Cancer Theme Newsletter

April - May 2016

University of BRISTOL
Elizabeth Blackwell Institute for Health Research

Life Factors could Increase Prostate Risk

An internal research team funded by the World Cancer Research Fund assessed sexual maturation using genetic markers for the first time. The team found these early puberty genes were associated with an increased risk of prostate cancer in later life.

Genes that could indicate sexual maturation were identified, and each man was given a score dependent on how many of these maturity genes were present. Measuring sexual maturation in this way allows for a possible causal link to be drawn between reaching puberty early and an increased risk of prostate cancer. This method is also more reliable than the conventional use of physical pubertal changes, which are imprecise and difficult to isolate.

The link between genetic factors that influence when boys enter puberty and prostate cancer could be due to the effect of early and prolonged increased levels of growth hormones, which are altered with puberty, although this remains to be examined.

Prostate cancer is the most common cancer in men in the UK, with more than 47,000 new cases each year. More than 10,000 men die of the cancer each year. Worldwide, it is the second most common cancer in men.

There are many questions around what could prevent prostate cancer… these results linking sexual maturation and prostate cancer risk could help fill some of the gaps .
Researcher Prof Richard Martin

Reference: Bonilla C *et al.* (2016). Pubertal development and prostate cancer risk: Mendelian randomization study in a population-based cohort. *BMC Medicine.* 14:66.

Early Career Researchers' Forum

A Cancer ECR forum launched in 2015 thanks to the efforts of Adam Chambers (MRC Clinical Research Fellow, CMM) and Hannah Taylor (Clinical Research Fellow, Biochemistry). Meetings occur approximately every two months and attendance has been encouraging, with excellent discussions and some useful networking taking place. The next gatherings are anticipated for early May and late June.

The forum aims to bring together junior cancer researchers, both clinicians and scientists, to facilitate collaboration. It is also hoped that discussions will encourage more clinicians to undertake a PhD at Bristol.

For more information contact Adam on ac14768@bristol.ac.uk

Inside this issue:

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EVENTS

Kamil R Kranc, Group leader, MRC Centre for Regenerative Medicine, University of Edinburgh Professor of Molecular Haematology; CRUK Senior Research Fellow

Hypoxia signalling pathways in normal and leukaemic stem cell functions

19 April 2016, 13.00 - 14.00. Kamil Kranc (MRC Centre for Regenerative Medicine, University of Edinburgh), C42, Biomedical Sciences Building

Building Research Partnerships Workshop

21 April 2016, 9.30 - 16.30. University of the West of England, Frenchay Campus, Dartington Suite, Wallscourt Farmhouse

Academy of Medical Sciences: poster and presentation prize event for ECRs

22 April 2016, 14.00 - 17.00. University of Bath

Global Challenges Research Fund workshops : Health

25 April 2016, 10.00 - 12.00. Room 4.10, Graduate School of Education

Professor Caterina La Porta, University of Milan

Obtaining NIHR Funding and the Application Process

25 April 2016, 10.00 - 16.00. University of Oxford

Cancer Stem cells in melanoma: a complex problem

26 April 2016, 12.00 - 14.00. Caterina La Porta (University of Milan, Center for Complexity & Biosystems), Bristol Centre for Complexity Sciences, 1-9 Old Park Hill (Ground floor)

Bristol Oxford Surgical Trials

27 - 29 April 2016. School of Social and Community Medicine.

Marie Sklodowska-Curie Fellowships: Q&A session

4 May 2016, 13.00 - 14.00. PMEU Team (Research Development), Seminar Room G13/14, Life Sciences

'Research without Borders', an exhibition of postgraduate research excellence

9 May 2016, 14.30 - 18.00. At-Bristol Science Centre

Professor Chris Jones, Team Leader, Institute for Cancer Research

Chris Jones, Institute of Cancer Research

10 May 2016, 13.00 - 14.00. Chris Jones (Institute of Cancer Research), C42 Biomedical Sciences Building

Epigenetic mechanisms for breast cancer risk
12 May 2016, 12.45 - 13.45. James Flanagan (Imperial College), LG08 Canynge Hall

GW4 Cancer Research Consortium: cross-institutional meeting
24 May 2016, 9.30 - 17.00. Bailbrook House Hotel, Bath

Sedentary behaviour and cancer: risk prognosis and putative mechanisms
15 June 2016, 14.00 - 15.00. Brigid Lynch (UoB), BRU Seminar Room, Education & Research Centre

Soapbox Science
16 July 2016, 10.00 - 17.00. Bristol.

Reach West
14 September 2016, 14.00 - 15.00. Richard Martin & Verity Leach (UoB), BRU Seminar Room, Education & Research Centre

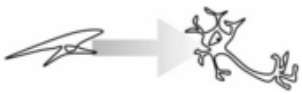
Dr James Flanagan, Non-clinical Senior Lecturer, Department of Surgery and Cancer, Imperial

NEWS

Human Cell Transformation Breakthrough

Pluripotent stem cells can be used to treat many different medical conditions and diseases. In the 9 years since the first artificial cells were created, scientists have only been able to discover a handful of further conversions for human cells. A computational algorithm called *Mogrify* was developed over 5 years by former PhD student Dr Owen Rackham and Prof Julian Gough, using data collected as a part of the FANTOM international consortium. The algorithm can be used to predict the cellular factors for cell conversions, thus bypassing the need to create stem cells.
The system was tested on two new human cell conversions, and succeeded first time for both. The speed with which this was achieved suggests *Mogrify* will enable the creation of a great number of human cell types in the lab. The ability to produce cell types will lead directly to tissue therapies of all kinds. This represents a significant breakthrough in regenerative medicine, and paves the way for life-changing medical advances within the next few years.

Rackham OJL et al. (2016). A predictive computational framework for direct reprogramming between human cell types. *Nature Genetics*. 48, pp331–335.



Dermal Fibroblast to Neuron

Mogrify *provides a landscape of cell types with the associated transcriptions factors to navigate from one part of the landscape to another*

Clinical Research and Imaging Centre

The Clinical Research and Imaging Centre (CRIC) has a new online facility. The page displays a comprehensive list of publications that have been drawn from research that has taken place at CRIC Bristol, many of which link to the online article.

CRIC is a joint venture between the University Hospitals Bristol NHS Foundation Trust and the University of Bristol. Facilities include a Siemens 3Tesla Magneton Skyra MRI scanner, a two-room sleep laboratory and four clinical investigation suites alongside a laboratory, meeting rooms, and access to high performance computing facilities.

Recent Appointment

Dr Kathreena M Kurian (pictured left) BSc, MD, MBBS, FRCPath(Neuro) Consultant Neuropathologist at Southmead, has recently been appointed an Honorary Reader in Brain Tumour Research within the School of Clinical Sciences

GW4 Cancer Research Consortium

The Consortium was awarded an Initiator Grant for Feb-May 2016 with leads: Drs T Perry & R Gill (Bath); Prof Raimondo Ascione (Bristol); Drs Chris Marshall & Derek Jones (Cardiff); and Prof John Terry (Exeter).

It aims to foster cross-disciplinary collaboration by capitalising on the breadth of complementary expertise and high-impact cancer research across GW4. Translating cancer discoveries into cures is a major public health challenge worldwide, and in the last two decades advances in diagnosis, treatment and care have led to longer survival times for a number of different cancers. As the ageing population continues to grow, cancer will only increase as a serious social and economic health challenge.

Within GW4 there is already substantial research effort into the environmental and lifestyles causes of cancer, the contribution of genetics, biochemistry and cell biological processes to the aetiology of a wide range of malignancies. There is also research into the prevention and pharmaceutical intervention in cancer.

They aim to identify resources required to underpin large strategic grant applications, and establish a cross-centre non-clinical doctoral training programme in cancer complementing the work of the GW4 Clinical Academic Training Community.

Recent Funding Successes

- A **GW4 Initiator grant** was awarded in Jan 2016 to the GW4 Cancer Research Consortium for a project to be led by Adele Murrell & Lorenzo Caggiano (Bath), Alan Clarke (Cardiff), Paul Martin & Axel Walther (Bristol), David Allard, Jacqueline Whatmore & Willie Hamilton (Exeter)
- Dr Sebastian Oltean received £2600 from **Breast Cancer Campaign** for *Does PRH inhibit EMT via direct activation of E-cadherin expression,* 01/11/2015 - 01/02/2016
- Prof Ann Williams, is in receipt of a **British Council** Newton Bhabha PhD placement: *Effect of Radiation on Cox-2 Mediated Signaling in Normal & Cancerous Cells,* £12,800, 01/04/2016 - 01/10/2016

Awards to Support Translational Research

A total of £650,000 was awarded to UoB from the MRC to support translational research. The award, which will be managed by the Elizabeth Blackwell Institute for Health Research, will provide flexible funding for early stage translational projects, to enable the development of academic-industry collaborations, and allow impact development. Two schemes recently sought outline proposals:

TRACK Awards will fund initial pilot studies to demonstrate the concept of a proposed solution to a health, clinical or product development need. They will support health related research projects which have translational/commercial potential but need to undertake an additional, specific piece of work before seeking proof of concept.

Confidence in Concept Awards will 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.

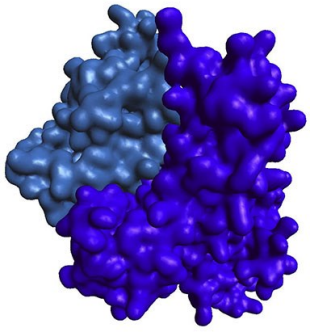
They are intended to accelerate the translation of discovery research into new therapies, diagnostics and medical devices by supporting preliminary work or feasibility studies.

The latest funding round resulted in an award for Dr Allison Blair to conduct a project entitled Development of pluronic micelle nano carriers for the treatment of childhood acute lymphoblastic leukaemia. The amount of £49,205 was granted and the research will will take place during 01/02/2016 - 01/10/2017.

Elizabeth Blackwell

Dr Alison Blair, Principal Clinical Scientist, School of Cellular and Molecular Medicine

Protein Interactions to Transform Drug Discovery



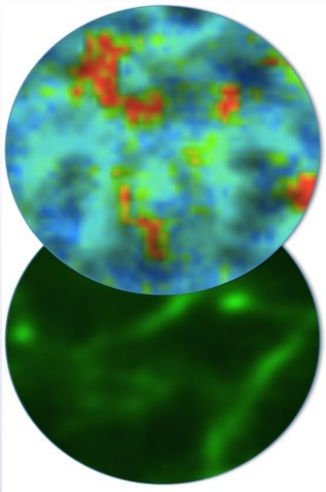
An x-ray crystallography image of a protein-protein interaction. © Prof Andrew Wilson, University of Leeds

A new programme involving researchers from the Universities of Leeds and Bristol along with the Northern Institute for Cancer Research, Newcastle University, AstraZeneca and Domainex, will develop new tools to understand which interactions between proteins in the human body are relevant to disease. Currently, only a handful of drugs in clinical use work by targeting protein-protein interactions. There are thought to be up to 600,000 protein-protein interactions that could be targets for new drugs, but we don't know which ones are most important, what is crucial for their interaction and how to target them. By understanding the 'social life' of proteins, significant strides could be made.

The project will create the tools to make this kind of drug discovery easier by analysing and categorising the important features of protein-protein interactions, which will provide the basis for discovering many new drugs for the treatment of disease.

A total of £3.4M has been awarded by the EPSRC to fund the research starting 1 Feb 2016 for 5 years.

Role of nuclear F-actin in regulating genome organisation and function



Part of a human cell nucleus. Green fluorescence shows nuclear F-actin and the coloured image is a map representing the states of genome (chromatin) packaging.

An international research team comprising scientists from the Universities of Bristol, Marburg (Germany) and Kinki (Japan) has been awarded a grant from the 2016 Human Frontier Science Program (HFSP).
The award, made after a rigorous year-long selection process, is designed to promote cutting edge research into complex biological systems. The team, comprising the laboratories of Prof Robert Grosse (Marburg), Dr Abderrahmane Kaidi (Bristol) and Dr Kei Miyamoto (Kikni), has been awarded US$ 1.05M to study the role of nuclear filamentous-actin.
Thanks to new advancements in cell imaging techniques, nuclear F-actin can be detected in cell nucleus in specific conditions, which raises the possibility that it may regulate genome organisation and function. The award will focus on testing this hypothesis and applying this knowledge to further understand fundamental biological processes, including genome organisation during cell division and cellular reprogramming.
The research will apply state-of-the art optogenetic tools for spatial and temporal control of nuclear F-actin, and simultaneously visualise genome dynamics in intact cells using cutting-edge cell imaging techniques. As part of this research Dr Kaidi's laboratory is developing and applying the microscopy-based assays for quantitative analysis of genome/chromatin dynamics.

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.

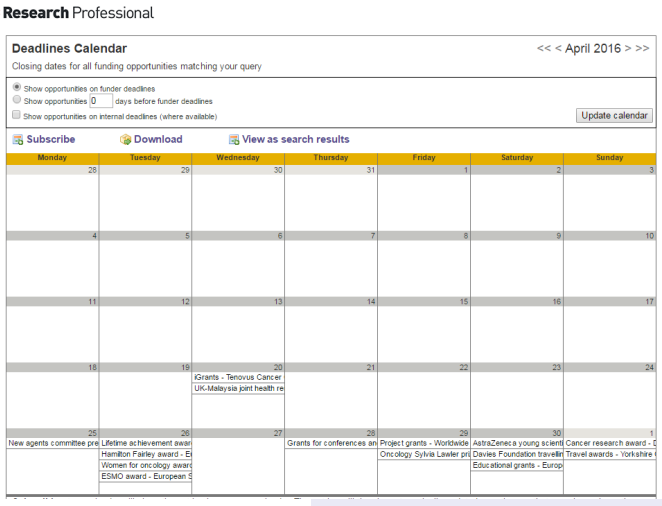
Returning Carers Scheme

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.

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.



Cancer Research UK

Pioneer award

Closing Date: none Award amount: £200,000

Supports high-risk, high-reward research projects that have a clear relevance to cancer, and enables the exploration of novel ideas which may lead to new discoveries or approaches. The award supports research that, due to its novelty and lack of supporting data, would be unlikely to secure fund-

ing through traditional mechanisms. Individuals and teams may apply regardless of background or vocation, across a breadth of disciplines. Investigators at all career stages, regardless of track record or publishing history, may apply.

Cancer Research UK
Small molecule drug discovery project awards

Closing Date: 09-May 16 Award amount: £300,000

Support research towards identification and validation of new targets, and the discovery of novel small molecule therapeutic and preventive agents. Milestone driven projects at all stages of drug discovery from target identification or validation to early preclinical studies will be supported, and preference will be given to applications at the target identification and target validation stages. Applications will be considered in associated assay or technology development and drug repositioning studies.

Children with Cancer UK
Clinical PhD and training studentships

Closing Date: 12-May-16 Award amount: £250,000

Enable clinicians to study towards a PhD or MRes research foundation qualification in the field of solid tumours, including the central nervous system, as well as taking their first steps on the path to becoming leaders in clinical research and education. Proposals must aim to:

- improve knowledge of the genetic and environmental causes and relevant biological mechanisms of childhood cancers, with a view to developing interventions to reduce the risks of development
- identify diagnostic and prognostic biomarkers for childhood cancers and develop systems for their introduction to clinical practice
- optimise and develop more effective and less toxic treatments for children with cancer, with a special focus on those forms of cancer that still carry a poor prognosis and develop mechanisms to introduce them rapidly to practice
- understand the long-term health implications of childhood cancer and its treatment and explore methods for interventions to reduce their impact

European Society for Medical Oncology
Translational research fellowships

Deadline: 12-May-16 Award amount: €80,000

Support research in oncology through training, career development and translational research projects. Each applicant must be:

- a full or junior ESMO member, or apply for membership
- an oncologist with at least one year experience in medical, radiation or surgical oncology
- be under the age of 40

Host institutes receive €1,000 towards administrative costs.

Department of Health
Health technology assessment programme – 16/12

Closing Date: 19-May-16 Award amount: unlimited

Proposals for one stage evidence synthesis under the commissioned funding stream of its health technology assessment programme. Proposals are sought on aids to cancer diagnosis in primary care.

Cancer Research UK
Clinician scientist fellowships

Closing Date: 23-May-16 Award amount: unspecified

Enable scientists to develop their clinical academic research career through a period of postdoctoral training, and will enable successful fellows to make the transition from doctoral research training to an independent clinical academic post. Applications will be considered from any area of CRUK's funding remit, with exception of clinical trials and drug discovery.

Applicants must have completed a higher degree, MD or PhD, in a cancer-relevant research area and be supported by an appropriate research group and supervisor.

Cancer Research UK
Population research committee project grants

Closing date: 27-May-16 Award amount: £100,000

Support projects that address cancer aetiology, early diagnosis, epidemiology, behavioural research, cancer prevention, statistics and methodology. Applications are open to scientists, clinicians or healthcare workers based in UK universities, medical schools, hospitals and eligible research institutions. Applicants must have three years' postdoctoral experience or equivalent, or a tenured post.

Cancer Research UK
Biotherapeutic drug discovery project awards

Closing Date: 01-Jun-16 Award amount: £300,000

Support milestone driven projects at all stages of drug discovery from target identification and validation to early preclinical studies. Applicants should discover and develop biological therapies, including:

- therapeutic antibodies
- cell based therapies
- viral therapies
- vaccines
- protein therapies
- gene therapies

GW4
Building Communities Initiator Funds and Accelerator Funds

Closing date: 06-Jun-16 Award amount: unspecified

The Building Communities programme is designed to build new, high-quality GW4 research communities or help existing collaborations to build on their work and secure long term sustainable funding.

Cancer Research UK
Biomarker project awards

Closing Date: 20-Jun-16 Award amount: £300,000

Support translational research studies that build upon the validation of biomarkers, with steps taken to qualify their use in the clinical setting. Applications are considered across the research areas of biomarker discovery, assay development, qualification, radiotherapy research, or imaging discovery and evaluation. Proposals may use invasive or imaging techniques and cover all types of biomarkers, including predisposition, screening, diagnostic, prognostic, predictive pharmacological and surrogate response. Applications in the following areas are particularly welcome:

- qualification of predictive biomarkers for conventional cytotoxics, including radiation
- early detection biomarkers
- circulating biomarkers – cells and nucleic acids, excluding proteomics

Cancer Research UK
Feasibility study project grants

Closing Date: 20-Jun-16 Award amount: £150,000

Fund investigator-led feasibility, phase II or pilot studies testing aspects of feasibility, tolerability or efficacy, including:

- single- or multi-centre prospective therapeutic, including investigational medicinal products and non-IMPs, and diagnostic or prevention phase II studies, potentially involving more than one national cancer research network, or several centres within a network
- academically-led feasibility studies in receipt of educational grants or free drugs from the pharmaceutical industry. Industry-sponsored trials cannot be reviewed under this scheme.

Cancer Research UK
Phase III clinical trial grants

Closing Date: 20-Jun-16 Award amount: £1M

These support investigator-led studies for cancer treatment directed at the tumour such as chemotherapy, radiotherapy and surgery with the principal objective of improving survival. This includes:

- phase III/IV therapeutic trials
- large-scale phase II trials that are over four years in duration or greater than £150,000 in total

Cancer Research UK
Prospective sample collections project grants

Closing Date: 20-Jun-16 Award amount: unspecified

Support prospective sample collections associated with clinical trials as well as strategy-enabling sample collections. Sample collections associated with a clinical trial that is about to commence or is ongoing are also accepted. Only funding for the collection of blood and paraffin tumour blocks is available. Under exceptional circumstances, funding for the collection of additional sample types may be provided.

Grants are available for up to 10 years. Sample collections with a guide price of £15 per paraffin block and £7.50 per blood sample are supported.

British Association for Cancer Research
Mid-Career Fellowships

Closing date: 30-Jun-16 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. Members may apply for a second award but this must be at least 3 years following the initial award.

Cancer Research UK
Career Development Fellowship

Closing date: 11-Aug-16 Award amount: salary for one postdoc and one technician + £150,000 for equipment

Enables scientists to set up their first independent cancer research group in any area of CRUK's funding remit, with the exception of drug discovery and clinical trials. Areas may include cancer biology, biomarker research, cancer aetiology, imaging research, pre-clinical research, early diagnosis, epidemiology, statistics and methodology, radiotherapy research, cancer prevention and immunology.

Post-doc and early-career researchers may apply. Applicants should have between three and eight years of research experience since completing their PhD at the time of applying.

Cancer Research UK
Career Establishment Awards

Closing date: 11-Aug-16 Award amount: salary for one postdoc and one technician + £150,000 for equipment

Enables new group leaders to enhance their cancer research in any area of CRUK's funding remit, with the exception of clinical trials and drug discovery. Areas may include cancer biology, biomarker research, cancer aetiology, imaging researcher, pre-clinical research, early diagnosis, epidemiology, statistics and methodology, radiotherapy research, cancer prevention and immunology.

Early-career researchers and established independent researchers may apply. Applicants should have at least three and no more than eight years of research experience after completing their PhD.

Cancer Research UK
Senior Cancer Research Fellowship

Closing date: 11-Aug-16 Award amount: unspecified

Enables scientists to establish or further develop an independent cancer research group in any area of the CRUK's funding remit, with the exception of clinical trials and drug discovery. Areas may include cancer biology, biomarker research, cancer aetiology, imaging research, pre-clinical research, early diagnosis, epidemiology, statistics and methodology, radiotherapy research, cancer prevention and immunology.

Established independent researchers may apply. Applicants should have between eight and 14 years of postdoctoral research experience since completing their PhD at the time of applying.

Department of Health

Health services and delivery research programme – researcher-led workstream: 16/52, 16/53

Closing date: 08-Sep-16 Award amount: unspecified

Supports research into the quality, appropriateness, effectiveness, equity and patient experience of health services. For this round, the emphasis is on large scale studies of national importance, such as research addressing issues of major strategic importance to the NHS, research likely to lead to changes in practice or having the potential to be applied to other conditions. Applicants may submit either a standard outline proposal or an evidence synthesis full proposal.

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

NIHR will fund HEIs at a maximum of 80 per cent of full economic costs, except for equipment worth over £50,000.

Medical Research Council

Clinical research training fellowship

Closing Date: 08-Sep-16 Award amount: unspecified

Enables clinically qualified, active professionals to undertake specialised or further research training in the biomedical sciences within the UK. Applications from basic studies to translational and developmental clinical research are welcome. The fellowship supports clinicians to undertake a higher research degree, while medically qualified applicants with a PhD can undertake early postdoctoral training enabling them to be competitive at the clinician

scientist fellowship level.

Veterinarians may apply if they have equivalent qualifications.

Cancer Research UK
Experimental Medicine Programme Awards

Closing date: 26-Sep-16 Award amount: £5M

Support investigator-led studies for ambitious translational research conducted in the clinical setting with the objective of optimising treatment and maximising patient benefit. Translational research considered within the scheme will typically be associated with, or lead to, one or more clinical trials. Involvement of an experienced clinical trials unit is expected. The programme is aimed at established independent researchers and clinicians.

Cancer Research UK
Late phase clinical trial awards

Closing Date: 26-Sep-16 Award amount: £1.5M

Support investigator-led studies for cancer treatment including chemotherapy, radiotherapy and surgery with the principal objective of improving survival. These are typically phase III trials, although large scale phase II trials, phase II/III trials and phase IV trials will also be considered. Trials should have clinical primary endpoints. Involvement of an experienced CTU is expected.

Cancer and Polio Research Fund
Research grants

Closing Date: 15-Oct-16 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. The fund does not usually support research in other fields but may consider proposals that are novel and that require pump-priming. Grants may be used for direct costs of research and to support research symposia or lectures for the dissemination of findings.

European Society of Surgical Oncology
Training fellowships

Closing Date: 31-Oct-16 Award amount: €10,000

Enable young surgeons to visit a specialist centre outside their own country in order to expand their experience and learn new techniques. Specialists, trainees or junior doctors under the age of 40 or in a training grade, with intention of specialising in a sub-speciality of surgical oncology may apply. Applicants must be or become members of the society before the start date of the award. European applicants may choose to visit European or non-European units. Eight standard training fellowships, worth €2,000 each, for stays of up one to three months are available, and one major training fellowship, worth €10,000 for stays of four to 12 months.

Dowager Countess Eleanor Peel Trust
Peel and Rothwell Jackson postgraduate travelling fellowships

Closing Date: 04-Nov-16 Award amount: £30,000

Enable researchers to spend up to one year at a centre of international excellence for the purpose of research, advanced study or the acquisition of a new clinical skill unlikely to be available in the UK. Candidates should be qualified and registered to practise in medicine, nursing or another health profession.

Great Britain Sasakawa Foundation
Butterfield awards

Closing Date: 15-Dec-16 Award amount: £15,000

Aim to encourage and facilitate exploratory exchanges and collaborations between qualified professionals in Japan and the UK, as well as investigation of scientific, clinical, social and economic aspects of medicine in which Japanese and British scientists, practitioners and policy makers may learn from each other. Applicants are normally expected to have an existing research record, but consideration will also be given to practitioners managers, carers or others in health-related fields. Preference will be given to those who have not previously been involved in a UK-Japan collaborations, and applications from early-stage researchers are particularly welcome. Areas currently of interest include health management; public health; health education; palliative care; stem cell technology; patient and carer involvement; cancer; and design for healthcare.

Substantial funds are also available for support of conferences and publications bringing together UK and Japanese expertise

FEATURED PUBLICATION

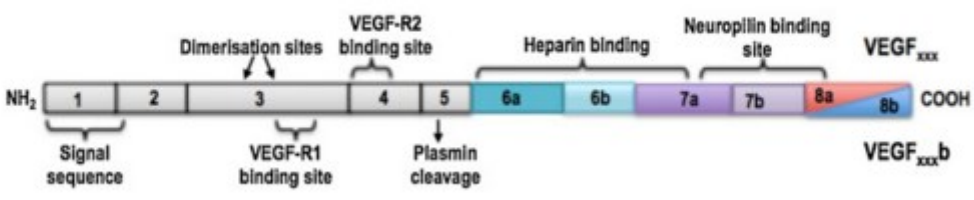
SRPK1 inhibition in prostate cancer: a novel anti-angiogenic treatment through modulation of VEGF alternative splicing

Mavrou A & Oltean S (2016). *Pharmacological Research*. 107, pp276-281

In the last 15 years there has been an increase in the use of drugs that target angiogenesis in cancers. The most well-known anti-angiogenic drug is Bevacizumab (Avastin), a humanised monoclonal antibody against vascular endothelial growth factor—A (VEGF-A) that is approved to be used in various cancers like colon cancer, non-small cell lung cancer or kidney cancer. However, following the initial excitement regarding the use of anti-angiogenics, they have not proven to induce a robust antitumoural treatment, with many clinical studies showing a modest progression-free survival and overall survival. Additionally, side effects of such treatments may be quite important. While there may be several explanations for this situation, it is more and more clear that we do not understand enough the vascular biology of tumours as well as many functional aspects of the molecules involved, therefore missing the chance to design more targeted treatments. This article discusses the current state of using anti-angiogenics in prostate cancer and our own work in finding a novel angle from which this problem may be solved.

Our human data on a cohort of 110 patients with PCa showed that SRPK1 expression is strongly associated with disease stage and invasion but not with Gleason score. This supports our findings in the pre-clinical studies that SRPK1 is a determinant of angiogenesis in PCa, as such it would not affect cell morphology (and therefore Gleason score) but contribute to its aggressiveness by stimulating angiogenesis.

The failure of clinical trials using antiangiogenics in PCa so far, despite strong evidence that angiogenesis is crucial for PCa progression, has pointed out that we need to understand better the various functions of angiogenic regulators and design better targeted treatments. Once such example might be the inhibition of SRPK1, which is highly expressed in PCa and drives expression of the pro-angiogenic VEGF splice isoforms, and not the beneficial anti-angiogenic ones, which are also inhibited by the current anti-VEGF therapies.



VEGF splice variants. Selection of a distal splice site (DSS) in the terminal exon results in formation of anti-angiogenic "b" isoforms.

RECENT PUBLICATIONS IN CANCER

Shaw TJ & Martin P (2016). Wound repair: a showcase for cell plasticity and migration: Cell dynamics. *Current Opinion in Cell Biology*. 42, pp29-37.

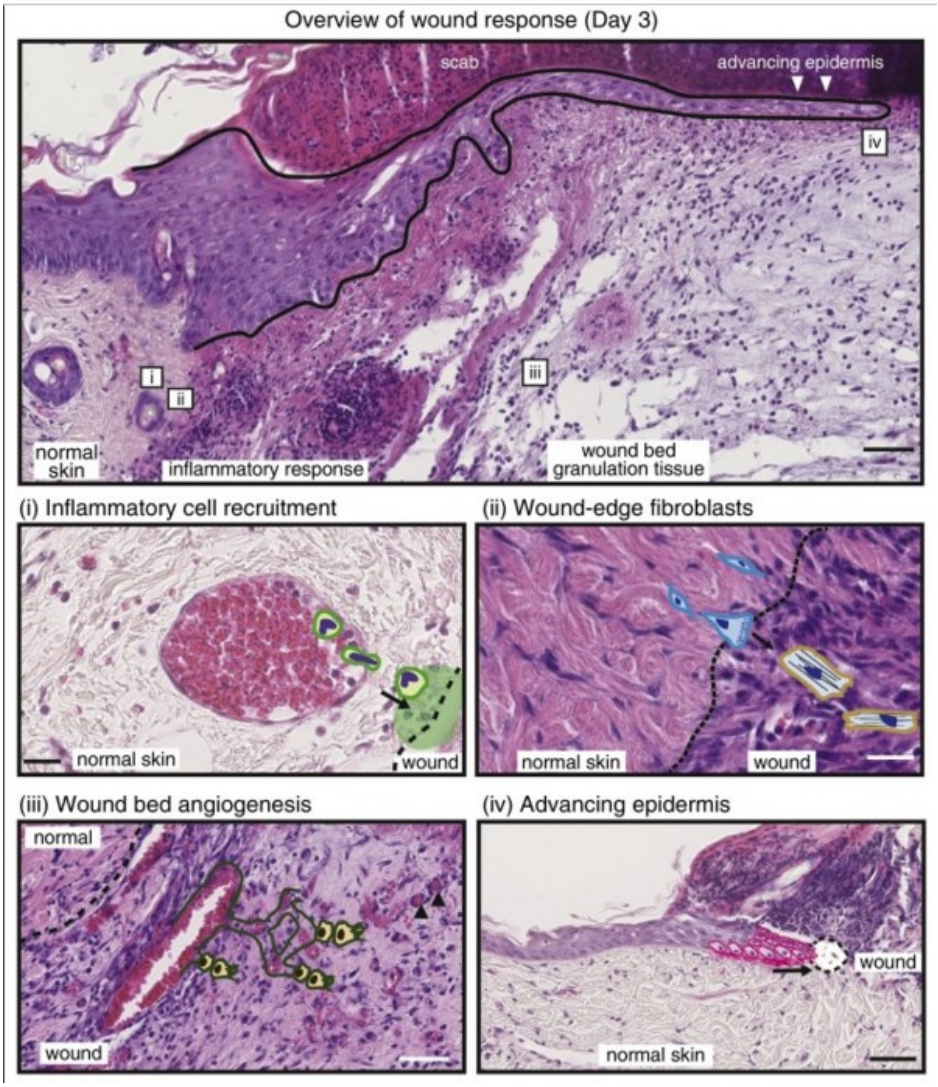
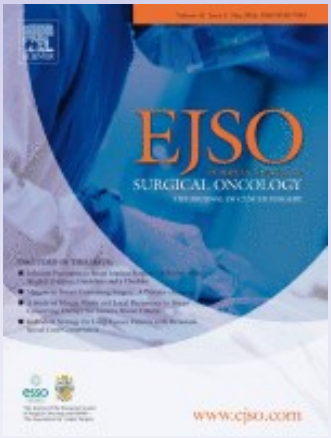


Image caption: *Histological overview of a wound, highlighting dynamic cell populations required for successful repair, Day 3 skin wound histology (H&E, excisional 4 mm wound to the shaved back skin of an adult male mouse). Scale, 50 μm.* ***(i)*** *Wound edge arteriole (Day 1) with wound-polarised adherence of leukocytes to the endothelial wall. Schematic illustrates diapedesis from the vessel and their subsequent migration towards the wound, and potent paracrine influence (green). Scale: 20 μm.* ***(ii)*** *Wound edge dermis of a Day 7 wound. Schematic illustrates dermal fibroblasts acquiring a migratory (blue) and subsequently contractile (myofibroblast — with stress fibres) phenotype. Scale: 50 μm.* ***(iii)*** *Extensive angiogenesis in a Day 5 wound bed (some vessels indicated with arrowheads). Schematic illustrates the branching and sprouting, led by tip cells (green), which results in a transient, dense vascular network in the wound granulation tissue. Scale: 50 μm.* ***(iv)*** *Wound edge epidermis (Day 1 wound — pink cells) migrating across the wound bed, boring a path between the granulation tissue and overlying scab. Schematic illustrates the reduction in keratinocyte cell:cell contacts, the involvement of suprabasal and follower cell, and production of new substratum as they progress. Scale: 50 μm.*

Winters Z, Afzal M, Rumpold G *et al.* (2016). International validation of the EORTC Patient-Reported Outcome Measure (PROM) in breast reconstruction (BRR): Evaluating health related quality of life (HRQL) and clinical



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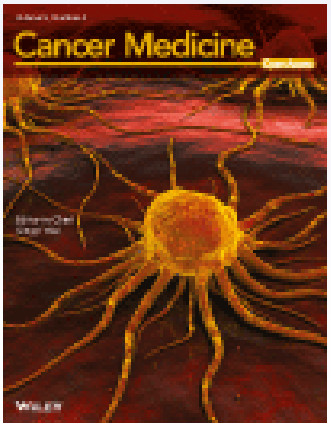

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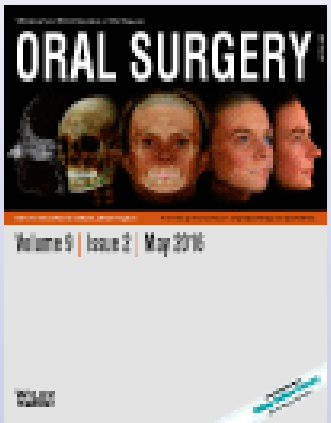

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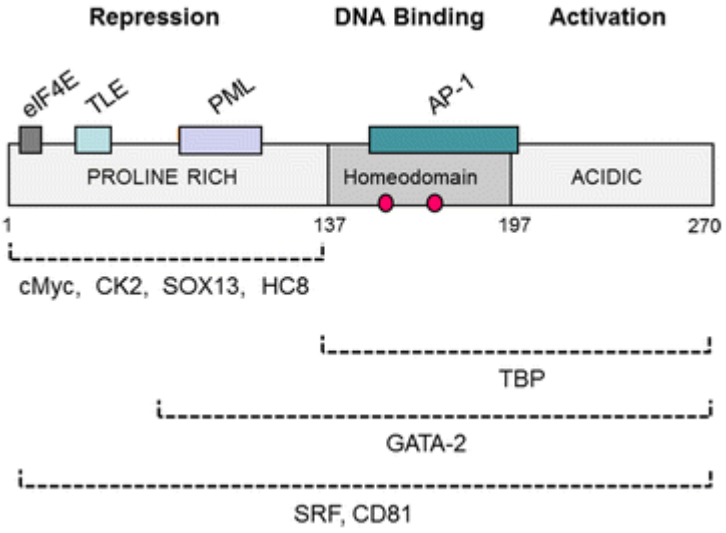

The PRH/HHEX protein and its interacting proteins. A diagrammatic representation of the human PRH protein. The PRH protein has three functional domains. The boxed andbracketed areas represent the regions of PRH that interact with the proteins indicated. Thebrackets indicate poorly mapped interactions. The filled circles represent residues that are phosphorylated by CK2.

Cancer Theme

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Elizabeth Blackwell Institute for Health Research

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Professor of Cell Biology

Theme Co-Lead:

Dr Axel Walther

Senior Lecturer and Head of Research, Bristol Cancer Institute

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- Dr Stephen Falk, *Consultant Clinical Oncologist*
- Dr Elinor Griffiths, *Senior Lecturer*
- Dr Sabine Hauert, Lecturer in Robotics, Engineering Mathematics
- Dr Zoe Holland, RED Facilitator
- Mr Andrew Hollowood, *Surgeon, University Hospitals Bristol*
- Prof Jeffrey Holly, *Professor of Clinical Sciences*
- Miss Ann Lyons, *General Surgery, North Bristol NHS Trust*
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- Prof Richard Martin, *Professor of Clinical Epidemiology*
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- Prof Christos Paraskeva, *Professor of Experimental Oncology and Head of School (Cellular and Molecular Medicine)*
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