well as taking their first steps on the path to becoming leaders in clinical research and education. PhD studentships are worth up to £250,000 for up to three years and MRes grants are worth up to £75,000 over one year.

**British Association for Cancer Research**

**British Association for Cancer Research/CRUK student travel awards**

Closing date: 30-Jun-17  
Award amount: £1,000

Enable student members to attend scientific meetings relevant to cancer research.

**Cancer Research UK**

**Multidisciplinary project award**

Closing date: 08-Aug-17 (deadline has been brought forward)  
Award amount: £500,000

Supports collaborations between cancer researchers and scientists from engineering and physical science disciplines. Projects may last for 4 years and funds cover salaries of postdocs, PhDs, technical staff, associated running expenses and equipment.

**Barn cancerfonden – Swedish Childhood Cancer Foundation**
Clinical project grants
Closing date: 11 Sep 17  
Award amount: unspecified

Support research projects of pronounced clinical character relevant for paediatric oncology including biology, epidemiology, registry research, diagnostics and treatment and nursing science including psychosocial research and preclinical, phase one and phase two studies. Grant covers monitoring costs, operating costs, equipment, publication costs, travel costs and salary costs for up to three years.

NIHR
Innovation challenge prizes – Wave 1: Cancer and Acorn challenges

Closing date: forecast 17-Sep-17  
Award amount: £150,000

Encourage, recognise and reward front line innovation, and drive spread and adoption of these innovations across the NHS. The following two challenges are available:

- cancer challenge, worth in total £100,000, recognises and awards initiatives that exemplify the modern patient pathway in cancer by demonstrating the following: an innovative and patient-focused approach to care that addresses a significant challenge in cancer management; an improvement in outcomes; providers, carers and commissioners collaborating effectively; a service that is affordable, sustainable and an efficient use of resources; strong potential to replicate across the NHS; clear delivery of the cancer strategy and the five-year forward view;
- acorn challenge, worth in total £50,000 of which up to £10,000 is available to each successful applicant, recognises and rewards small ideas that have the potential to make a big difference to patients, including new care pathways, services or technologies in any area.

Cancer and Polio Research Fund
Research grants

Closing date: 15 Oct 17  
Award amount: unspecified

Support research into cancers, with particular reference to the causes, development and treatment of these diseases, or research into polio and other crippling diseases. Grants may be used for direct costs of research and to support research symposia or lectures for the dissemination of findings.
Genome-wide DNA methylation analysis identifies MEGF10 as a novel epigenetically repressed candidate tumour suppressor gene in neuroblastoma


Figure: Genome-wide DNA methylation analysis of neuroblastoma. (A) Dendrogram using Pearson’s correlation coefficient, analysing all probe ratios from the MCIP/microarray analysis of human neural crest cells (hNCC) and four neuroblastoma cell lines (SK-N-AS, SHSY-5Y, IMR32, and BE(2)-C). MYCN amplification, ALK mutation, and neuroblastoma cell type are indicated next to the cell line names. (B) Venn diagram of overlap between lists of methylated genes having a probe ratio of greater than log2 0.5 found in hNCC, MYCN-amplified, and non-amplified cell lines. (C) Gene ontology profiles of the hNCC-unique methylated genes (hNCC), genes shared between hNCC and neuroblastoma cell lines (shared), and cell line-unique genes (NB).

Neuroblastoma is a childhood cancer in which many children still have poor outcomes, emphasising the need to better understand its pathogenesis. Despite recent genome-wide mutation analyses, many primary neuroblastomas do not contain recognizable driver mutations, implicating alternate molecular pathologies such as epigenetic alterations. To discover genes that become epigenetically deregulated during neuroblastoma tumorigenesis, we took the novel approach of comparing neuroblastomas to neural crest precursor cells, using genome-wide DNA methylation analysis. We identified 93 genes that were significantly differentially methylated of which 26 (28%) were hypermethylated and 67 (72%) were hypomethylated. Concentrating on hypermethylated genes to identify candidate tumor suppressor loci, we found the cell engulfment and adhesion factor gene MEGF10 to be epigenetically repressed by DNA hypermethylation or by H3K27/K9 methylation in neuroblastoma cell lines. MEGF10 showed significantly down-regulated expression in neuroblastoma tumor samples; furthermore patients with the lowest-expressing tumors had reduced relapse-free survival. Our functional studies showed that knock-down of MEGF10 expression in neuroblastoma cell lines promoted cell growth, consistent with MEGF10 acting as a clinically relevant, epigenetically deregulated neuroblastoma tumor suppressor gene.
The Cancer Theme is led by a Steering Group:

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

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

- Dr Sabine Hauert, Engineering Mathematics
- Dr Zoë Holland, RED Facilitator
- Prof Richard Martin, Professor of Clinical Epidemiology
- Prof Caroline Relton, Professor of Epigenetic Epidemiology
- Prof Ann Williams, Professor of Experimental Oncology
- Catherine Brown, Theme Administrator

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