## Cancer Network Newsletter July - August 2017

## **Royal Society report on machine learning**

The Royal Society released a report in April 2017 entitled Machine *learning: the power* and promise of computers that learn by example. Machine learning is a branch of artificial intelligence that allows computer systems to learn directly from examples, data, and experience. Through enabling computers to perform specific tasks intelligently, machine learning systems can carry out complex processes by learning from data, rather than following preprogrammed rules. Recent years have seen significant advances in machine learning, which have raised its capabilities across a suite of applications. Increasing data availability has allowed machine learning systems to be trained on a large pool of examples, while increasing computer processing power has supported the analytical capabilities of these systems. Within the field itself there have also been algorithmic advances, which have given machine learning greater power. As a result of these advances, systems which only a few years ago performed at noticeably belowhuman levels can now outperform humans at some specific tasks.

**Dr Sabine Hauert was** an active member of the working group which spent 18 months putting the report together. One of the benefits of the technology that was highlighted is its potential use in medi**cine**, for example to improve diagnosis of cancer. In healthcare, machine learning could help provide more accurate diagnoses and more effective healthcare services, through advanced analysis that improves decision-making. One example of this function comes from breast cancer diagnoses, which typically include an assessment by pathologists of a tissue sample. A machine learning system trained on tissue images was able to achieve a higher accuracy than pathologists, by finding and utilising features of the image that were predictive but had not previously been used in the pathology assessments. In doing so, the system was able to help doctors more accurately assess a patient's prognosis. Sabine wrote an article for BBC News, published 25 April 2017, which mentions the use of machine learning in cancer. Below: Sabine and her "swarm"



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cancer-research @bristol.ac.uk	
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July - August 2017

## **EVENTS**

Cancer Early Career Researchers Forum 21 July 2017, 12.30 - 13.30. Adams Chambers and James Yarmolinsky F40, Biomedical Sciences Building

**Metabolic Dysfunction and Cancer: Molecular Epidemiologic Approaches** 25 July 2017, 12.00 - 13.00. Dr Marc Gunter (Head of Section of Nutrition and Metabolism, International Agency for Research on Cancer), Room OS6, Oakfield House

Curiosity funding scheme information event 25 July 2017, 12.00 - 16.30. At-Bristol Science Centre

PreScribed (a Life Written for Me) 15 - 25 August 2017, 15.30 - 16.30. The Sanctuary, Edinburgh

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

West of England Genomic Medicine Centre 2017 annual event 1 September 2017, 10.00 - 16.00. Sandford Education Centre, Cheltenham

Workshop: Above and Beyond and Research Capability Funding grants 5 September 2017, 8.00 - 9.00. Tutorial Room 3, Research & Innovation, Education & Research Centre, UHBristol

Integrating Inherited Cancer Syndromes into Cancer Care 6 September 2017, 8.45 - 16.30. The Royal Marsden Education and Conference Centre, London

Workshop: Above and Beyond and Research Capability Funding grants 12 September 2017, 8.00 - 9.00. Tutorial Room 6, Research & Innovation, Education & Research Centre, UHBristol

Tableau software workshop (data visualisation using Tableau)13 September 2017, 9.30 - 17.00. Seminar room, Beacon House

Workshop: Above and Beyond and Research Capability Funding grants 14 September 2017, 13.00 - 14.00. Tutorial Room 6, Research & Innovation,



(Product Consultant, Tableau)







### Cancer Network Newsletter



#### Education & Research Centre, UHBristol

**Early Detection of Cancer Conference** 20 September 2017, 9.00 - 17.00. The Hilton Cambridge City Centre

#### **Big Data in Biology and Health 2017**

25 - 27 September 2017. Keynote: Sarah Teichmann (Wellcome Trust Sanger Institute), Wellcome Genome Campus, Saffron Walden

**Enhancing Facilitation Workshop** 27 September 2017, 8.45 - 13.00. UWE, Frenchay Campus

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

**UHBristol Research & Innovation Showcase** 31 October 2017, 10.30 - 16.00. Education Centre, Upper Maudlin Street

**Elizabeth Blackwell Annual Public Lecture** 2 November 2017, 16.00 - 19.30. Prof Helen Stokes-Lampard FRCGP

### Health: The design, planning and politics of how and where we live conference 25 January 2018, 9.30 - 17.00. UWE Bristol, Frenchay Campus

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



From top: Irene Ghobrial (Dana-Farber Cancer Institute, speaker at the Early Detection of Cancer Conference), Sarah Teichmann, Stephen Robinsion, Helen Stokes-Lampard











University of the West of England

# **Cancer Research Forum**



## Are you interested in Cancer research?

Early career cancer researchers from all backgrounds get together to learn about each other's work

## Speakers:

Adam Chambers – Radiosensitivity in rectal cancer

James Yarmolinsky – Mendelian randomization in cancer research

Friday 21<sup>th</sup> July 12.30pm – 1.30pm

Room F40, Biomedical Sciences Building (by St Mike's Hill)

University of Bristol

Bringing together scientists and clinicians working in cancer

Cake, Tea and Coffee provided.

Email adam.chambers@nhs.net or bieev@bristol.ac.uk

For enquiries and to register interest

## NEWS

## **Cerami Award to Sir Paul Nurse**

Northwell Health's Feinstein Institute for Medical Research and Molecular Medicine has announced that the seventh Anthony Cerami Award in Translational Medicine will be awarded to Sir Paul Nurse, Director of The Francis Crick Institute and Chancellor of the University of Bristol.

The award is in recognition of his research, which identified protein molecules that control the division of cells in the cell cycle currently being examined as a therapy to stop or prevent cancer cell growth. Dr Nurse's research led to the critical discovery that the protein cyclindependent protein kinase (CDK), found both in yeast and in human genes, controls the cell cycle. Knowledge of the cell cycle is critical to the treatment of cancer.

Most cancers are caused by the uncontrolled cell division due to damage to the controls regulating cell growth and reproduction, or by damage to how the cell replicates and grows. Leading drug companies are utilising the understanding of the role that CDK plays in cell growth to test new therapies to stop cancer cell growth. The Cerami Award, which includes a \$20,000 prize, is conferred semi-annually by the editors of *Molecular Medicine*. A monograph authored by Dr Nurse, *A Journey in Science: Cell Cycle Control*, is available online.



## New Head of School for CMM

Prof Anne Ridley FMedSci FRS has been confirmed as the new Head of School for Cellular and Molecular Medicine. She is currently Head of the Cell Motility and Cytoskeleton Section in the Randall Division of Cell and Mo-



lecular Biophysics at King's College London. She will succeed Prof Chris Paraskeva when she takes up her post in January 2018.

Prof Ridley's academic career has included postdoctoral research at MIT and at the Institute of Cancer Research in London, a professorship at the Ludwig Institute for Cancer Research at UCL and, since 2007, a post as Professor of Cell Biology at King's College London. Her awards include the British Society of Cell Biology's Hooke Medal and the Lilian-Bettencourt Prize for the Life Sciences.

She became a fellow of the Royal Society of Biology in 2009, and a fellow of the Academy of Medical Sciences in 2012. She became an honorary fellow of the Royal Microscopical Society in 2014 and a fellow of the Royal Society in 2017. Dr Abderrahmane Kaidi (CMM) from the **Royal Society**, an International Exchanges Award: *Therapeutic targeting of chromatin in cancer stem cells*. £6,000; project dates 13/03/2017 to 13/03/2018.

Dr Kathreena Kurian (SOCS) from the David Telling Charitable Trust for Identifying circulating tumour cells and DNA in the blood: an analysis of their diagnostic and prognostic significance in correlation with biopsy findings. £24,170; project dates 01/11/2015 to 01/11/2018. Prof Richard Martin (SSCM)

from **Cancer Research UK** for Prostate cancer screening and treatment of localised disease: implications of recent and emerging trial results for practice and policy in the UK and internationally. £15,000; project dates 01/01/2017 to 01/03/2017.

Dr Kathreena Kurian (SOCS) from the North Bristol NHS Trust, a PhD in Brain Tumour Research. £120,000; project dates 01/10/2017 to 01/10/2020.

**Prof Christoph Wuelfing** 

## **Recent funding successes**

(CMM) from the **Wellcome Trust** for *The vesicular localisation of the co-inhibitory receptors PD-1 and LAG 3 in anti -tumour immunity.* £2,000; project dates 03/07/2017 to 03/09/2017.

Profs Richard Martin and Jenny Donovan (SSCM) from **Cancer Research UK** for *Evalu*ating the long-term effectiveness and cost effectiveness of population-based screening and treatment for prostate cancer: the CAP and ProtecT *RCTs.* £961,404; project dates 01/08/2017 to 01/01/2022.

### **Cancer Research UK 2017 Research Engagement Award**

Dr Kaitlin Wade of the MRC Integrative Epidemiology Unit has been awarded this year's **CRUK Research Engagement** Award in the category of Rising Star. This prize was initiated by CRUK to recognise those who show extraordinary commitment to engaging the public and sparking enthusiasm and interest in cancer research. Kaitlin was nominated through her work with the Integrative Cancer **Epidemiology Pro**gramme (ICEP); over the past

two years she has gone to great efforts to establish multiple public engagement activities and frameworks and her relentless enthusiasm for engagement the public with MRC IEU research has been a key to many of other academic staff becoming involved.

"Public engagement is such an important part of scientific research that often gets overlooked - it's quite easy to become introverted when running analyses, writing papers and applying for specific grants but sometimes it means you lose focus of the 'big picture' – public engagement enables us to experience and communicate our ultimate goal of improving population health"

Image © CRUK; Kaitlin is second from left



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## **Elizabeth Blackwell Institute funding**

Emily Milodowski (VetSci) was recently awarded a Clinical Primer for Identifying predictive biomarkers for the therapeutic efficacy of check point inhibitors in the treatment of metastatic melanoma patients. Clinical primers are aimed at medical, veterinary and dental clinical graduates and are designed to give outstanding early career clinicians the chance to experience a world-class research environment for the first time. Emily will begin her placement later this year.

Postgraduate Discipline Hopping Fellowships are designed to support a small number of postgraduate researchers currently enrolled on one of the University of Bristol Wellcome Trust-funded 4 year PhD programmes, who receive funding that enables them to 'discipline hop' and experience a new field. Recently in receipt of an award is Mark Olenik (Maths, below) for Mathematical modelling of cell competition in cancer.



**Confidence in Concept awards** fund larger proof of concept studies which provide robust evidence to funders of the feasibility of a proposed solution to a health, clinical or product development need. They are intended to accelerate the

translation of discovery research into new therapies, diagnostics and medical devices by supporting preliminary work or feasibility studies to establish the viability of an approach – before seeking more substantive translational funding. Recently in receipt of such an award is Jaap Velthuis (Physics, below) for Development of novel silicon diode dosimetry devices for radiotherapy verification.



## Informatics service support for research

The Elizabeth Blackwell Institute for Health Research (EBI), through its Wellcome Trust ISSF Award, and match funded by UoB, invested in two posts that are openly available to help support all health and biomedical researchers across the University in their informatics needs.

Dr Stephen Cross (left), Research Associate in Microscopy Image Processing and Analysis, Wolfson Bioimaging Facility:

The primary purpose of my role is to assist users with processing and analysis of microscopy images; typical examples of which include 3D segmentation of cells, characterisation of protein co-localisation using the overlap of fluorescent signals and tracking cells and measuring their mobility. Email Stephen to discuss your project.

Dr David Lee (right), Research Associate in Bioinformatics,

Life Sciences: My speciality is analysing, predicting and comparing the structures and functions of proteins. More recently, I have expanded my expertise at Bristol into transcriptomics, proteomics and statistics and can now assist with truly comprehensive analyses. Email David to discuss how he could collaborate with you on your project.



### **Evaluating novel therapies for leukaemia**

Researchers lead by Dr Allison Blair (pictured in background) developed a model for testing leukaemia drugs that promises to provide more reliable indications of clinical effectiveness, which involves injecting patient material directly into immune-compromised mice. The mouse model was used to demonstrate that the natural medicine parthenolide (PTL) can eliminate human leukaemias. Previous research may have overlooked the therapeutic potential of the drug because in vitro tests of PTL

yielded disappointing results. This was the first time that human leukaemias have been shown to be eradicated in mice and illustrated the importance of using animal models of human leukaemia for drug evaluation studies. The next step was to validate the mouse model by testing whether the results matched those from real patients. The project went ahead with funding from the EBI Translational Acceleration and Knowledge Transfer award. They inoculated immunedeficient mice with samples from children with leukaemia from different clinical risk groups and measured the rate at which the disease established. Then they treated the mice with conventional drugs or combinations of drugs used to treat the children and monitored their response. Another group of mice acted as control. The team compared the results with how each child responded to the treatment. Overall the model gave a true representation of disease progression. More info

A Phase 3 study evaluating *Opdivo* 3 mg/kg versus *Yervoy* 10 mg/kg in patients with stage IIIb/c or stage IV melanoma who are at high risk of recurrence following complete surgical resection met its primary endpoint at a planned interim analysis, demonstrating superior recurrence-free survival (RFS) in patients receiving Opdivo compared to Yervoy.

The CheckMate -238 trial, sponsored by Bristol-Myers Squibb, is important news for the oncology community; despite surgical intervention and new treatment options, many of these patients still experi-

## Phase 3 clinical trial success

ence disease recurrence.

The trial is an ongoing Phase 3, randomized double-blind study of Opdivo versus Yervoy in patients who have undergone complete resection of Stage IIIb/c or Stage IV melanoma. The trial randomized 906 patients to receive either Opdivo 3 mg/kg intravenously every two weeks or Yervoy 10 mg/kg IV every 3 weeks for four doses and then every 12 weeks until documented disease progression or unacceptable toxicity, up to a maximum treatment duration of one year. The primary endpoint is RFS defined as the time between randomization

and the date of first recurrence or death. *Opdivo* is a programmed death-1 (PD-1) immune checkpoint inhibitor that is designed to harness the body's own immune system to help restore anti-tumour immune response. By harnessing the body's own immune system to fight cancer, Opdivo has become an important treatment option across multiple cancers.

The UHBristol Haematology and Oncology Centre Clinical Trials Unit recruited 4 patients to the trial. (PI: Dr Chris Herbert, pictured in background). More info

### **Cancer Research UK news**

### Strategy progress report

In 2014 CRUK published a strategy with the ambition to accelerate progress and see 3 in 4 patients surviving cancer within 20 years. The strategy set out our priorities and outlined the approaches they would take to achieve this. A progress report, published in June 2017, sets out a highlevel view of progress since the strategy's launch. Alongside ongoing dialogue with the UK and international research community, they have sought input and challenge on their progress from supporters, patients and those affected by cancer. The aim is not just to support the best research, but to ensure that their focus and priority areas are those that will transform outcomes for patients.

The four objectives include:

*PREVENT*- More than 40% of all cancers diagnosed in the UK are attributed to lifestyle and environmental factors, but achieving large-scale behaviour change is a huge challenge. CRUK are tackling cancer prevention in a holistic way, from tobacco control to preventive treatments.

*DIAGNOSIS*- Earlier diagnosis of cancer offers the greatest potential for transformational improvements in patient outcomes. They pledged to take a leading role in this area, leveraging the range and breadth of their expertise and infrastructure.

TREAT – They recognised a need for therapeutic innovation covering a breadth of treatments – drugs, radiotherapy and surgery – and bringing in new perspectives, mechanisms and methods. They will continue to invest in treatment innovations, and to lobby for more rapid adoption of them into the healthcare system.

*OPTIMISE* – The aspiration is to make precision medicine a reality in the UK, with patient treatment decisions being made on a truly individual basis, and for doctors to have access to a wide range of effective treatment combinations.

### Early Detection Research Committee

CRUK are convening a new Early Detection Research Committee that will award funding for research into the early detection of cancer. They are challenging the research community to focus efforts, drawing together disparate activity across many areas of cancer research and across disciplines – including biomedical sciences, physical sciences, engineering, mathematics and industry – to bring in new thinking and build novel early detection research projects. The Committee will consider early detection research as investigations that enable the detection of cancer, or precancerous states, at the earliest possible time point at which an intervention might be made. The ambition is to build to an annual investment of £20 million in this area by 2021.Initially, the committee's remit will include:

*Project awards*- Catalytic awards to stimulate and support new lines of early detection research, of up to £500k for up to 3 years; and

Programme awards- High-level support for ambitious research programmes to enable significant progress in early detection research of up to £2.5m for up to 5 years.

### **New chief clinician**

### Prof Charles Swan-

ton (pictured in background) has been appointed as CRUK's new chief clinician. Prof Swanton, who will also join the charity's executive board later this summer, now leads a team at the Francis Crick Institute working on an internationally acclaimed clinical study, TRACERx, analysing how lung cancer develops. The Image Data Resource (IDR) is a collaboration between the Open Microscopy Environment (OME) based at Dundee, the Universities of Cambridge and Bristol and the European Bioinformatics Institute. IDR brings together biologists, imaging specialists, big data scientists and computer scientists.

A team headed by Prof Jason Swedlow (Dundee) has built this public database that collects and integrates imaging data related to experiments published in leading scientific journals. This means that 'Big Data' from imaging experiments conducted by scientists all over the world that were previously too large and difficult to share are now publicly available.

Access to primary research data is vital but comparing and analysing image datasets is notoriously difficult due to file size and complexity. They are rarely publicly available and different means of collating and storing image data mean they cannot be easily reproduced, compared or re-

### Image Data resource

#### analysed.

IDR automates these processes and pulls individual pieces of related research together to create a vast bank of knowledge that can save researchers time, effort and money while highlighting previously unexplored areas with the potential to solve scientific mysteries. This free resource is the first general biological image repository that stores and integrates data from multiple modalities and laboratories. More info

The UHBristol Haematology and Oncology Centre Clinical Trials Unit are the first to recruit globally for A Study of CYP-001 for the Treatment of Steroid-Resistant Acute Graft Versus Host Disease.

Allogeneic stem cell transplantation is a potentially curative treatment for patients with cancer and bone marrow failure although is associated with significant serious side effects. Acute graft versus host disease (aGvHD) is the result of the donor immune system, mediated by lymphocytes attacking the recipient tissues, and is one of the most

serious complications of allogeneic transplantation. This typically occurs within the first 3 months following transplant and affects up to two thirds of transplant recipients. Significant aGvHD is treated with corticosteroids although up to half of patients require subsequent lines therapy. Currently available treatments for steroid refractory aGvHD are often ineffective and there is no standard of care and the mortality for patients with resistant aGvHD is high. Mesenchymal Stem Cells (MSC) are able to inhibit a range of inflammatory cells including

### **Clinical Trial recruitment success**

lymphocytes, natural killer cells and dendritic cells, on which basis they have been investigated as a possible treatment for aGvHD. Results of previous studies using MSC in aGvHD have been mixed. The study will assess the safety, tolerability and efficacy of two infusions of MSC (CYP 001) produced using a novel technology to facilitate cell expansion without loss of efficacy.

The Bristol PI is Dr James Griffin.

## Prehabilitation

Programmes to improve people's health before surgery have mostly been exercisebased, with limited studies showing mixed results. The role of diet, for example, has been little studied, and the same is true of managing medicines and pre-existing conditions. Dr Maria Pufulete (top left background) led collaborative research to identify interventions that improve postoperative recovery and decrease the length of hospital stay.

The project won funding from EBI's Research for Health Challenge scheme in response to a challenge from Dr Sanjoy Shah (right bottom background),

Consultant in Intensive Care Medicine at UHB NHS Foundation Trust, to develop a 'prehabilitation' programme for patients having major cancer surgery. The prehabilitation programme initiated by Dr Shah aims to develop a multicomponent intervention; it reached a stage where there was a need to identify which interventions work best; describing the population of patients undergoing surgery, in terms of baseline characteristics and post-operative complications; describing preoperative assessment practice across different hospitals; and discussing the concept of prehabilitation with local patient and public involvement (PPI)

groups.

Alongside the project, prehabilitation is now offered to UBH patients undergoing surgery for thoracic, ovarian and urological cancers, and is being extended to other cancers. The work has attracted the support of cancer charities, and a paper on the systematic review, which comprised the first stage of the project, was published in Systematic Reviews in May 2016.

More info

## **Transforming treatment of autoimmune diseases**

There is a problem with the traditional treatment of autoimmune and inflammatory conditions. Steroid therapy doesn't always work, and immunosuppressant drugs can have toxic side effects. Dr Richard Lee (in background) and his team are working to overcome this thanks to an EBI **Translational Acceleration and** Knowledge Transfer award, by exploring technology used in cancer therapy to target steroid-resistant immune cells and avoid damaging healthy nonimmune tissues. This involves

combining the active therapeutic agent (in this case an immunosuppressant) with a monoclonal antibody that targets a protein (antigen) specifically found on disease causing cells. These therapeutic pairings are known as antibody drug conjugates (ADCs).

The team had already identified a group of steroidresistant immune cells as candidates for therapeutic targeting in a range of inflammatory conditions. They now proposed to deliver a cal-

cineurin inhibitor in an ADC directed at a cell surface protein (CCR6) which they had identified as particular to steroid resistant cells. Pilot data needed to develop this resulted in a partnership with a UCL spinout, Polytherics (now Abzena), to produce the ADC. Their project is also being developed in partnership with US National Institutes of Health. The work resulted in a US patent application by UoB for ADCs for steroid refractory inflammatory disease. More info

## ELIZABETH BLACKWELL FUNDING

### EBI MRC Confidence in Concept Scheme (CiC)

Support health related translational projects. Funding is available to support projects which are at the stage of proof of concept (Confidence in Concept Awards). Applicants successful at the outline stage will be invited to submit a full application for concept development funding.

### Deadline for outline applications: 28 July 2017

### EBI Research for Health challenge

Aims to encourage healthcare practitioners and University of Bristol researchers to work together to develop innovative thinking around clinical problems.

### Call for solutions opens 26 July 2017

### 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 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.



Elizabeth Blackwell Institute for Health Research





## **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

Closing date: None

Award amount: US\$3,400

### July - August 2017

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.

### **European Association for Cancer Research** Meeting bursaries

Closing date: 31-Jul-17

Award amount: €500 + registration

Enable early-career scientists to attend and present at the association's conference. Bursaries include registration fees and funds up to €500 each to support travel and accommodation costs.

### Cancer Research UK

Multidisciplinary project award

Closing date: 08-Aug-17

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.

### HEE/NIHR Integrated Clinical Academic (ICA) scheme

Closing date: 06-Sep-17

HEE/NIHR ICA Internship (2017/18); Post-Doctoral Award (2017/18); Transitional Awards (2017/18)

### Department of Health including NIHR

Health services and delivery research programme – researcher-led workstream: 17/45, 17/49

Closing date: 07-Sep-17

Award amount: unspecified

Supports research into the quality, effectiveness and accessibility of health services, including evaluations of how the NHS might improve delivery of services. The workstream has a continued interest in the following research areas: primary care interventions, very rare diseases, long-term conditions in children, applied research into mesothelioma

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.

#### 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.

### Joint University Hospitals Bristol Research Capability Funding and Above and Beyond grants

Closing date: 25-Oct-17

Award amount: £25,000

### UHBristol Research Capability Funding (RCF)

Used to help NHS organisations attract, develop and retain high quality research active staff. Funds can be used to a) Fund Research Sessions/PAs (for medical and non-medical staff) to allow time to prepare NIHR research grant applications; and/or b) Fund the generation of preliminary or underpinning data to support an NIHR application; a "pump-priming" grant.

### Above and Beyond

Above and Beyond generously allocate funds to research in UHBristol, and the call is now open for Above and Beyond research grants (up to £20,000). These grants aim to promote high quality biomedical research in UHBristol. Applications are welcomed from any medical or non-medical UHBristol employee, or university academic (Universities of Bristol and the West of England) holding an honorary contract with UHBristol.

## **FEATURED PUBLICATION**

### The small molecule inhibitor YK-4-279 disrupts mitotic progression of neuroblastoma cells, overcomes drug resistance and synergizes with inhibitors of mitosis

### Kollareddy M, Sherrard A, Park JH, Szemes M, Gallacher K, Melegha Z, Oltean S, Michaelis M, Cinatl Jr J, Kaidi A and Malik K. *Cancer Letters*. 403, pp74-85

Neuroblastoma is a biologically and clinically heterogeneous pediatric malignancy that includes a high-risk subset for which new therapeutic agents are urgently required. As well as MYCN amplification, activating point mutations of ALK and NRAS are associated with high-risk and relapsing neuroblastoma. As both ALK and RAS signal through the MEK/ERK pathway, we sought to evaluate two previously reported inhibitors of ETS-related transcription factors, which are transcriptional mediators of the Ras-MEK/ERK pathway in other cancers. Here we show that YK-4-279 suppressed growth and triggered apoptosis in nine neuroblastoma cell lines, while BRD32048, another ETV1 inhibitor, was ineffective. These results suggest that YK-4-279 acts independently of ETS-related transcription factors. Further analysis reveals that YK-4-279 induces mitotic arrest in prometaphase, resulting in subsequent cell death. Mechanistically, we show that YK-4-279 inhibits the formation of kinetochore microtubules, with treated cells showing a broad range of abnormalities including multipolar, fragmented and unseparated spindles, together leading to disrupted progression through mitosis. Notably, YK-4-279 does not affect microtubule acetylation, unlike the conventional mitotic poisons paclitaxel and vincristine. Consistent with this, we demonstrate that YK-4-279 overcomes vincristine-induced resistance in two neuroblastoma cell-line models. Furthermore, combinations of YK-4-279 with vincristine, paclitaxel or the Aurora kinase A inhibitor MLN8237/Alisertib show strong synergy, particularly at low doses. Thus, YK-4-279 could potentially be used as a single-agent or in combination therapies for the treatment of high-risk and relapsing neuroblastoma, as well as other cancers.



SK-N-AS, GIMEN, SK-N-BE(2)-C and SH-SY5Y representative mitotic structures (Red: microtubules, Green: chromosomes) from three independent replicates. Diverse microtubule organisation is evident from

the images. All DMSO treated cells showed typical metaphase equatorial plates and progressed through mitosis and segregated chromosomes within the nine-minute time frame, whereas YK-4-279 cells were mostly stuck at prometaphase.

## CONTACTS



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The Cancer Theme is led

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bristol.ac.uk /cancer

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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



