There is a wide range of exceptional cancer research taking place in the University. Bristol researchers focus on the cancers that affect the lives of many of our loved ones, including childhood leukaemia, breast cancer, prostate cancer, lung and bowel cancers. The work is spread between many different approaches – ranging from the development of new diagnostic tests and drug treatments through to epidemiological research into what predisposes some people to getting cancer in the first place.

We focus on core strengths in cancer cell biology, genetic and lifecourse epidemiology and health services research, in partnership with Bristol NHS Trusts and the University of West of England.
Core information set for oesophageal cancer surgery

The mainstay of curative treatment for oesophageal cancer is surgery, which may be combined with neoadjuvant chemotherapy or chemoradiotherapy. Although many advances in surgery for oesophageal cancer have occurred over the past decade, long-term outcomes are generally poor and perioperative risks remain high. The risk of in-hospital death after oesophagectomy is between 2 and 4%, with serious complications occurring in about 20% of patients. Surgery also has an immediate major detrimental impact on health-related quality of life. The 5-year survival rate after surgery is in the region of 30–50% and health-related quality of life deficits persist in long-term survivors. The decision to undergo this surgery, therefore, is difficult. It is informed by discussion between surgeons and patients about short-term risks and long-term outcomes. It includes consideration of tumour stage, patient co-morbidities, and surgeon and patient preferences. It is now widely accepted that decision-making between surgeons and patients should be shared, with an exchange of information. Although there is an emphasis for surgeons to provide high-quality information to inform decisions, the actual information provided in consultations is largely unknown; standards for information provision and methods for informed consent for surgery are limited. Indeed, the driver behind many consultations focuses on the medicolegal requirements for surgeons to discuss inherent risks of surgery rather than focus on patient information needs.

Recent surveys in oesophagogastric cancer and other cancer sites have examined patients’ preferences for information. Generally patients prefer more rather than less information. Patients want surgeons to raise sensitive issues (such as prognosis) in consultations rather than having to request this information themselves. The amount of information that could be communicated before surgery, however, is large and it is unclear what information is critical to inform understanding. There may also be a danger of overwhelming patients with data, which may reduce understanding. One method for focused provision of information before surgery is to identify a ‘core information (disclosure) set’ for a specific procedure. Core information represents the minimum information to be given by a clinician in all consultations for a particular operation. The idea of the core information set was described over 30 years ago when ‘core disclosure’ was recommended. It was suggested that a core disclosure set would include information of importance to key stakeholders (patients and surgeons) and be feasible to communicate in a regular clinical consultation. Although a seminal idea, it has received little attention.

This study sought to develop a core information set for surgeons to use in consultations with patients.
before surgery for oesophageal cancer, and consider how it might be used to improve shared decision-making and informed consent.

EVENTS

3rd Annual Congress of the European Society of the Translational Medicine
1 September 2015, 9:00. Vienna, Austria

Metabolism in Cancer and Stromal Cells

Chemoprevention meeting
9 September 2015, 11:00 - 16:00. For details email ann.c.williams@bristol.ac.uk

Pharmaceutical and Biotechnology Industry Event
15 September 2015, 10:00. Wills Memorial Building

One Science: Life at the Interface - Wellcome Trust
22 September 2015, 10:00. Wellcome Collection, London

West of England Academic Health Science Network Annual Conference
15 October 2015, 9:30. Cheltenham Racecourse

Cancer Research UK Integrative Cancer Epidemiology Programme (ICEP) Launch Event and public lecture

Dr Peter Campbell (Head of Cancer Genetics and Genomics, Wellcome Trust Sanger Institute): title tbc
3 December 2015, 16:00. The Seminar Room, Second Floor, Oakfield House

University Hospitals Bristol Research & Innovation Day
4 December 2015, 9:30.

NEWS

The five year Discovery Programme was an initiative between the Universities of Bristol, Cambridge, Bangor, Durham, Oxford, Exeter and Bristol NHS Clinical Commissioning Group. Funded by the National Institute for Health Research (NIHR), the study explored different aspects of the patient journey to a cancer diagnosis. The group’s final recommendations, presented at a symposium held in London on 2 June, suggested that the UK can improve cancer diagnosis in several ways:
Improving patient awareness campaigns resulting in earlier diagnoses and improved patient outcomes

- Bringing patients into the decision making process by explaining risks, investigations and options
- Supplying GPs with data and decision support tools to give them the potential to be more proactive and cancer aware

Programme Manager Dr Jon Banks confirmed that over 20 papers had been published during the project, a number of which have been used by NICE to formulate its guidelines.

Recent Bristol Cancer-related papers:

According to a recent study lead by Dr Matthew Ridd, the time taken to diagnose bowel and lung cancers could be shortened by seeing a different doctor to their regular GP. The study, funded by Cancer Research UK, determined that although seeing a known GP may slightly delay diagnosis, following-up new symptoms with the same doctor was found to result in a quicker diagnosis. The findings highlight a need for more research to establish in what circumstances seeing a different doctor for possible cancer symptoms could potentially speed up the time to diagnosis. Said Matthew, “These findings provide some evidence that GPs should follow up patients who present with potential cancer symptoms to make sure they receive a timely diagnosis. Interestingly, we also found that your regular doctor might not be the best person to spot those symptoms in the first place. So in some cases getting a second opinion from a different doctor could speed up the time to diagnosis.”


The body’s inflammatory response to wounds following cancer surgery or biopsy have found that these procedures may cause growth signals to be delivered to any remaining cancer or pre-cancerous cells which may negatively influence disease progression. Tissue damage has been implicated as a possible trigger in the development of various cancers. Until now, little was known about how local wounding, following cancer surgery, biopsy collection or ulceration, might impact on disease progression. The study, led by researchers from the Universities of Bristol and Aarhus, investigated how inflammatory cells react to cancerous wounds. The team first used zebrafish larvae that were genetically modified to sporadically produce pre-cancerous cells in their skin. They found that their inflammatory cells, primarily a type called neutrophils, were rapidly diverted from wounds to the pre-cancerous cells and this led to increased growth at the pre-cancerous site.
Their results showed the process was dependent upon these inflammatory immune cells and was, at least in part, due to the release of a factor called prostaglandin-E2 derived from the immune cells promoting cancer cell growth, which is, interestingly, a key target of the anti-inflammatory action of aspirin. In an adult Zebrafish model of chronic wounding, they also showed that repeated wounding led to a greater incidence of local melanoma formation.

Led by Professor Paul Martin and funded by the Wellcome Trust, Cancer Research UK and the Biotechnology and Biological Sciences Research Council, the study’s results were published in the *EMBO Journal*.


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**Recent Bristol Cancer grants awarded:**

A multi-centre bid entitled *Understanding the diagnostic pathway for brain tumours in adults and its potential impact on clinical care and outcomes* has been approved by The Brain Tumour Charity. The Bristol leads are Professors Yoav Ben-Shlomo and Will Hollingworth.

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**Congratulations are extended** to Dr Philip Haycock who has been awarded a CRUK Population Research Postdoctoral Fellowship following an interview. Philip will be contributing to the *Integrative Cancer Epidemiology Programme* and will be spending the next three years *Appraising the causal relevance of fatty acids in cancer through two-sample Mendelian randomization*.

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**MINI MD**

The UoB Mini MD programme is a new initiative led by Dr Axel Walther to give early career basic scientist researchers with an interest in cancer an opportunity to learn about clinical issues, treatments and pathways. PhD students beginning basic science programmes related to cancer will spend several half day sessions over a two week period visiting outpatient clinics, surgical theatre sessions and teaching sessions on clinical issues to gain a better understanding of the potential relevance to patients of their current research, help them shape the science questions to be better aligned with clinical issues, and build the relationships with clinicians to drive forward translational research. The programme will be run as a pilot beginning in October 2015, with limited places but with a view to
expanding it in the coming years. There are no costs associated with this programme. PIs with any students expected to start in October 2015 should contact Axel Walther for details.

**FUNDING OPPORTUNITIES**

A calendar of potential funding opportunities for Cancer has been set up via Research Professional which details the funding opportunity according to submission deadline for the whole year. This calendar is accessible via their website and will be updated automatically according to the search criteria for Cancer Studies and Oncology. Other areas can be added by request- please email the theme with suggestions and/or comments.

**EPSRC funding changes**
The EPSRC have updated their on-going refresh of priority areas for Fellowships. For Healthcare Technologies please note the following expected calls: Fellowship call to be announced (August - September 2015); a pilot call for Healthcare Technologies Fellowships aligned to their recently published strategy (early and established career stage). To be removed, effective from 01-Oct-15 are: Regenerative Medicine (early and established career stage); Diagnostics (early and established career stage); Therapeutics (early and established career stage).

**Cancer Research UK**

**Pioneer Award**
A new rapid-response scheme for high risk-high reward ideas that would not normally be funded through existing mechanisms. Funding is on the quality of the idea and applications can be from anyone regardless of career stage. Projects supported by the Award will have a clear relevance to cancer and enable the exploration of novel ideas, which may lead to new discoveries or approaches. Research proposals will highlight that they are tackling a problem that could currently be considered intractable, and that have the potential to be paradigm shifting in cancer research. Funding for clinical trials will not be considered. The Pioneer Award is not intended to support preliminary data gathering and/or proof-of-principle studies.
Award Amount: £200,000  Deadline: none

**Institut Curie**

**Foreign postdoctoral fellowships**

Enable young postdoctoral researchers to conduct cancer research in one of the institute’s laboratories for up to one year.

Award amount: unspecified  Deadline: none

**Medical Research Council**

**Discovery awards**

Support discovery research in areas with potential for development, which are strategically sound within the institution’s strategy and are important nationally. Applicants are encouraged to explore how awards could be used to develop interdisciplinary interactions, for example by linking with physical sciences, mathematics and social sciences.

Awards support recruitment or initial development of new PIs at junior or senior levels, or linked pilot work or technology and methods development. Institutions are expected to initiate and build critical mass and capacity in otherwise underexplored, high-potential areas of research, which may not yet compare to more established fields but have a clear vision for development.

Award amount: £1M  Deadline: 10-Aug-15, please note this falls under the University’s Major Bids process, internal deadline 29-Jun-15.

**Cancer Research UK**

**Phase III Clinical Trials Grants**

Support studies for cancer treatment directed at the tumour, such as chemotherapy, radiotherapy and surgery, with the principal objective of improving survival. The clinical trials awards and advisory committee accepts investigator-led studies including phase III/IV therapeutic trials and large-scale phase II trials that are over four years in duration or greater than £150,000 per year.

Award amount: £100,000  Deadline: 29-Jul-15

**Cancer Research UK**

**Prospective sample collections project grants**

Support prospective collections of samples associated with clinical trials as well as strategy enabling sample collections. Only funding for the collection of blood and paraffin tumour blocks is available. Under exceptional circumstances, where specific justification is provided, funding for the collection of
additional sample types will be available. Funding is available for up to 10 years. Sample collection with a guide price of £15 per paraffin block and £7.50 per blood sample is supported.

Award amount: see text  Deadline: 29-Jul-15

**Cancer Research UK**

**Feasibility study project grants**

Fund investigator-led 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, however, industry-sponsored trials cannot be reviewed under this scheme.

Award amount: £150,000  Deadline: 29-Jul-15

**GW4**

**Initiator Fund** - for workshops, sandpits or other community building or collaborative activities. This can be used as a stand-alone award or could be a step towards other funding sources.

**Accelerator Fund** - for collaborative pump priming activities which will normally position the community to win major external funding and/or measures of academic esteem. Applicants for the Accelerator Fund will either have successfully completed the Initiator stage or provided evidence of recent activities that have enabled the scoping of research ideas to a level appropriate for direct submission to the Accelerator Fund.

A GW4 research community should involve at least three GW4 institutions, with communities involving all four partners preferred. Where less than four are involved this will need to be justified. Each application will need to articulate the added value of working across GW4.

Award amount: unspecified  Deadline: 31-Jul-15

**Leukaemia & Lymphoma Research**

**Clinician scientist award**

Enables PhD-qualified haematologists in training to combine postdoctoral research with the completion of specialist training. Applicants are asked to contact the Research Director prior to submitting an application.

Award amount: specialist registrar grade  Deadline: 01-Aug-15

**Cancer Research UK**

**Early diagnosis advisory group grants**
Support policy relevant research or activities that are adding to the scientific evidence base to achieve earlier cancer diagnosis and enable access to treatment. Proposals should address one of the following four topic areas:

- assessment of the impact of new National Institute for Health and Care Excellence guidance
- empowering patients to seek help and describe their symptoms
- evidence to inform future public awareness and behaviour campaigns
- alternative routes to diagnosis

Collaborations, including international ones, are encouraged, as are proposals that use innovative, multidisciplinary and rapid approaches using pre-existing data sources are encouraged.

Grants are worth up to £100,000 per year for a maximum period of 18 months.

Award amount: £100,000  Deadline: 14-Aug-15

**Children with Cancer**

**Project grants**

Awarded for any research project which addresses one or more of the following specific research objectives:

- to improve knowledge of the genetic and environmental causes and relevant biological mechanisms of childhood cancer
- to identify diagnostic and prognostic biomarkers for childhood cancer
- to 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
- to understand the long-term health implications of childhood cancer and its treatment

International collaborations will be considered but researchers from the UK must hold a leading role.

Grants may be used to fund staff costs, and the purchase of equipment and consumables.

Award amount: £250,000  Deadline: 20-Aug-15 (expected)

**Cancer Research UK**

**Research bursaries for clinicians and professions allied to medicine**

Provide short-term funding to allow clinicians and other health professionals to get involved in research projects early in their career. Clinicians, nurses, health professionals and pre-PhD candidates of any nationality may apply, but they must have been resident and working in the European Economic Area for three years immediately before application and intend to pursue a medical career in the UK.

Award amount: £25,000  Deadline: 21-Aug-15

**Cancer Research UK**

**New agents committee preclinical combination grants**
Support preclinical *in vitro* and *in vivo* studies of new drug combinations, including novel combinations with radiotherapy and established drugs. The output of the grant should be *in vitro* and *in vivo* combination data supporting a clinical trial of the novel combination therapy in cancer patients. The applicant or one of their team members should be a clinical investigator with relevant early clinical oncology trials expertise.

**Award amount:** £50,000  
**Deadline:** 25-Aug-15

**Cancer Research UK**  
**Preclinical combination grants**  
Fund preclinical *in-vitro* and *in-vivo* studies of new drug combinations, including novel combinations with radiotherapy and established drugs for cancer patients. Applications are open to non-clinical researchers, established independent researchers, clinicians and early-career researchers. At least one of the members in each team must be a clinical investigator with relevant early clinical oncology trials experience.

**Award amount:** £50,000  
**Deadline:** 25-Aug-15

**Bayer**  
**Grants for targets**  
The initiative aims to encourage research on novel targets and disease-related biomarkers in the fields of oncology, gynecology, cardiology, hematology and ophthalmology. The following different types of grants, depending on the specifics of the target and its development phase will be awarded: support grants worth between €5,000 and €10,000 will be awarded to advance research on targets that are at a very early stage of discovery; focus grants worth between €10,000 and €125,000 will be awarded for more mature ideas, such as addressing specific aspects of a target as a first step towards transferring it to the drug discovery process. Researchers from universities, other academic research institutes and start-up companies from all over the world are welcome to apply.

**Award amount:** €125,000  
**Deadline:** 31-Aug-15

**Cancer Research UK**  
**Multidisciplinary project award**  
Supports collaborations between cancer researchers and scientists from engineering or physical science disciplines. The research themes within remit for this award include:

- direct application of physics, engineering, chemical or mathematical concepts to address the underlying physical processes of cancer, including tumour initiation, growth and metastasis;
- development and translation of technologies for direct applications in, or a clear path to, a direct application in the prevention, diagnosis or treatment of cancer.
The award is awarded jointly to principal investigators from engineering or physical science disciplines, and PIs who are working in cancer research. Applications should ideally include a minimum of two PIs working in distinct scientific disciplines, at least one PI working in cancer research at any career stage, and at least one PI from an engineering or physical science discipline at any career stage.

Award amount: £500,000 Deadline: 01-Sep-15

**Cancer Research UK**

**Career development fellowship**

Offers outstanding scientists support to set up their first independent cancer research group. Applications will be considered from any area of CRUK’s funding remit, with the exception of end-of-life care and clinical trials. Funding support is provided for salaries for the fellow, one postdoctoral researcher and one technician, as well as for associated running expenses and equipment costs up to £25,000.

Award amount: unspecified Deadline: 15-Sep-15

**Cancer Research UK**

**Career establishment awards**

Support new group leaders in enhancing their cancer research. Applicants must be the sole principal investigator for their project. The awards support salaries and associated running expenses for one postdoctoral researcher and one technician, and equipment costs up to £25,000, over a maximum duration of six years.

Award amount: unspecified Deadline: 15-Sep-15

**Wellbeing of Women**

**Research training fellowships**

Designed to further the training of medical graduates embarking upon a career in obstetrics and gynaecology. Fellowships will support training in basic science, clinical or translational research in topics which include gynaecological cancers. Fellows will normally be expected to enrol for a higher degree. It is hoped that applicants will be based in a department that has at least a silver Athena Swan award.

Fellowships are tenable for up to three years and must be undertaken in the UK or Ireland. Funding will cover the cost of a full-time salary at specialist registrar level or equivalent, as well as registration fees for a higher degree.

Award amount: £200,000 Deadline: 19-Sep-15 (expected)
Dutch Cancer Society – KWF Kankerbestrijding

Unique opportunities
Support both breakthrough research projects and unique high-risk research projects on oncology that aren’t financed through regular research instruments.

Two types of grants are available: unique breakthrough projects grants – for projects with high potential to lead to a breakthrough in cancer research that do not fit in any of the current KWF grant programmes; unique high-risk project grants – for innovative projects that are mainly based on theoretical findings and that have the potential to lead to a breakthrough in cancer research.

The main applicant should be appointed at the Dutch institute where the programme will be implemented for its entire duration and have extensive research experience and a proven track record within the relevant fields. Collaboration with third parties is encouraged. For breakthrough projects collaborating with international parties is allowed, however foreign institutions may not act as the main applicant. Both types of research must mainly be undertaken in the Netherlands.

Award amount: €150,000 for high-risk; no limit for breakthrough          Deadline: 21-Sep-15

Bone Cancer Research Trust

Research fellowships
For individuals committed to a career in academic clinically related research in bone cancers. They support a specific clearly described piece of research in collaboration with a recognised researcher in the field. Joint applications are expected from supervisors and candidates.

Award amount: £225,000          Deadline: 26-Sep-15 (expected)

UHBristol

Small grants scheme
Research Capability Funding is designed to lead on to future NIHR applications. Above and Beyond funding can be earlier stage more translational research, though should (eventually) be of benefit to UHBristol patients. They are open to university-based researchers, as long as they collaborate with a UHBristol employee, or have an honorary contract with UHBristol.

Award amount: €250,000          Deadline: Oct-15 (exact date tbc)

World Cancer Research Fund International

Regular grant programme
Provides funding for research on the link between diet, nutrition, body composition, physical activity, and cancer prevention and survival. Two types of grants are available:

- investigator initiated grants, worth a maximum of £250,000 for up to four years
- pilot grants worth up to £60,000 for up to two years
Grants are awarded to principal investigators based at institutions in any country outside the Americas. International collaborations and applications from low and middle income countries are particularly encouraged.

Award amount: £250,000  Deadline: 09-Oct-15

**Cancer and Polio Research Fund**

**Research Grants**
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.

Award Amount: not specified  Deadline: 15-Oct-15

**Cancer Research UK**

**Population research committee project grants**
Support projects that address clinical and public health epidemiology, educational and behavioural research in areas of prevention, screening and early diagnosis, clinical trials methodologies or statistics, and secondary physical effects of treatment.

Award Amount: £100,000  Deadline: 15-Oct-15

**Cancer Research UK**

**CRUK and Bupa Foundation Cancer Prevention Fund**
Supports postdoctoral researchers and healthcare professionals who conduct research into behavioural and lifestyle changes that can prevent people from getting cancer. Applications must have the potential to be translated into practice or influence policy.

Award Amount: not specified  Deadline: 23-Oct-15

**Worldwide Cancer Research**

**Project grants**
Support fundamental and translational research into the causes, mechanisms, diagnosis, treatment and prevention of cancer.

Award Amount: £250,000  Deadline: 31-Oct-15
Leukemia and Lymphoma Research
Bennett Fellowships
Awarded to outstanding clinical and non-clinical qualified postdoctoral researchers to establish themselves as independent investigators in any aspect of haematological research relevant to the charity’s mission. Fellowships are up to five years in duration together with one research assistant or postdoctoral post.

Award Amount: not specified                           Deadline: 01-Nov-15

Bowel and Cancer Research
Small grants
Support research projects that provide proof-of-principle preliminary data such that applicants can use the findings to apply for more funding from a national public funder. The aim is to fund research to save lives and improve the quality of life of individuals diagnosed with bowel cancer or other bowel conditions or functional problems. The project must focus on a specific research question that delivers patient benefit. At least one grant will be awarded for a cancer-related subject. Research should be within experimental medicine, innovation or clinical trials.
Grants are worth up to £50,000 over a maximum period of 18 months. Overhead or other indirect costs will not be supported.

Award Amount: £50,000                           Deadline: 07-Nov-15 (expected)

Cancer Research UK
Cancer Immunology Project Awards
Applications can be in any area of immunological research, providing the cancer relevance is clearly articulated in the proposal, including any of the following key areas:

- Cellular and molecular immunology, including but not limited to mechanisms of tolerance; the regulation of immune function, and; the development of memory
- Inflammation, allergy, transplantation and auto-immunity (how the basic understanding of relevant mechanisms involved could drive forward our understanding of cancer)
- The immune response to infection
- The interaction of immune cells with tissues
- Immunity and disease susceptibility/resistance

This award does not support the development of new biotherapeutics or immunomodulatory agents.

Award amount: £300,000                           Deadline: 10-Nov-15
Cancer Research UK

Clinician scientist fellowship

This enables scientists to develop their clinical academic research career. The fellowship provides salaries for the fellow and one research assistant, and associated running expenses for up to four years.

Award amount: Not specified  Deadline: 20-Nov-15

PUBLICATIONS


Image caption: src42A Is Required Specifically and Autonomously for Macrophage Wound Responses in Drosophila Embryos. (A) Stills and trajectories of red-stinger-labeled macrophages taken at 20 min after wounding from movies of inflammatory responses to wounds in control and src42AE1 mutant embryos. (B) Scatterplots of directionality toward the center of wounds and average speed (per macrophage, per embryo) during wound responses show that macrophages in src42AE1 mutants essentially ignore wounds (B’) but that their ability to move at normal speeds is unaffected (B”). (C) Representative stills of GFP-labeled macrophages (green) at wound sites at 20 and 60 min after wounding in control embryos and embryos expressing a dominant-negative version of Src42A in macrophages. (D) Scatterplot of wound responses shows numbers of macrophages per μm2 of wound area normalized according to control averages. Scale bars represent 20 μm. Central lines and error bars on scatterplots represent mean and SD, respectively; ns, not significant; *p < 0.05 and **p < 0.001 via Mann-Whitney test (B) or one-way ANOVA followed by Sidak’s multiple comparisons test (D); Mϕ, macrophages; white ovals depict wound edges.


Image caption: This study reveals how innate immune cells, in particular neutrophils, that are initially drawn to a wound can subsequently be attracted away to nearby early- and late-stage cancer cells and drive their proliferation. Both chronic and acute wounds exacerbate cancer growth; tissue damage in larval zebrafish, or cancer surgery in adults, draws in neutrophils and macrophages; neutrophils are recruited from wounds to nearby pre-neoplastic cells and deliver trophic signals; neutrophil presence correlates with tumour cell proliferative index and indicates poor prognosis in ulcerated human melanoma.


CONTACTS

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- Zoe Holland - Research Development Manager for the Faculty of Medical and Veterinary Sciences

Steering Group:

Theme Lead:
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Theme Lead:
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- Dr Elinor Griffiths, Senior Lecturer
- Mr Andrew Hollowood, Surgeon, University Hospitals Bristol
- Professor Jeffrey Holly, Professor of Clinical Sciences
- Miss Ann Lyons, General Surgery, North Bristol NHS Trust
- Dr Nick Maskell, Reader in Respiratory Medicine
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