Cancer Theme Newsletter

November - December 2016

University of BRISTOL
Elizabeth Blackwell Institute for Health Research

Research Paper of the Year in *Palliative Medicine*

Jeff Round's paper *Estimating the cost of caring for people with cancer at the end of life: A modelling study* was awarded 'Research Paper of the Year' in *Palliative Medicine (29;10: 899-907)* in June 2016. Jeff joined the Health Economics Bristol group in Dec 2015 from University College London.

Using a modelling based approach, the work tried to capture the costs to the NHS and society of caring for people during the terminal phase of illness. Of interest was the high proportion of costs borne by informal caregivers. The results were also notable for the degree of uncertainty in the data, arising from lack of data on people at the end of life and the challenges of defining the end of life period. Jeff has further contributed to the economics of end of life care with the publication in early 2016 of an edited book, *Care at the End of Life: An Economic Perspective*, containing contributions from leading researchers in this area.

Student Health Sciences Research journal

The *INSPIRE Student Health Sciences Research Journal* is produced by a team of student editors from Bristol, Exeter, Plymouth and Cardiff and plays a key part of a collaborative project under the national INSPIRE scheme funded by the Wellcome Trust and administered by the Academy of Medical Sciences.

The scheme aims to encourage student doctors, dentists and vets to consider a career in research, and encourages publication of their work. Since the scheme began in 2013 the south-west INSPIRE partnership has supported more than 70 vacation studentships as well as prize awards. Together with local matched funding, this has enabled students to undertake research projects under the supervision of senior scientists and clinicians. Following a competition in 2015, a team of seven senior editors came together to set up the journal from scratch in order to provide a platform for publication of student project results, as well as to have direct experience of academic peer review.

The first issue of the journal is available online.

Inside this issue:

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EVENTS

8th Annual 'Research, Audit & Quality Improvement' Day
18 November 2016, 9.00 - 17.00. Engineers' House, Clifton

Careers Beyond Biomedical Research: Publishing and Editing
23 November 2016, 13.00 - 14.00. Natasha Bray (Associate Editor, Nature Reviews), E29 Biomedical Sciences Building

Annual Scientific Meeting of the Integrative Cancer Epidemiology Programme
23 November 2016, 9:00 - 12:30. Oakfield House

Elizabeth Blackwell Institute Biomedical and Health Research Industry Day
24 November 2016, 9.00 - 16.00. Wills Memorial Building

Cabot Institute Annual Lecture 2016: Ideas to change the world
25 November 2016, 18.00 - 19.45. Prof Tom Scott (Transforming our energy), Dr Eric Morgan (Resilient and sustainable livestock), Prof Keri Facer (Connected Communities), Great Hall, Wills Memorial Building

Modulation of alternative splicing as a novel therapeutic avenue in cancer
29 November 2016, 13.00 - 14.00. Dr Sebastian Oltean (UoB), C42 Biomedical Sciences Building

University Hospitals Bristol Research Showcase
30 November 2016, 9.30 - 15.30. Lecture Theatre 1, UH Bristol Education and Research Centre

Careers Beyond Biomedical Research: Clinical Research
30 November 2016, 13.00 - 14.00. Jason Parker (Senior Director of Technology, Quintiles) and Louise Peverley (Clinical Research Associate, PPD Winchester), E29 Biomedical Sciences Building

Statistics Clinic - 30 November 2016
30 November 2016, 14.00 - 15.30. SM3 Mathematics

Bristol Conversations in Education - Using computers to teach statistics to reluctant researchers
30 November 2016, 13.00 - 14.00. Prof William Browne, room 4.10, 35 Berkeley Square

Early Career Researchers' event / Annual Symposium and Stephen Frankel Lecture 2016: hosted by Population Health

From top: Natasha Bray, Keri Facer, Sebastian Oltean, Louise Peverley

From top: Dr Gonçalo Bernardes, Dr Alan Parker, Prof Ricjhard Vile

1 December 2016, 8.45 - 18.30. Engineers' House, Clifton Down

Vascular Biology: Past, present and future
2 December 2016, 9.00 - 18.00. Wills Hall

Chemical Pharmacology of Protein Conjugates and Natural Products
5 December 2016, 10.00 - 11.00. Dr Gonçalo Bernardes (University of Cambridge), LT3 Chemistry Building

GW4 Cancer Immunology at Christmas
5 December 2016, 16.30 - 18.30. Approved by the Royal Society of Biology, may be counted as 3 CPD credits. Dr Alan Parker (Cancer and Genetics, Cardiff University): *How to train your oncolytic adenovirus*; Prof Richard Vile (Mayo Clinic): *Development of experimental cancer therapies based on stimulating antitumor immune responses*. Sponsored by the British Society for Immunology and Cardiff University Division of Cancer and Genetics.

Statistics Clinic - 14 December 2016
14 December 2016, 14.00 - 15.30. SM3 Mathematics

Cancer Research UK Early Diagnosis Research Conference
23 February 2017, 9.30 - 17.30. Radisson Blu Portman Hotel, London

Excellence in Medicine Day
24 February 2017, 10.00 - 16.30. Wills Memorial Hall

Third International Symposium on Immunotherapy
12 May 2017, 9.00 - 17.00. The Royal Society, London

ICVI Institute for Cancer Vaccines & Immunotherapy
Changing Lives Through Research

NEWS

ProtecT publishes first results

The largest UK trial of treatment for prostate cancer, ProtecT has ascertained that active monitoring is as effective as surgery and radiotherapy for the disease, in terms of survival at 10 years. Results show that all three treatments result in similar, and very low, rates of death from prostate cancer. Surgery and radiotherapy reduce the risk of cancer progression over time compared with active monitoring, but cause more unpleasant side-effects. This is the first trial to evaluate the effectiveness, cost-effectiveness and acceptability of three major treatment options: active monitoring, surgery (radical prostatectomy) and radiotherapy for men with localised prostate cancer.

The team measured mortality rates at 10 years, cancer progression and spread, and the impact of treatments reported by men. They found that survival from localised prostate cancer was extremely high, at approximately 99 per cent, irrespective of the treatment assigned. The rate of cancer progression and spread was reduced by more than half in men in the surgery and radiotherapy groups, compared with active monitoring; cancer progression occurred in one in five in the active monitoring group, as opposed to less than one in 10 in the surgery and radiotherapy groups. However, surgery and radiotherapy caused unpleasant side-effects, particularly in the first year after treatment.

More info...

Bio-ink for 3D Printing with Stem Cells

A new stem cell-containing bio-ink allows 3D printing of living tissue. The ink contains two different polymer components: a natural polymer extracted from seaweed, and a sacrificial synthetic polymer used in the medical industry. The latter causes the bio-ink to change from liquid to solid when under raised temperatures; the former provides structural support when cell nutrients are introduced.

Lead researcher Dr Adam Perriman explained the challenges in designing the bio-ink, which went through several iterations before being finalised:

You need a material that is printable, strong enough to maintain its shape when immersed in nutrients, and that is not harmful to the cells. The special bio-ink formulation was extruded from a retrofitted benchtop 3D printer, as a liquid that transformed to a gel at 37°C, which allowed construction of complex living 3D architectures.

The team were able to differentiate the stem cells into osteoblasts and chondrocytes to engineer 3D printed tissue structures over five weeks, including a full-size tracheal cartilage ring.

What was really astonishing was when the cell nutrients were introduced, the synthetic polymer was completely expelled from the 3D structure, leaving only the stem cells and the natural seaweed polymer. This, in turn, created microscopic pores in the structure, which provided more effective nutrient access for the stem cells.

Armstrong JP *et al.* (2016). 3D Bioprinting Using a Templated Porous Bioink. *Advanced Healthcare Materials*. Published online 22 June 2016.

NIHR Biomedical Research success

University Hospitals Bristol NHS Foundation Trust, in partnership with the University of Bristol, has been awarded £21.8M over five years by the National Institute for Health Research (NIHR) to fund cutting-edge research. The Biomedical Research Centre (BRC) will come into being in April 2017 and will allow the two existing Biomedical Research Units (BRUs) to continue the world class research they have been carrying out in the areas of Cardiovascular Disease and Nutrition, Diet and Lifestyle. Alongside this UH Bristol have been funded in three new themes – Surgical Innovation, Mental Health and Perinatal and Reproductive Medicine. The partnership is one of 20 NHS and university partnerships across England to have been awarded funding; each BRC will host the development of new, ground-breaking treatments, diagnostics, prevention and care for patients in a wide range of diseases like cancer and dementia.

Immune cells remember first meal

Whilst an inflammatory response is beneficial for human health, many human diseases (including atherosclerosis, cancer and arthritis) are caused or aggravated by an overzealous immune response. A greater understanding of what activates the immune response will help design novel therapies to treat these inflammatory disorders.

A study lead by Dr Helen Weavers found that immune cells must first become activated by eating a dying neighbouring cell before they are able to respond to wounds or infection. In this way, immune cells build a molecular memory of this meal, which shapes their inflammatory behaviour. The team dissected the mechanism by which the memory is generated and found that ingestion of the dying cell activates signalling via a calcium flash, which leads to an increase in the amount of damage receptor Draper. High levels of this receptor enable the primed immune cell to sense the damage signals that entice them towards a wound during inflammation. Without this priming, the cells are blind.

Understanding how one signal (in this case a dying cell) can influence the ability of an immune cell to respond to a subsequent signal is a major step towards finding novel ways to clinically manipulate immune cells away from sites of the body where they are causing the most damage.

Weavers H *et al.* (2016). Corpse Engulfment Generates a Molecular Memory that Primes the Macrophage Inflammatory Response. *Cell.* 165(7), pp1658-1671

High Blood Pressure Study Requires Volunteers in the 35-60 year age range

What is this study?

This is a study investigating whether brain blood flow autoregulation is preserved in hypertension. The study involves ~1 hour of screening at CRiC Bristol and ~2 hours on a Thursday afternoon at the Bristol Heart Institute for an MRI scan of the head and chest during lower body negative pressure.

Contact?

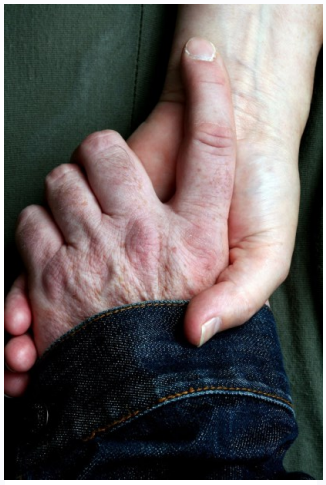
If you are think you might be eligible, please contact Sandra Neumann (t: 0117 342 1503) for more information.

Health Research Strategy Committee

Professor Iredale, Pro Vice-Chancellor for Health, has created a new Health Research Strategy Committee with broad membership across the Faculties of Health and Biomedical Sciences including Deans, Faculty Research Directors, Heads of Schools and the Elizabeth Blackwell Institute. The committee will be chaired by the new Director of Research for Health, Professor Jeremy Tavaré (pictured right). The Committee will debate and develop a unified health research and innovation strategy across the two faculties and take an overview of its delivery by the Faculties and Schools with support from the Research and Enterprise Development team.

A Picture of Health - illustrate your research

Researchers across UoB are invited to share images of their health research inspired by a series of six themes: growing up and growing older; conflict; care and caring; consumption; green; wellbeing. The best images will be displayed in weekly themed collages on Picture of Health from Jan 2017. Free 1hr workshops on Smartphone Photography will be held on 3 and 8 Nov 2016, 12:00-13:00. Deadline for submissions is 2 December 2016.



NIHR Doctoral Research Fellowship

An NIHR Doctoral Research Fellowship has been awarded Dr Anna Bibby (pictured left) with Profs Nick Maskell and Rachael Gooberman-Hill as co-supervisors. The amount of £418,414 will go towards *Treating mesothelioma with Intra-pleuraLbacterial immunoTherapy (the TILT Trial): A feasibility study using the 'Trial within a Cohort' methodology*. The study will explore intra-pleural immunotherapy using the streptococcal preparation OK-432 in patients with mesothelioma; it will use an innovative and highly pragmatic methodology called the 'Trial Within a Cohort' or 'TWIC' design and will include embedded qualitative interviews with participants to explore their experiences of participating in the trial.

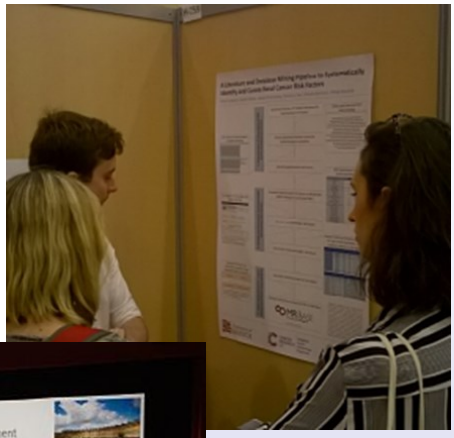
Society of Endocrinology Early Career grant

Awarded to Dr Felicity Stubbs (pictured right), this £10,000 early career grant will go towards *The role of glucocorticoids on P53 dependent cell-cycle control.* Synthetic glucocorticoids are widely used clinically due to their potent anti-inflammatory properties. Glucocorticoids are known to promote cell cycle arrest through the P53 pathway. However there have been suggestions of another essential key 'player' which could mediate this mechanism by directly interacting with the glucocorticoid receptor (GR) and P53. The team will be performing co-immune-precipitation studies, proteomics and flow cytometry cell cycle analysis to determine whether this key 'player' is ARID1a, a chromatin remodelling complex protein commonly mutated in a variety of cancer types, shown to regulate cell cycle arrest, and reported to directly interact with GR and P53.

ICEP at IACR

Thirteen members of the Integrative Cancer Epidemiology Programme (ICEP) attended the International Agency for Research on Cancer (IARC) conference held 8-10 June 2016 in Lyon. Topics ranged from the global burden of cancer; challenges in primary prevention; the roles of tobacco, alcohol, nutrition, obesity and exercise in cancer; DNA damage, repair and mutagenesis; attributable risks; and genetics and epigenomics.

Of those attending, Caroline Bull, Dr Rebecca Richmond, Dr Vanessa Tan and Ryan Langdon had posters illustrating their work on lipids, epigenetics, recall by genotype analyses and an automated pipeline for harmonising data of the hypothesised risk factors for cancer. Dr Sarah Lewis presented within the Mechanisms of Carcinogen Evaluation session on *linking diet, nutrition and physical activity to cancer: a systematic review framework for integrating evidence from human, animal and other mechanistic studies.* Within the Bioinformatics session, Dr Kaitlin Wade showcased *MR-Base: an online platform for Mendelian randomization using summary data* and on the final day, Prof George Davey Smith discussed *causality and chance in the origins of cancer.*



Cancer Research UK lab tours June 2016

Cancer Research UK fundraisers and supporters visited the Learning and Research building at Southmead Hospital in June to explore the laboratories investigating cancer. The visitors were welcomed by Alexa Bishop (CRUK's Research Engagement Manager) who introduced the event and explained how fundraisers' money was used to support the research carried out and introduced the Integrative Cancer Epidemiology Programme (ICEP). Prof Jeff Holly and Dr Claire Perks then presented on how cancer occurs, develops and interacts in the body. Images, videos and slides were used to help explain to the public what research is being carried out in the labs and how this new knowledge can be used to help understand and prevent cancer.

This led onto the lab tours where the public were split up into four groups wearing colour-coded lab coats and rotated around four work stations to see and interact with the research in the laboratories:

- How do we capture migrating cancer cells and investigate them in the lab?
- Measuring biomarkers: Pipetting challenge!
- Visualising cancer using imaging techniques
- Lab techniques for protein analysis: understanding the building blocks of cancer

EBI / Wellcome Trust Fellowship Success

Tom Dudding of the School of Oral and Dental Sciences has been awarded a prestigious Wellcome Trust Clinical Research Training Fellowship for *Reassessing the association between vitamin D and head & neck cancer risk and progression.*

These Fellowships allow clinicians the opportunity to undertake funded full-time PhD research, with structured training and mentorship, while maintaining their clinical practice

Tom's research will use innovative epidemiological techniques to clarify the recently identified link between vitamin D and risk and progression of head & neck cancer, and to identify intermediates that have the potential to be future therapeutic targets. He will be working with the MRC Integrative Epidemiology Unit and the CRUK Integrative Cancer Epidemiology Programme under supervisors Profs Richard Martin and Steve Thomas, Dr Nic Timpson & Dr Paul Brennan from the International Agency for Research on Cancer (Lyon). As well as formal training in epidemiology, the award will allow Tom to attend international courses and conferences, and spend time at the IARC in Lyon.

Double honours for Zoe Winters

Breast cancer Consultant Surgeon Zoe Winters has been formally appointed to the Board of Directors at the International Society for Quality of Life Research (ISOQOL). This is a great honour and endorsement of Zoe's work in the field and internationally.

Zoe has also been nominated to the medical selection committee for the Foundation for the Nordic Prize in Medicine due to her expertise in breast cancer research. This annual prize, which comes with SEK 1M (approx. £100k), will this year be split between

awards for prostate cancer research and breast cancer research. The expert reviewers will evaluate the nominations and suggest Prize winner (s) to the Board of the Research Foundation, as a basis for the decision by the Board.

Award to study brain tumour biology

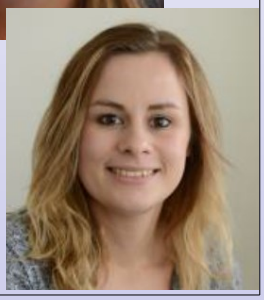
The Pathological Society of Great Britain and Ireland has awarded a £9989 small grant to Dr Harry Haynes for *shRNA mediated PPARa knock down in a xenograft model of human glioblastoma*. Harry is a PhD student and Clinical Research Fellow with the Brain Tumour Research Group under supervisor Dr Kathreena Kurian. This award is an adjunct to his PhD funding which will enable collaboration with colleagues at the University of Leeds. It is hoped that this work will lead to further elucidation of the key roles of the PPAR transcription factors in brain tumour biology.

Liverpool collaborations

Profs Caroline Relton, Richard Martin and Steve Thomas visited the North West Cancer Research Centre at the University of Liverpool for some interesting discussions with a group of Head & Neck cancer specialists. Richard and Caroline also presented a seminar entitled Integrative Cancer Epidemiology: Using (epi)genomic data in cancer prediction, prevention & prognosis.

CRUK Award

Drs Suzi Gage (above right) and Becky Richmond (below right) have been awarded £171,478.95 from Cancer Research UK to investigate *DNA methylation in e-cigarette users versus cigarette smokers and never-smokers*.



NCRI Cancer Conference presentation

Dr Luke Robles and Ellie Shingler presented a poster at the above event, which showcases the latest basic, translational and clinical cancer research, between 6-9 November 2016 in Liverpool.

The PrEvENT Feasibility Trial - Results of the Qualitative Feasibility Analysis

Abstract:
With a growing body of evidence identifying diet and low physical activity as risk factors for prostate cancer development and progression, the Prostate Cancer: Evidence of Exercise and Nutrition Feasibility Trial (PrEvENT) aimed to assess a physical activity and nutrition based intervention in men undergoing radical prostatectomy.

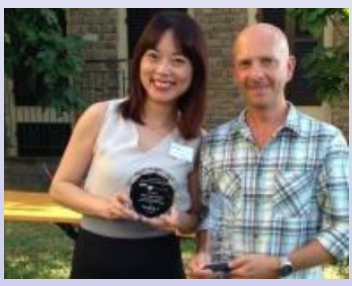
This qualitative analysis provides insight into the opinions and experiences of the acceptability of the PrEvENT nutrition and physical activity intervention from the participants themselves. It outlines that the interventions delivered were acceptable to this sample of participants, as were the data collection methods utilised. It has also highlighted some considerations to be taken into account for the design of further behavioural change interventions in this population group.

More than just a Biobank

The Bristol Biobank doesn't just provide access to samples; they can also provide lab support to help you run research via their dedicated lab technician, who can process samples prior to storage or shipment. You can also apply to run your research projects under their generic REC approval, ensuring all the relevant governance and ethics issues are taken care of. In addition to Biobanking they also have a short term storage facility for samples not under an REC approval.

If you would like to hear more about any of these options please contact bristol-biobank@bristol.ac.uk

Ingram Olkin Award



Presented to Prof Julian Higgins by the Society for Research Synthesis Methodology, the award recognises his important contributions to Cochrane. The Ingram Olkin Award recognises an individual who has made distinguished lifetime achievement in research synthesis methodology, and represents the highest honour bestowed by the Society.

Adjuvant treatment changes for pancreatic patients

The European-wide Espac 4 Trial for pancreatic cancer began in 2009 and is being carried out at the Bristol Haematology and Oncology Centre. The trial is looking to see whether the addition of capecitabine to the standard post-surgical chemotherapy regime of gemcitabine alone improves survival. Pancreatic cancer can be split into two types: ductal and the rarer periampullary. The primary outcome has been published and has shown very good results. This is the type of data that prompts a change in clinical practice with the promise that the patient group will now be able to benefit from the increased survival rate this new regime can give. The patient long term survival could be increased from 16% to 29%.

Read more on the BBC news website.

Soft robotics for throat surgery

Surgical removal of the voice box is a potentially life-saving treatment for thousands of laryngeal cancer patients It is also a mutilating procedure, which means that patients may no longer be able to speak, swallow or cough. In addition to the direct cost of the procedure and significant follow up costs, there is a large social and personal cost to both the patient and their family. The procedure often renders the patient with a permanent stoma in their neck, little or no voice and a severely impaired sense of taste and smell, as well as putting them at much greater risk of airway blockage from food and drink that may enter the trachea. Patients are currently unlikely to return to both work and society, with a consequent negative impact on patient quality of life and increase in social costs.

Prof Jonathan Rossiter (top right) and Dr Andrew Conn (bottom right) used their Elizabeth Blackwell Institute Knowledge Transfer award to investigate new ways to overcome these severe surgical effects. Together with colleagues from UCL they developed new robotics technologies designed to work seamlessly with the human body.

The team developed an artificial respiration system that simulated breathing with different physiological parameters. This allowed them to prototype robotic larynx replacements and analyse their performance. The newly designed device offers a way to restore important functional capabilities of the larynx and to avoid the implantation of conventional, uncomfortable and ill-fitting alternatives.

Read more...

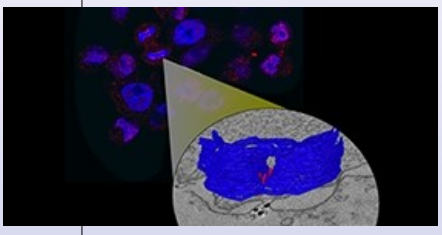
European Research Council funding

Following the result of the referendum on 23 June 2016, the International Team in Research Development wish to confirm that there will be no immediate impact with regards to Horizon 2020 funding. All existing grants will continue to run as normal and anything currently under submission or in the granting process will also continue as normal. The UK will continue to be an EU member state for two more years at least and during this time we will be eligible to apply to each and every call under Horizon 2020.

If the UK does withdraw from the EU there is the possibility of negotiating associated status to H2020, like Norway and Israel. Universities UK will be leading discussions around this with the government, and Bristol will be fully engaged with this process as well as via the Russell Group. If no agreement can be reached then this would likely mean the UK could no longer access H2020 funding but this would not come into effect until October 2018 at the earliest, based on current predictions.

In summary, in the short term it is very much business as usual and we would encourage everyone to continue to apply. If anyone has any concerns contact the EU and overseas team.

Microscopy facilities opened



A new purpose-built microscopy suite to accommodate expansion of the Wolfson Bioimaging Facility was officially opened by Paul Ramsbottom, Chief Executive of the Wolfson Foundation, on 8 July 2016. Currently housing 22 imaging systems covering a broad range of advanced fluorescence and electron microscopy techniques, the Facility has a growing reputation within the UK and across Europe. The arrival of new systems including multiphoton, super-resolution and fluorescence lifetime imaging alongside expansion of confocal and widefield microscopy meant that the expanded facility could no longer be housed within existing space.

A donation of £1M by the Wolfson Foundation was vital in helping to create six purpose-built microscope rooms to accommodate new equipment. The new imaging suite is situated adjacent to existing microscope rooms and provides the controlled and stable environment required for high-resolution microscopy. The facility has also recently increased the level of support it offers for image processing and analysis to equip its users with the expertise to fully quantify and interpret microscopy data.

Details of the facilities are available on the website.

Add-Aspirin study hits recruitment targets

Add-Aspirin is a large randomised clinical trial taking place in the UK and India. It will recruit 11,000 participants to help find out whether regular aspirin use after treatment for an early stage cancer can prevent the cancer from coming back and preventing deaths. The Bristol Haematology and Oncology Centre is the second highest recruiting centre out of 147 sites, and third highest in terms of data return which is currently 98%. Verity Henson from the Bristol Cancer Institute is leading the study and has shared some recruitment hints and tips:

Having a good screening process has been the most effective way to identify eligible participants. We approach participants and give them information a month or so before they are due to complete treatment or after cycle 2 of their chemotherapy. We also screen potential participants at routine appointments to avoid participants having too many extra hospital visits. It helps to be approachable, enthusiastic and knowledgeable about the study!

Find a clinical research study app

The Clinical Research Network Business Intelligence team has launched a new version of the public Open Data Platform *Find a Clinical Research Study* app.

The purpose of this app is to provide a tool for clinical research professionals to search for CRN Portfolio studies using specific parameters, such as specialty or study design. The search results then enable the user to view a publicly available, one-page summary of information about each study. The app can be downloaded online.

The UK Clinical Trials Gateway remains the chosen NIHR platform for providing patients and the public with information about clinical research studies taking place in the UK.

In the new *Find a Clinical Research Study* app, you can search by:

- CPMS Study ID, IRAS ID, MRec, EUdraCT
- Study title or short name
- Research summary or inclusion/exclusion criteria keywords

Other search values include:

- Study design
- Open to new sites
- Eligibility
- Study Status
- Phase
- Specialties/sub specialties

The major difference between *Find a Study* v2 and its predecessor is that this version no longer features a "map search" function. This will be re-established at a later date, with other enhancements where appropriate.

If you have any questions or suggestions concerning the new app, contact ODP@nihr.ac.uk

University Cancer Research Fund

Each year this fund seeks out the most innovative ideas in cancer research by funding projects and ideas in their early stages that have the promise to develop into high impact research. One such project funded in the 2016 call went to Dr Jason Johnson for *MicroRNA-20a retards angiogenesis and prostate cancer progression.* The £4900 award will support the project for one year (Sep '16-Sep '17).

Engineering the future of cancer treatment

The EBI Catalyst Fund provides pump priming for the most promising and ambitious ideas across the widest interdisciplinary boundaries. One such award was granted to Dr Sabine Hauert from Engineering Mathematics for *Microfluidic testbed for the fast prototyping of nanoparticle distributions in tumour-like environments*.

One of the many new developments in cancer research comes from nanoscience; bioengineers are designing nanoparticles that can deliver treatments and diagnostics directly to tumours, raising the prospect of much more precise and effective interventions. However, the behaviour of each nanoparticle varies depending on size, shape, coating and cargo, etc. and on the interactions in the body that result. And when trillions of such nanoparticles are involved in each case, their collective behaviour in the complex environment of a tumour is crucial to the success of the treatment. But that behaviour can be difficult to predict.

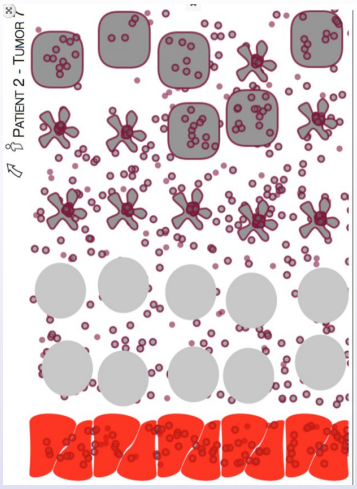


Image © Sabine Hauert

For example, nanoparticles can be engineered to accumulate specifically in cancer cells, but may only accumulate in the first cells they encounter rather than penetrating further into the tumour. Similarly, particles delivered via convection-enhanced delivery (CED) may not accumulate in the right concentrations throughout the tumour to be effective. One of the biggest challenges is to find an accurate way to visualise the behaviour of nanoparticles, since neither *in vitro* nor *in vivo* experiments provide enough detail.

One possible solution emerged at a workshop hosted by the Elizabeth Blackwell Institute, which considered clinical applications for nanomedicine, exploring the design and testing of micro-nano systems, and discussing future opportunities in swarm engineering. This resulted in a proposal for a cross-disciplinary project bringing her together with Drs Andy Collins and Adam Perriman (UoB) and Mr Barua and Dr Bienemann (Southmead).

First they developed a preliminary computational model that would predict tissue penetration in brain tumours depending on variables such as nanoparticle injection speed, drainage, and binding properties. They also built up a small library of fluorescent nanoparticles, each with well-defined properties and designs, for use on their newly designed microfluidic testbed. Using gelatin to simulate the tissue-like environment, they were able to monitor the distribution of nanoparticles under a microscope, and to capture it on high-definition video. Preliminary experiments were also performed *in vivo* (rat brain) using quantum dots and pluronic micelle nanocarriers. Results showed the clear impact of nanoparticle charge on their anchoring in the brain tissue.

Read more...

Free law clinics for young cancer patients

Working in partnership with CLIC Sargent, the UK's leading cancer charity for children and young people, University of Bristol Law Clinic students will help parents of children living with cancer negotiate some of the legal obstacles that come with the diagnosis.

To do this, the partnership has established regular Law Clinic drop in sessions for families of children living with the disease at Sam's House, one of CLIC Sargent's Home from Homes accommodation for families and young people, while they have treatment at Bristol Royal Hospital for Children (BRHC). The move follows research from CLIC Sargent's recent *Cancer Costs* campaign, which found that, on average, families of a child undergoing active cancer treatment spends an extra £600 a month. This financial impact of cancer can be devastating. For parents of children living with cancer, understanding their legal position can help alleviate some of the pressure that comes with the diagnosis.

Through regular drop in sessions, Law Clinic students will provide parents with advice on topics such as rights for benefits for carers, disability living allowance for children and more. Sessions began on 6 October 2016. The project is supported by CLIC Sargent social workers, who provide practical and emotional support to children, young people and their families. Their services include financial support, grants, benefit information and a wide range of information on cancer and its impact.

Read more...

Cancer Research Paper of the Year

The publication of a study led by Dr Matthew Ridd, Consultant Senior Lecturer in Primary Health Care, is one of the winners of the Royal College of General Practitioners (RCGP) Research Paper of the Year 2015. The award gives recognition to an individual or group of researchers who have undertaken and published an exceptional piece of research relating to general practice or primary care. Now in its 20th year, winners of each category were invited to present at the RCGP Annual Conference held in October 2016 in Harrogate. Matthew won for Category 1: Cancer, Patient-doctor continuity and diagnosis of cancer: electronic medical records study in general practice (Published 1 May 2015).

£7.5M boost for Health Research

University of BRISTOL
Elizabeth Blackwell Institute for Health Research

The Elizabeth Blackwell Institute (EBI) has been awarded the Wellcome Trust's Institutional Strategic Support Fund (ISSF), designed to support biomedical research and related activities in the UK over the next five years. The ISSF award of £3.75M is being matched by the University. It is the third and largest ISSF award for the EBI and recognises the successful work the Institute has delivered during the previous five years.

The Institute will continue to invest in supporting the next generation of health research leaders by offering fellowships and support for clinical and non-clinical early career researchers. Clinical researchers in particular will benefit from opportunities offered by the EBI and the recently announced Wellcome Trust-funded clinical PhD programme for the South West.

The Institute will also prioritise work on diversity and inclusion, as well as public engagement with focus on building capacity, creating and developing partnerships to co-design and increase the impact of the University's research.

Treatment of stomach infections

A team from the Technical University of Munich, University of Duisburg-Essen at Essen University Medical Centre and UoB have discovered a new approach to infections related to *Helicobacter pylori*. Infections of *H. pylori* commonly occur during childhood, colonising the human stomach; once obtained the bacterium stays in the stomach throughout life and is associated with an increased risk of stomach cancer, gastritis and duodenal ulcers. It can be fatal unless treated with particular antibiotics. Antibiotics, however, kill all of the gut's flora and there is increasing resistance to them.

The team found that *H. pylori* attach to the epithelial cells in the gastric mucosa and they detected a highly specific and exceptionally strong variant of this adhesion, in which the bacterial surface molecule, HopQ, binds to the Carcinoembryonic Antigen-related Cell Adhesion Molecules (CEACAM) inside the stomach. In contrast to previously known binding partners, this bond is independent of sugar structures. They found that this ensures that it is stable in the acidic environment of the stomach. CEACAMs are not produced in healthy stomach tissue, but primarily when there is an inflammation of the gastric mucosa caused by the *H. pylori* infection. The adhesion of the bacterium to stomach cells could be prevented with a soluble version of HopQ or parts of the protein, and the damaging effects of the germ could potentially be suppressed.

Read the paper in *Nature Microbiology*.

ELIZABETH BLACKWELL INSTITUTE 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.

Clinical Primer Scheme

This scheme is aimed at is aimed at exceptionally motivated clinically qualified medical and veterinary trainees who are at an early stage of their career and is designed to give them the chance to experience a world-class research environment for the first time. Applicants must either be fully-qualified medical doctors and will have started, or be ready to start, their specialist training OR have completed a degree in veterinary medicine or veterinary science; an intercalated degree or other research experience (e.g. undergraduate vacation project) is also desirable. All applicants should be entitled to work within the European Economic Area (EEA).

Deadline for applications is 15 December 2016.

GW4 - Clinical Academic Training programme

The Wellcome Trust-funded GW4 Clinical Academic Training programme (GW4-CAT) is a new scheme that brings together the Universities of Bristol, Cardiff and Exeter in developing the next generation of clinical academics. Within the programme, exceptional early career medical, veterinary and dental graduates will have the chance to undertake an interdisciplinary PhD training in one of over 50 world-leading research groups in population health, cardiovascular sciences, neuroscience, mental health, infection, immunity & repair, cancer or molecular cell biology.

Deadline for applications is 25 November 2016.

University of BRISTOL

Elizabeth Blackwell Institute for Health Research

FUNDING OPPORTUNITIES IN CANCER

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.

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.

Department of Health including NIHR
Health services and delivery research programme – researcher-led workstream: 16/116, 16/115

Closing date: 12-Jan-17 Award amount: unspecified

This programme supports research into the quality, appropriateness, effectiveness, equity and patient experience of health services. NIHR will fund HEIs at a maximum of 80 per cent of full economic costs, except for equipment worth over £50,000, and non-HEIs at 100 per cent of full economic costs. The workstream has a continued interest in the following research areas: dementia; surgical and implantable devices; primary care interventions; very rare diseases; antimicrobial resistance; long-term

conditions in children; applied research into mesothelioma; multimorbidities in older people; prevention and treatment of obesity.

Union for International Cancer Control
Yamagiwa-Yoshida memorial international study grants

Closing date: 15-Jan-17 Award amount: US$10,000

Enable cancer investigators from any country to carry out bilateral research projects abroad that exploit complementary materials or skills, including advanced training in experimental methods and special techniques. Between 14 and 16 grants are available yearly and support a maximum study period of three months.

European Society of Surgical Oncology
Methods in clinical cancer research workshop educational grants

Closing Date: 08 Feb 17 Award amount: unspecified

Support young oncology surgeons in attending a workshop on methods in clinical cancer research in Zeist in the Netherlands from 17 to 23 June 2017. The one-week intensive residential training offers the opportunity to learn the essentials of clinical trials and network with clinical oncologists from across the globe. Junior clinical oncologists in any clinical research speciality area may apply. Five grants are available to cover 60 per cent of the participation costs.

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

Closing date: 28 Feb 17 Award amount: £1000

Enable student members to attend scientific meetings relevant to cancer research. Awards are worth up to £1,000 for overseas meetings and up to £500 for meetings in the UK, and may be used towards economy class travel, registration fees and accommodation.

British Association for Cancer Research
Mid-career fellowships

Closing Date: 28 Feb 17 Award amount: £3,000

Enable fellows to visit a laboratory in order to advance an ongoing programme or facilitate a collaboration that may lead to new programmes of work. Applicants must have 15 years continuous BACR membership, and be over 40 years old.

Cancer Research UK
Pontecorvo prize for best PhD thesis

Closing date: 31 Mar 17 Award amount: £500

Awarded to a CRUK funded student who has produced the best PhD thesis and made the most outstanding contribution to scientific knowledge in their field of research, leading to publications in major peer reviewed journals. The prize is worth £500, and includes a free place at the following National Cancer Research Institute conference.

Royal Society of Medicine
Oncology Sylvia Lawler prize

Closing Date: 14-Apr-17 Award amount: £250

Recognises the best clinical papers or poster presentations based on a clinical or basic scientific research project. Clinical research may include audit data, imaging studies and outcomes of surgical procedures. Translational studies such as genomic studies of clinical samples should be submitted for the basic or translational science prize.

Barncancerfonden – 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.

FEATURED PUBLICATION

Insulin Receptor Isoform Variations in Prostate Cancer Cells

CM Perks, HA Zielinska, J Wang, C Jarrett, A Frankow, MR Ladomery, A Bahl, A Rhodes, J Oxley and JMP Holly. *Frontiers in Endocrinology*: Cancer Endichronology, 28 September 2016.

Men who develop prostate cancer (PCa) increasingly have one of the co-morbidities associated with a Western lifestyle that are characterized by hyperinsulinemia, hyperglycemia and increased expression of insulin-like growth factors-I (IGF-I) and IGF-II. Each have been associated with poor prognosis and more aggressive cancers that exhibit increased metabolism and increased glucose uptake. The insulin receptor (IR) has two splice isoforms IR-A and IR-B: IR-A has a higher affinity for IGF-II comparable to that for insulin, whereas the IR-B isoform predominantly just binds to insulin. In this study, we assessed alterations in the IR-A and IR-B isoform ratio and associated changes in cell proliferation and migration of PCa cell lines following exposure to altered concentrations of glucose and treatment with IGF-II and insulin. We observed that where IR-B predominated insulin had a greater effect on migration than IGF-II and IGF-II was more effective when IR-A was the main isoform. With regard to proliferation IGF-II was more effective than insulin regardless of which isoform was dominant. We assessed the abundance of the IR isoforms both in vivo and in vitro and observed that the majority of the tissue samples and cell lines expressed more IR-A than IR-B. Alterations in the isoforms in response to changes in their hormonal milieu could have a profound impact on how malignant cells behave and play a role in promoting carcinogenesis. A greater understanding of the mechanisms underlying changes in alternative splicing of the IR may provide additional targets for future cancer therapies.

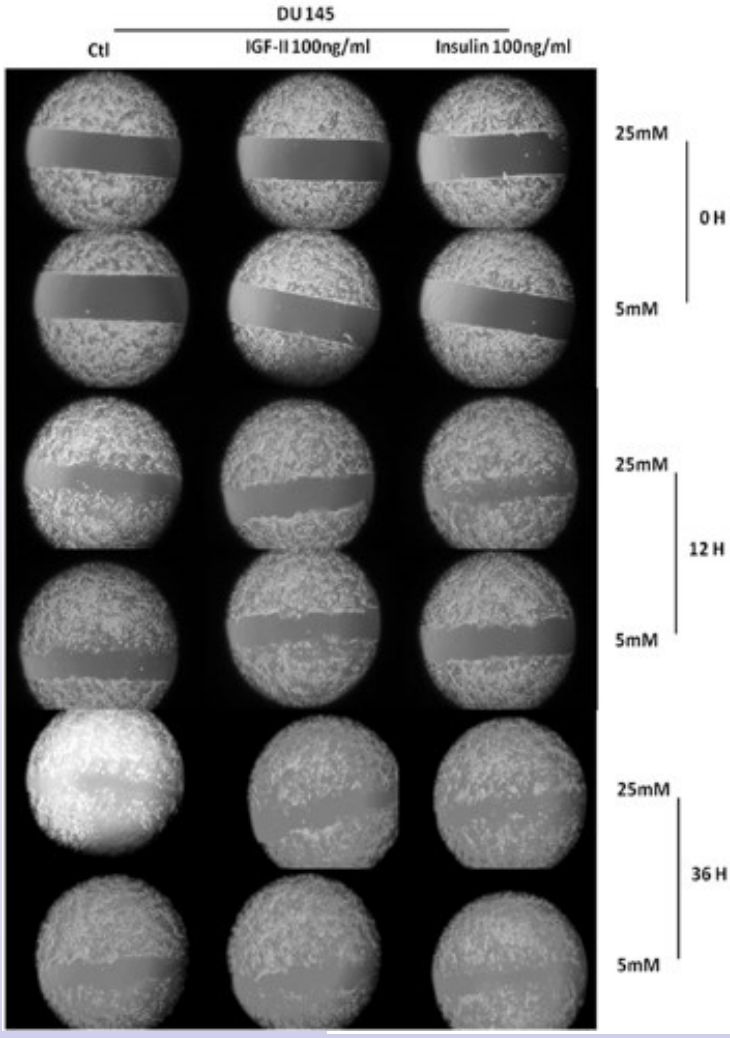


Image caption: DU145 cells were seeded into culture-inserts in 6 well plates in 5 mM GM. After 24 h, cells were treated with either 100 ng/ml IGF-II or insulin in either 25 mM or 5 mM-glucose containing SFM. Pictures were taken at time 0, 12, and 36 h. These are representative of experiments repeated three times.

Cancer Theme

University of BRISTOL

Elizabeth Blackwell Institute for Health Research

Theme Co-Lead:

Professor Paul Martin

Professor of Cell Biology

Theme Co-Lead:

Dr Axel Walther

Senior Lecturer and Head of Research, Bristol Cancer Institute

The Cancer Theme is led by a Steering Group:

- Dr Sabine Hauert, *Engineering Mathematics*
- Dr Zoe 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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