Join us at the 2015 NCRI Cancer Conference

The largest cancer research meeting in the UK

Meet experts including:
Amy Abernethy (USA)
Anna Barker (USA)
Malcolm Brenner (USA)
Kristian Helin (Denmark)
Tim Hunt (UK)
Carl June (USA)
Charles Sawyers (USA)
Dennis Slamon (USA)
Harald zur Hausen (Germany)

Key dates

30 March – 5 June
Abstract submission

13 April – 31 July
Earlybird registration

3 August – 26 August
Late breaking abstract submission

1 August – 25 September
Standard registration

Programme and Exhibition Guide 2014

2–5 November 2014
BT Convention Centre, Liverpool, UK
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The Scientific Committee and organising team are grateful to all the NCRI partners for their continuing commitment to the concept of a multidisciplinary cancer conference and for their financial support.

NCRI Partners

- Association of the British Pharmaceutical Industry
  www.abpi.org.uk
- Biotechnology and Biological Sciences Research Council
  www.bbsrc.ac.uk
- Breakthrough Breast Cancer
  www.breakthrough.org.uk
- Breast Cancer Campaign
  www.breastcancercampaign.org
- Cancer Research UK
  www.cancerresearchuk.org
- Chief Scientist Office, Scottish Government Health Directorates
  www.cso.scot.nhs.uk
- Children with Cancer UK
  www.childrenwithcancer.org.uk
- Department of Health
  www.dh.gov.uk
- Economic and Social Research Council
  www.esrc.ac.uk
- Leukaemia & Lymphoma Research
  www.leukaemialymphoma-research.org.uk
- Ludwig Institute for Cancer Research
  www.ludwig.ox.ac.uk
- Marie Curie Cancer Care
  www.mariecurie.org.uk
- Macmillan Cancer Support
  www.macmillan.org.uk
- Medical Research Council
  www.mrc.ac.uk
- National Institute for Social Care and Health Research
  www.nischr.org.uk
- Northern Ireland Health & Social Care - R&D Office
  www.publichealth.hscni.net
- Prostate Cancer UK
  www.prostate-cancer.org.uk
- Roy Castle Lung Cancer Foundation
  www.roycastle.org
- Tenovus Your Cancer Charity
  www.tenovus.org.uk
- The Wellcome Trust
  www.wellcome.ac.uk
- Worldwide Cancer Research
  www.worldwidecancerresearch.org
- Yorkshire Cancer Research
  www.yorkshirecancerresearch.org.uk

Join us next year: 1–4 November 2015
conference.ncri.org.uk
Map of the BT Convention Centre

Side view of venue

Cityside entrance: hotels and car parking

Registration area

Riverside balcony

Exhibition, poster sessions, Spotlight Theatre, social media hub and refreshment area

Riverside entrance

First floor

Plenary lectures

Hall 2

Registration area

Hall 1A

1B

1C

Download the app for the latest updates
Welcome

Message from the Chair and Director of the National Cancer Research Institute

On behalf of the NCRI Partners, we are pleased to welcome you to Liverpool.

The NCRI is a partnership of UK cancer research funders who, collectively, spend more than £500m on cancer research in the UK each year. By working together to help coordinate and collaborate on research, we ensure that these funds are used to the best effect.

What's special about the NCRI is that we bring together a broad range of Partners that cover the entire spectrum of cancer research. We coordinate and collaborate on a number of different initiatives in response to areas of need. No two initiatives are the same; each involves different groups of funders, addressing different types of challenges and often in many different ways. Please make sure you find time to visit our stand in the Exhibition Hall and hear more about our work.

In many ways the NCRI Cancer Conference epitomises what we do. It brings together colleagues like you from across the research spectrum – from basic to translational and indeed clinical research – from a variety of institutions to learn, share best practice and forge new collaborations.

With a record number of abstracts submitted, this 10th Conference promises to showcase more research than ever before: we encourage you to make the most of this opportunity. This year, we have received generous support towards even more prizes for excellent research than in the past. The new Spotlight Theatre, located directly in the exhibition hall, will host many prize winners, all showcasing their latest research. The Spotlight Theatre programme on page 16 – and indeed the new Conference app - contains more details of these sessions.

This 10th Conference gives us an occasion to reflect: a retrospective highlighting key milestones and the impact of the Conference has been set up in the Galleria on the ground floor. We hope it inspires you. Please join the scientists who have already shared their thoughts and add your views to the board.

Our utmost gratitude goes to colleagues on the Scientific Committee for putting together the stimulating programme you are about to experience, and of course the speakers themselves who have travelled from all over the world to come and speak in Liverpool. Last but not least we must acknowledge the NCRI Partners, Sponsors and Exhibitors whose enduring support allows us to maintain the Conference’s excellence.

Have a great Conference

Dr Harpal S Kumar
Chair, National Cancer Research Institute

Dr Karen Kennedy
Director, National Cancer Research Institute
On behalf of the Scientific Committee, I am thrilled to welcome you to the 10th NCRI Cancer Conference. There could not be a more befitting place than the cosmopolitan and vibrant city of Liverpool to host the myriad of cancer researchers you are about to hear from.

The multi-disciplinary programme we have put together features the most recent and exciting scientific developments from around the globe and from across the research spectrum. Whether you are a basic, translational, clinical scientist or work in any other cancer research speciality, it will be tempting to just join sessions that focus on your area of practice. I urge you to be brave and look beyond the boundaries of your daily research and engage with fellow participants from other disciplines and other institutions.

The new ideas, new friendships and new collaborations that you will generate are really what make this Conference unique. Along with many of us who have attended several NCRI Cancer Conferences, I know you will feel reinvigorated, and go home on Wednesday ready to continue the fight against cancer for the benefit of patients.

Over the next few days, you will have a choice between more than 150 speakers from across the globe, more than 800 abstracts and more than 60 stands to visit. To mark the 10th Conference, the Scientific Committee have made a special effort to design a programme which looks back on achievements and reflects on future opportunities. Different types of sessions – plenaries, symposia, parallel sessions, workshops – should keep the discussions upbeat. Use the Conference app to schedule which sessions to attend, which posters to see and which stands to visit.

Following the success of the past two years, Tuesday will again see sessions programmed in association with the Royal College of Radiologists. It will also be the day for the ever-popular Clinical Trials Showcase which provides updates on practice-changing trials. And for the fifth year in a row, also on Tuesday, we will welcome around 50 A-level students from local schools to further their understanding of research and inspire the next generation to follow a career in science.

I am grateful to all speakers from around the globe who will make this 10th NCRI Cancer Conference a very special one. And of course to all my colleagues on the Scientific Committee for their continuing support and dedication to crafting this exciting programme. I am also very grateful to the NCRI team for making organising this conference both fun and easy and for keeping me on track.

Have a great Conference.

Professor Richard Marais
Chair, 2014 Scientific Committee
Director, Cancer Research UK Manchester Institute, UK

PS: Make sure you share your experience with colleagues back in your institutions and indeed with the wider scientific community. If you are on Twitter, remember to use #NCRI2014 – the best tweet wins a prize.
The NCRI is grateful to the Scientific Committee for their support in developing the programme and maintaining the high standards of this Conference.
Support grants are provided towards the 2014 programme, which has been designed independently by your peers (see Scientific Committee on page 10).

Almac  
AstraZeneca  
Bayer  
Braintrust  
Brain Tumour Research  
Breakthrough Breast Cancer  
Bristol-Myers Squibb**  
British Association of Cancer Research  
British Association of Surgical Oncology  
Cancer Research UK  
Cancer Research UK and Manchester Institute  
Cancer Research UK and Medical Research Council  
Oxford Institute for Radiation Oncology  
Celgene  
Children’s Cancer and Leukaemia Group  
European Association for Cancer Research  
Lilly  
Manchester Cancer Research Centre  
Medical Research Council  
National Institute for Health Research  
NIHR Clinical Research Network: Cancer  
Nature Reviews Clinical Oncology  
SIRT UK Network  
Pancreatic Cancer Research Fund  
Pancreatic Cancer UK  
Pfizer Oncology  
Prostate Cancer UK  
Teenage Cancer Trust  
The Company of Biologists  
The Institute of Cancer Research  
The Royal College of Radiologists  
Randox  
Roche  
Sanofi  
Wellcome Trust

* Amgen Oncology has provided sponsorship for this conference. Amgen Oncology has a stand at the conference and a symposium but has had no input into the main programme, topics or awards.
** Satellite Symposium sponsored by Bristol-Myers Squibb

Join us next year: 1–4 November 2015  
conference.ncri.org.uk
Useful information

A retrospective – celebrating the 10th NCRI Cancer Conference
This year’s 10th Conference is an opportunity to reflect about the past and look forward to what will shape the future of cancer research. The retrospective exhibition in the Galleria presents views from fellow scientists and researchers; it is meant as an invitation for you to share your thoughts too – whether publicly via the interactive boards, on twitter or indeed in person with fellow participants.

Accommodation
For accommodation enquiries, please visit the Accommodation desk in the registration area.

Browsing abstracts
All abstracts are available to view on the Conference app and online at http://conference.ncri.org.uk/abstracts/2014

Car parking
Convenient parking is available opposite the BT Convention Centre at a cost of £12 per 24 hours.

Choose your session
While every attempt has been made to put popular sessions in large rooms, some sessions may be oversubscribed on the day. Entry is on a first come first served basis, so please arrive early at your chosen session.

As a courtesy to speakers and other delegates, please remember to turn off your mobile phone before entering the lecture halls.

Please wear your delegate badge at all times while at the venue and social events.

Cloakroom and lost property
A cloakroom is provided at the entrance of the BT Convention Centre. NCRI does not accept any liability for lost property. Please visit the BT Convention Centre helpdesk in the entrance to report or reclaim lost property.

CPD certificates
The 2014 NCRI Cancer Conference has been approved by the Federation of Royal Colleges of Physicians for 24 category 1 (external) CPD credits. Please complete the appropriate section of the electronic Conference survey to request your certificate. Certificates will only be sent electronically and may take up to 10 working days.

Exhibition hall
The exhibition runs from Sunday 2 November to Tuesday 4 November in Hall 2 of the BT Convention Centre. Exhibitors contribute significantly to the financial sustainability of the Conference. Please make sure you visit relevant exhibitors and acknowledge their support. A full list and a map are provided from page 162 of this book.

Download the NCRI Cancer Conference app
Keep up to date and connected throughout the event by downloading the NCRI Cancer Conference app.
- View the agenda and explore sessions
- Build your personalised schedule
- Browse and search abstracts
- View maps of the venue
- See who is exhibiting and visit them at their stands
- Networking options
- Make notes on the app and email them to yourself

For help with downloading or using the app, ask at the General Enquiries desk.

Feedback
Your feedback helps us tremendously when planning future Conferences. Please take a few minutes to complete the online survey, which will be sent to you after the Conference.

If you want to leave feedback immediately, please contact the General Enquiries desk.

Download the app for the latest updates
General enquiries
Please visit the General Enquiries desk situated in the registration area between Sunday 2 and Wednesday 5 November, where NCRI Cancer Conference staff will be happy to help. Contact us on +44 (0)151 707 4640. Out of Conference hours, please call: +44 (0)7852 651 451 or +44 (0)7539 477 109.

Messages
A message board is available in the main registration area. To leave a message with the Conference staff, please call +44 (0)151 707 4640.

Press office
The Conference press office is located in Room 5 on the first floor. To contact the press team, please call: +44 (0)151 707 4642/4643/4644/4645. Out of Conference hours, please call: +44 (0)7050 264 059.

Passport competition
Your bag contains a passport competition book. Once your book has been stamped by all of the participating exhibitors, drop it into the competition box situated outside Hall 2 on the Exhibitors Helpdesk for a chance to win some great prizes.

Recycling facilities
The BT Convention Centre is one of the most eco-friendly meeting venues in the UK. Please use the facilities provided to recycle paper. If you wish to recycle your bag, badge and lanyard, pass them to the Conference staff.

Registration
Registration is situated on the first floor and is open:
- Sunday 2 November 13.00–19.30
- Monday 3 November 07.45–19.30
- Tuesday 4 November 07.45–19.30
- Wednesday 5 November 08.15–13.00

Poster sessions
Posters must be put up by 08.30 on the day of your poster session and remain on your poster board until 17.40.

Posters are available for informal viewing throughout the allocated day of their presentation. Presenters are encouraged to provide handouts for when they are not present to speak to participants.

To avoid overcrowding during the poster presentation times, poster presenters are asked to stand with their posters for only half of the session as noted in the timetable below:

**Poster session A: Monday 3 November**
- Odd number posters: 12.30 – 13.20
- Even number posters: 13.20 – 14.10

**Poster session B: Tuesday 4 November**
- Odd number posters: 12.30 – 13.20
- Even number posters: 13.20 – 14.10

Posters must be taken down by 16.30 on the allocated day, as posters left up after this time will be removed. The Conference team is not responsible for storing posters that have been removed.

Taxis
A taxi rank is situated on the riverside entrance of the BT Convention Centre. Alternatively, please call +44 (0)151 298 2222 or +44 (0)151 207 2222.

Twitter competition
Let’s get NCRI trending. Use #NCRI2014 to tweet your experiences, thoughts and highlights of the Conference. Follow us @NCRI. The best tweet of the Conference will win a prize.

Join us next year: 1–4 November 2015 conference.ncri.org.uk 13
Choosing the right session

Plenary lectures
These feature experts from the UK and overseas, invited by the Scientific Committee to give plenary lectures. All have been briefed to give talks that are accessible to a diverse scientific audience. Their talks may address a broad area of work, summarise their own research, or discuss an important area of policy relating to cancer. There are plenary lectures on each of the four days of the Conference.

10th Conference celebratory talks
Two special sessions on Monday 3 and Tuesday 4 November have been designed by the Scientific Committee to allow us to take a closer look at progress over the past ten years and future possibilities in key areas of cancer research.

Clinical Trials Showcase
The Scientific Committee select abstracts on clinical trials from those that are submitted. Trials selected for presentation in the Clinical Trials Showcase are often practice-changing, of high quality and/or are presenting new data.

Symposia
Each symposium comprises three talks from speakers of international standing around a broad theme. The aim is to consider one topic from three different angles, with a mix of disciplinary approaches. A symposium may cover basic, translational and clinical research, or it may reach into areas such as social and behavioural studies, as well as approaches to prevention. Symposia should help you to see your own work within a broader context of studies beyond your own expertise.

Parallel sessions
These more specialist sessions mainly attract professionals in the areas on which they focus. On each day there will be one parallel session intended to be accessible to a lay audience, though professionals frequently attend these sessions too. Parallel sessions cover a range of themes; see page 15 for further information.

Workshops
Workshops are organised on a demand-led basis and vary somewhat in format. Some are educational or commercially-led training sessions, while others debate a hot topic or discuss the availability of research resources such as biosamples or datasets. Workshops are intended to include much more audience participation and are essentially discussion forums.
Session themes

**Diagnosis and therapy**
Screening technologies and diagnostic markers. Estimation of prognosis and identification of individuals at increased risk of cancer.
Factors associated with stage of diagnosis and clinical outcome.
All types of therapy and all phases of development and testing.

**Epidemiology and prevention**
Population-based research aimed at understanding causation, incidence, trends, and risk (such as environmental and genetic risk).
Research on prevention e.g. lifestyle and nutritional factors, including individual and community interventions.

**Health services research**
Quality and cost of healthcare and coordination of care.
Development and testing of healthcare delivery methods.
Access to healthcare including primary care and screening services.

**Information, patients and the public**
Public policy issues, ethics and confidentiality.
Education and communication about cancer.
Involvement of patients and public in deciding research priorities.
Patient-led research.

**Survivorship and end-of-life care**
Living with and beyond cancer: physical, psychological and social impacts and their management.
Research into care at the end of life.

**The cancer cell and model systems**
Molecular and cellular mechanisms of oncogenesis and tumour suppression.
The tumour microenvironment.
Cell biology relevant to cancer.

**Tumour-specific research**
Tumour-specific research, including basic, translational, and clinical approaches.
Research applied to specific patient groups, such as paediatric patients, and older people with co-morbidities.
New for 2014: Spotlight Theatre

Located directly in the exhibition hall, the new Spotlight Theatre will showcase featured products, services and excellent science.

On Sunday, you will benefit from special presentations by some key exhibitors. On Monday and Tuesday, the Spotlight Theatre will showcase research by a number of prize winners, as well as talks of general interest.

Programme at a glance

**Sunday 2 November**

18.30 – 18.50 Teenage Cancer Trust Stephen Sutton Prize: Final results from the QUASAR2 trial, a multicentre, international randomised phase III trial of bevacizumab and capecitabine in the adjuvant setting of colorectal cancer (CRC)

19.00 – 19.30 Integrated DNA Technologies: Superior sequencing coverage and uniformity in affordable gene panels that you can customise

**Monday 3 November**

10.30 – 10.45 ACP McElwain Prize: A neoadjuvant window study of metformin's effects on breast cancer metabolism

12.30 – 13.00 British Association of Surgical Oncology (BASO) Surgery Prize and Cancer Research Excellence through Surgical Trials (CREST) Award

13.00 – 13.30 British Association of Cancer Research (BACR) AstraZeneca Young Scientist Frank Rose Award: Genome analysis of clonally transmissible cancers in dogs and Tasmanian devils

15.45 – 15.55 ACP McElwain Prize: RORyt+ innate lymphoid tissue inducer cells promote lymphatic invasion in triple negative breast cancers


19.30 – 20.00 Trends in pathology and The Royal College of Pathologists prize

**Tuesday 4 November**

10.30 – 10.45 Macmillan Cancer Support: Using Macmillan and NCIN's Local Cancer Intelligence tool to inform regional improvement

12.45 – 13.45 The Royal College of Radiologists proffered paper presentations

Download the app for the latest updates
The Royal College of Radiologists at the Conference

The Royal College of Radiologists (RCR) is delighted to be working with the NCRI for the third consecutive year, delivering sessions by a world-class faculty to the 10th NCRI Cancer Conference on Tuesday 4 November. Join your RCR colleagues for these talks. See the full programme for Tuesday from page 80.

12.20 – 14.10, Hall 2
Poster viewing, including a dedicated radiotherapy and radiobiology section. Download the app for full details.

12.45 – 13.45, Spotlight Theatre
Proffered paper session
One of the presentations in this session will be awarded an RCR Ross Prize for the best oral presentation, as judged by an RCR judging panel.

14.10 – 15.40, Room 3B
High precision radiation therapy
Hosted by Diana Tait, The Royal Marsden NHS Foundation Trust, London, UK and The Royal College of Radiologists

Introduction by the host

Stereotactic ablative radiotherapy (SABR): a local therapy poised to fight metastatic cancer
Robert Timmerman, University of Texas Southwestern Medical Center, Dallas, USA

Proton therapy: pushing the frontiers of radiotherapy
Tony Lomax, Centre for Proton Therapy, Paul Scherrer Institut, Villigen, Switzerland

Image guided radiation therapy
Uwe Oelfke, The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK

Discussion
16.00 – 17.40, Room 3B

Biology of the radiation response
Hosted by Gillies McKenna, Cancer Research UK and Medical Research Council Oxford Institute for Radiation Oncology, UK

Introduction by the host

A modern interpretation of the 5 Rs of radiobiology and their impact on clinical practice
Kevin Harrington, The Institute of Cancer Research, London, UK

The Royal College of Radiologists Ross Prize winner: selected from RCR proffered paper session in the Spotlight Theatre

Combining radiotherapy with DNA repair inhibitors in the lab and the clinic
Anthony Chalmers, University of Glasgow, UK

Genetic screens exploring tumour radiosensitivity
Geoff Higgins, Cancer Research UK and Medical Research Council Oxford Institute for Radiation Oncology, UK

Discussion
Networking

In the past few years 95% of colleagues said they would recommend the Conference to others. And this is not just because of the variety and quality of the science presented: networking – whether planned or serendipitous – is an essential motive for many to come to the Conference year in, year out. Here are some of the key events for you to network with old colleagues, meet fellow participants and speakers and start new collaborations:

Opening reception
Sunday 2 November, 18.00 – 20.00, Hall 2
Join fellow participants for a light supper and drinks in the exhibition hall. Use this opportunity to visit exhibitors and hear about the latest initiatives, services and products from over 60 organisations.

Exhibition hall, jobs board and posters
From 18.00 on Sunday 2 November for all refreshments and meals, until 16.20 on Tuesday 4 November, Hall 2
See the newest initiatives, as well as some of the best products and services available to cancer research professionals in the exhibition hall, and talk to expert staff about your needs. The exhibition hall is the place to meet fellow participants: all meals and poster sessions will take place in the hall, and a jobs' board will be available. The new Spotlight Theatre (see programme on page 16), located directly in the Exhibit Hall will provide short sessions to fuel conversations.

A retrospective – celebrating the 10th NCRI Cancer Conference
Throughout the Conference, Galleria (Ground floor)
This year’s 10th Conference is an opportunity to reflect about the past and look forward to what will shape the future of cancer research. The retrospective exhibition in the Galleria presents views from fellow scientists and researchers; it is meant as an invitation for you to share your thoughts too – whether publicly via the interactive boards, on twitter or indeed in person with fellow participants.

Conference dinner (ticketed event)
20.00 onwards, Tuesday 4 November, The Echo Arena, BT Convention Centre
This is a chance for you to relax and another opportunity to connect with fellow participants on the last evening of the Conference. At time of print, limited tickets were available for this event – please enquire before noon on Tuesday 4 November at the payments desk in the registration area as only ticket holders will be admitted.
Prizes at the Conference

**ACP McElwain prize**  
Monday 3 November

- **10.30 - 10.45**  
  Spotlight Theatre  
  A neoadjuvant window study of metformin’s effects on breast cancer metabolism  
  **Simon R Lord**, University of Oxford, UK

- **15.45 - 15.55**  
  Spotlight Theatre  
  RORyt+ innate lymphoid tissue inducer cells promote lymphatic invasion in triple negative breast cancers  
  **Sheeba Irshad**, King’s College London School of Medicine, Guy’s Hospital, UK

**AstraZeneca Young Investigator Prize**  
Monday 3 November

- **Poster A268**  
  Notch mutation creates super-competitor clones and field change in oesophageal epithelium  
  **Maria Alcolea**, University of Cambridge, UK

**British Association of Cancer Research (BACR) AstraZeneca Young Scientist Frank Rose Award**  
Monday 3 November

- **13.00 - 14.00**  
  Spotlight Theatre  
  Genome analysis of clonally transmissible cancers in dogs and Tasmanian devils  
  **Elizabeth P Murchison**, University of Cambridge, UK

**British Association of Surgical Oncology (BASO) Surgery Prize**  
Monday 3 November

- **12.30 - 13.00**  
  Spotlight Theatre  
  Gemcitabine-loaded and antibody-tagged superparamagnetic iron oxide nanoparticles as targeted drug vehicles in pancreatic cancer cell lines  
  **Sumit Nandi**, University of Liverpool, UK

**British Association of Cancer Research (BACR)/Gordon Hamilton-Fairley Young Investigator Award**  
Monday 3 November

- **12.20 - 14.10**  
  Poster session A  
  This prize will be selected from posters BACR1-BACR31.

**Cancer Research Excellence through Surgical Trials (CREST) Award**  
Monday 3 November

- **12.30 - 13.00**  
  Spotlight Theatre  
  Prize to be presented.
Prizes at the Conference

**Children’s Cancer and Leukaemia Group (CCLG) Award**

Poster BACR29, Monday 3 November and presentation in the ‘Molecular profiling of childhood cancers’ parallel session, 16.00 – 17.40, Tuesday 4 November

Routine molecular subgrouping of medulloblastoma: bridging the divide between research and the clinic using low-cost DNA methylomics

**Edward Schwalbe**, Northern Institute for Cancer Research, Newcastle University and Northumbria University, UK

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**The Company of Biologists Travel Awards**

- Posters A151 and A152
  - **Madison Rose**, Salaam Bombay Foundation, Bombay, India

- Poster A155
  - **Safia Awan**, Aga Khan University, Karachi, Pakistan

- Poster A163
  - **Fatma Zuhrotun Nisa**, Gadjah Mada University, Indonesia

- Poster A285
  - **Kai Dun Tang**, Queensland University of Technology, Brisbane, Australia
  - **Nguyen Tran Bao Chi**, Hung Vuong Hospital, Vietnam

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**European Association for Cancer Research Travel Awards**

- Poster A19
  - **Tanusree Paul**, Institute of Pharmacology of Natural Products and Clinical Pharmacology, University of Ulm, Germany

- Poster A135
  - **Benedicte Kirkøen**, Cancer Registry of Norway, Oslo, Norway

- Poster A272
  - **Barbara Mair**, CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria

- Poster LB48
  - **Hassan Fazilaty**, Instituto de Neurociencias de Alicante, Spain

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**National Cancer Research Institute (NCRI) Prize Awards**

See poster boards with a purple rosette on them on Monday 3 and Tuesday 4 November.

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**The Royal College of Pathologists prize**

Monday 3 November, 19.30 – 20.00, Spotlight Theatre

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**Royal College of Radiologists (RCR) Ross Awards**

The RCR Ross Award for the best poster will be selected from posters RCR1-RCR10, Tuesday 4 November.

The RCR Ross Award for the best oral presentation will be selected from the RCR proffered paper session, Tuesday 4 November, 12.45 – 13.45, Tuesday 4 November.

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Prizes at the Conference (continued)

- **Teenage Cancer Trust Stephen Sutton Prize**
  Sunday 2 November

  **18.30 - 18.50**
  Spotlight Theatre

  First prize: Final results from the QUASAR2 trial, a multicentre, international randomised phase III trial of bevacizumab and capcitabine in the adjuvant setting of colorectal cancer (CRC)
  **Rachel Kerr**, University of Oxford, UK

  Second prize: Lifestyle and lifestyle changes as predictors of 10-year all-cause and cancer specific mortality in individuals aged 50 to 55 years
  **Paula Berstad**, Cancer Registry of Norway and Telemark Hospital, Norway

- **Wellcome Trust bursaries for participants from Low and Middle Income Countries (LMIC)**

<table>
<thead>
<tr>
<th>Poster</th>
<th>Name</th>
<th>Institution</th>
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<tbody>
<tr>
<td>A76</td>
<td>Sanjit Agrawal</td>
<td>Tata Medical Center, West Bengal, India</td>
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<tr>
<td>A113</td>
<td>Mohsen Soliman</td>
<td>National Research Center, Cairo, Egypt</td>
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<td>A140</td>
<td>Shalu Jain</td>
<td>National Institute of Pathology, New Delhi, India</td>
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<td>A158</td>
<td>Amen Bawazir</td>
<td>Aden Cancer Centre, Yemen</td>
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<td>B30</td>
<td>Happiness Aweto</td>
<td>University of Lagos, Nigeria</td>
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<tr>
<td>B82</td>
<td>Hemantha Amarasinghe</td>
<td>National Cancer Control Programme, Ministry of Health, Colombo, Sri Lanka</td>
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<tr>
<td>B128</td>
<td>Ramandeep Arora</td>
<td>Max Super-Speciality Hospital and Cankids... Kidscan, New Delhi, India</td>
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*BMJ Open* is an Open Access general medical journal with an extensive topic collection in Oncology.

As an NCRI delegate, you are eligible for a 20% discount off the article publishing charge. Use the code **MAFUEE9** upon payment.*

**Visit our stand** to learn more about the benefits of publishing with *BMJ Open*

*Offer valid on submissions made between 2 November 2014 and 5 February 2015*
Programme at a glance

**Workshops**

- **14.00 – 15.00**
  - **Room 3A**
  - **Hititng the headlines – Communicating cancer research in the media**
- **14.00 – 15.00**
  - **Room 3B**
  - **Science pick ‘n’ mix: an introduction to the science at this year’s conference**
  - Hosted by **Elaine Vickers**, Science Communicated Ltd, Sheffield, UK

**Welcome address**

- **15.20 – 15.30**
  - **Hall 1A**
  - **Introduction from the Director of the NCRI and the Chair of the 2014 Scientific Committee**
  - **Karen Kennedy**, Director of the National Cancer Research Institute and **Richard Marais**, Chair of the 2014 Scientific Committee

**Plenary lecture**

- **15.30 – 16.10**
  - **Hall 1A**
  - **Targeting phosphoinositide 3-kinase for cancer therapy**
  - **Lewis C Cantley**, Weill Cornell Medical School, Cornell University, New York, USA

**Networking and refreshment break**

- **16.10 – 16.40**
  - **Registration area and Galleria**

**Plenary lectures**

- **16.40 – 17.20**
  - **Hall 1A**
  - **Communicating risk and uncertainty to patients and the media**
  - **David Spiegelhalter**, University of Cambridge, UK
- **17.20 – 18.00**
  - **Hall 1A**
  - **Genomically-inspired treatment of lymphoma by targeting oncogenic signalling**
  - **Louis M Staudt**, National Cancer Institute, Bethesda, USA

**Workshops**

- **18.00 – 19.30**
  - **Room 3A**
  - **Genomic medicine in metastatic breast cancer: reality or hype?**
  - Hosted by **Andrew Tutt**, The Institute of Cancer Research, King’s College London and Breakthrough Toby Robins Breast Cancer Research Centre, London, UK
- **18.00 – 19.30**
  - **Room 3B**
  - **Cancer Research UK Centre for Drug Development Phase I trial design**
  - Hosted by **Sarah Halford** and **Gary Acton**, Cancer Research UK Centre for Drug Development, London, UK

**Opening reception, networking, exhibition viewing and Spotlight Theatre**

- **18.00 – 20.00**
  - **Hall 2**
  - **Including celebratory welcome by the Wrexham Tenovus Sing with Us choir, made up of cancer patients and their supporters. Light supper and refreshments will be served.**
Plenary abstracts

Targeting phosphoinositide 3-kinase for cancer therapy

**15.30 – 16.10**
Hall 1A

**Lewis C Cantley,**
Weill Cornell Medical School, Cornell University, New York, USA

Phosphoinositide 3-kinase (PI3K) is a central enzyme in a signalling pathway that mediates cellular responses to insulin and other growth factors. The signalling pathway involving insulin, PI3K and the downstream components of AKT and mTOR is highly conserved from worms and flies to humans and genetic analysis of the pathway has revealed a conserved role in regulating glucose metabolism and cell growth. Germline mutational events that lead to hyperactivation of the PI3K pathway result in hamartoma syndromes and cancers. Sporadic activating mutations in PIK3CA, encoding the p110alpha catalytic subunit of PI3K or inactivating mutations in PTEN (a phosphoinositide 3-phosphatase that reverses the effects of PI3K) are among the most common events in solid tumours. More than thirty drugs that target PI3K and other components of this pathway are in clinical trials for a variety of cancers. It is likely that PI3K pathway inhibitors will need to be combined with other drugs to be broadly effective. We have employed genetically engineered mouse models that develop cancers due to mutations in genes in the PI3K pathway and are using these models to explore the efficacy of PI3K pathway inhibitors as single agents or in combination with other drugs. The role of PI3K inhibitors for treating cancers in these mouse models and in human trials will be discussed.

**Lay abstract**
Phosphoinositide 3-kinase (PI3K) mediates glucose uptake into muscle and fat and other tissues in response to insulin, IGF1 and other growth factors. Thus, it plays a major role in the growth of all tissues during human development. Sporadic activating mutations in the gene encoding PI3K (PIK3CA) or inactivating mutations in PTEN, a gene that reverses the effects of PI3K, are among the most common events in solid tumours. These mutations allow tumours to take up glucose and use it for tumour growth. More than thirty drugs that target PI3K and other components of this pathway are in clinical trials for a variety of cancers. It is likely that PI3K pathway inhibitors will need to be combined with other drugs to be broadly effective. We have been using pre-clinical models to determine how best to determine what patients are most likely to benefit from treatment with PI3K inhibitors as single agent drugs or in combination with other drugs. The role of PI3K inhibitors for treating cancers in pre-clinical models and in human trials will be discussed.

Communicating risk and uncertainty to patients and the media

**16.40 – 17.20**
Hall 1A

**David Spiegelhalter,**
University of Cambridge, UK

None of us know what is going to happen, but acknowledging uncertainty about the future can be tricky. Sometimes numbers can be put on the chances of various possible outcomes, both good and bad, but the language and metaphors used can make a difference in people's perceptions. And often the chances are themselves uncertain.

I shall look at how different agencies are communicating risk and uncertainty, both in medicine and outside. Recent psychology research suggests that using ‘natural frequencies’ – such as “what we would expect to happen in 100 people like you” – can help avoid some biases. I will consider the use of such language in the new leaflets from the NHS Screening Programme, which attempt to present both potential harms and benefits of screening in a uniform way and, in a bold innovation, do not explicitly recommend screening but suggest people ‘consider the offer’.

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colncri.org.uk
The media love stories about how mundane exposures can lead to dread consequences - ‘cats cause cancer’ being a classic example. I will look at how such presentations serve to manipulate emotions, and suggest some alternative metaphors that could lead to a more balanced assessment of risk.

Genomically-inspired treatment of lymphoma by targeting oncogenic signalling

Diffuse large B cell lymphoma (DLBCL) is a heterogeneous diagnostic category that is comprised of two prominent molecular subtypes, termed activated B cell-like (ABC) and germinal center B cell-like (GCB). These DLBCL subtypes are now viewed as molecularly distinct diseases since they arise from distinct stages of normal B cell development, require distinct recurrent genetic abnormalities to become malignant, have distinct cure rates with current chemotherapy regimens, and respond differentially to targeting agents. We defined a ‘chronic active’ form of B cell receptor (BCR) signalling that activates NF-κB in ABC DLBCLs. Such ABC DLBCLs are killed by knockdown of BCR signalling components, such as the kinase BTK or components of the BCR itself. Over one fifth of ABC DLBCLs have mutations affecting the CD79B or CD79A subunits of the BCR that augment BCR signalling. To attack chronic active BCR signalling therapeutically, we initiated clinical trials in relapsed/refractory DLBCL of ibrutinib, an irreversible and highly selective inhibitor of BTK. Ibrutinib monotherapy induced a high rate of complete and partial responses in ABC DLBCL, while GCB DLBCL tumours rarely responded. Given its excellent safety profile and selective mechanism of action, we are hopeful that ibrutinib can be combined with both chemotherapy and other signalling modulators to achieve cures for these patients. Several rational combinations of targeted agents for the therapy of ABC DLBCL will be presented.
Workshops

Hitting the headlines – communicating cancer research in the media

14.00 – 15.00
Room 3A
Kat Arney, Cancer Research UK, London, UK

From the perspective of cancer researchers, funders and healthcare providers, it’s vital that accurate, understandable information about cancer gets out to the public – whether it’s progress in research, improvements in treatment and survival, or information about risks and prevention. There’s an increasing array of media outlets available to do this – from traditional newspapers, TV and radio to online options such as blogs, podcasts and social media. In this session, aimed at researchers, medical professionals and research-funding organisations, we’ll be exploring how cancer stories make their way from the pages of academic journals into these various media, and how Cancer Research UK’s science media team helps to achieve this. We’ll also provide tips and tricks on how to effectively engage with traditional and ‘new’ media and the wider public about your research, and discuss some of the issues and benefits involved.

Science pick ‘n’ mix: an introduction to the science at this year’s Conference

14.00 – 15.00
Room 3B
Elaine Vickers, Science Communicated Ltd, Sheffield, UK

Do words like PI3K, KRAS wild-type, biomarkers, metabolomics, genomics and tumour heterogeneity leave you scratching your head in confusion?

Well never fear!

Elaine will explain many of the words, concepts and ideas behind this year’s plenary lectures, symposia and parallel sessions.

Similar to her workshop last year, ‘A beginner’s guide to targeted cancer treatments’, Elaine will use diagrams and illustrations to provide clear, easy-to-understand explanations of complicated biological concepts.

The workshop is geared towards non-scientists, such as doctors, nurses, trials staff and patients who would like to get the most out of this year’s Conference.

Elaine will also be running a second workshop on Tuesday morning: ‘A beginner’s guide to cancer immunotherapy’.

Genomic medicine in metastatic breast cancer: reality or hype?

18.00 – 19.30
Room 3A

1,000 women die each month in the UK as a result of metastatic breast cancer. This alarming statistic highlights the urgent need for better treatments, so that women and men diagnosed with this form of the disease can live longer and healthier lives.

The advent of more affordable sequencing technologies is allowing us to move away from characterising the few known genetic markers associated with breast cancers and instead gives us information on entire tumour genomes. The dream of using these data to inform treatment choice is coming closer to a reality.

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conference.ncri.org.uk
Whilst the field of cancer genomics is in its infancy we ask: Is medicine able to keep up with the pace of this technology? Will this be financially viable for all? Will genomic data ever inform the treatment of metastatic breast cancer? This debate will seek to answer these questions and many more through an interactive discussion between the audience and panel.

**Panel**

Chair: **Andrew Tutt**, The Institute of Cancer Research, King's College London and Director of the Breakthrough Toby Robins Breast Cancer Research Centre

Speaking for genomic therapies: **David Cameron**, Edinburgh Cancer Research Centre, UK and **Iain MacPherson**, Institute of Cancer Sciences, Glasgow, UK

Speaking against genomic therapies: **David Miles** and **Andreas Makris**, Mount Vernon Cancer Centre, Middlesex, UK

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**Cancer Research UK Centre for Drug Development Phase I trial design**

18.00 – 19.30

Room 3B

Hosted by **Sarah Halford** and **Gary Acton**, Cancer Research UK Centre for Drug Development (CDD), London, UK

Over the past decade The Cancer Research UK Centre for Drug Development (CDD) (formally the Drug Development Office [DDO]) has significantly strengthened its capacity, capability and conceptual vision. Our approach to early stage drug evaluation has evolved from predominantly investigator-led academic studies, to a contemporary pipeline which is strategically driven and potentially practice changing.

This workshop will present the current criteria by which proposals are evaluated within the CDD to ensure that we only accept those where we can see a clear pathway of progression to later stage clinical trials.

Participants will learn how to maximise their chances of a successful application through the submission of study designs with a significant biomarker component, as well as other pharmacodynamic methodologies permitting early assessment of future viability. Case examples will be presented of rejected and accepted applications, to demonstrate the importance of well defined, mechanistically relevant patient populations, robust outcome criteria, early use of combination treatment strategies and most importantly, a convincing rationale for how the proposal might translate into a future development programme attractive to potential partners.

**Gary Acton is the author of Sympathy for the Devil: The Definitive True Story of Cancer Biotechnology and Its Battle Against Disease, Death and Destruction.**
Spotlight Theatre

**18.30 – 18.50**

**Teenage Cancer Trust Stephen Sutton Prize**

Presentation of the Teenage Cancer Trust Stephen Sutton Prizes, followed by a presentation from the winner of the first prize.

First prize: Final results from the QUASAR2 trial, a multicentre, international randomised phase III trial of bevacizumab and capecitabine in the adjuvant setting of colorectal cancer (CRC)

Rachel Kerr, University of Oxford, UK

Second prize: Lifestyle and lifestyle changes as predictors of 10-year all-cause and cancer specific mortality in individuals aged 50 to 55 years

Paula Berstad, Cancer Registry of Norway and Telemark Hospital, Norway

**19.00 – 19.30**

**Integrated DNA Technologies: Superior sequencing coverage and uniformity in affordable gene panels that you can customise**

Traditionally, researchers using NGS target capture technologies faced a tradeoff between off-the-shelf probe pools or panels that may not exactly meet experimental needs, and high-cost custom designed gene probe pools or panels. In this talk, you will learn how IDT xGen® Lockdown® Probes help you capture just your selected target regions of interest, with a high degree of uniformity and specificity. Furthermore, you can mix probes to individual target regions to build and optimise your own panels, or augment existing panels. This flexibility provides the same high degree of uniform coverage with lower cost. Learn how the xGen Predesigned Capture Pools will allow you to:

- Start with small reaction volumes to design and optimise new panels at lower cost, with less waste
- Build a cost-effective custom panel targeting specific UTR, introns, or intergenic regions of interest, in addition to CDS
- Enhance existing panels with expanded target space or improved capture
- Design your own custom plate from probes for each gene target in a separate well
Meet colleagues involved in clinical research:

- clinicians
- research nurses
- patient representatives
- data managers.

You will:

- see updates on current NCRI trials
- hear results of closed trials
- foster collaborations in future national trials
- network and enhance your professional development.

For more information contact the NCRI CSG Secretariat ncricsg@ncri.org.uk
For commercial opportunities contact ncriconference@ncri.org.uk
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2014/15 NCRI Clinical Studies Groups (CSG) Annual Trial Meetings
7 November 2014
Lymphoma CSG
17 November 2014
Children’s Cancer and Leukaemia CSG
2 December 2014
Upper GI CSG
4 March 2015
Colorectal CSG
5 March 2015
Breast CSG
Summer 2015
Haematological Oncology CSG

Upcoming meetings

The UK’s largest online network of doctors
A trusted source of medical education, research and communication
Programme at a glance

**Workshop**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
<th>Details</th>
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<tbody>
<tr>
<td>08.00</td>
<td>BACR educational workshop: Tools for image analysis in cancer research</td>
<td>Room 11</td>
<td>BACR educational workshop: Tools for image analysis in cancer research</td>
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**Introduction to the programme**

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<th>Time</th>
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<tbody>
<tr>
<td>08.50</td>
<td>Message from the Chair of the Scientific Committee</td>
<td>Hall 1A</td>
<td>Richard Marais, Cancer Research UK Manchester Institute, UK</td>
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</tbody>
</table>

**Plenary lectures**

Chaired by Caroline Dive, Cancer Research UK Manchester Institute, UK

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<tr>
<th>Time</th>
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<th>Location</th>
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<tbody>
<tr>
<td>09.00</td>
<td>Quantitative oncology: biologically informed and clinically actionable</td>
<td>Hall 1A</td>
<td>Peter Kuhn, University of Southern California, Los Angeles, USA</td>
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<tr>
<td>09.40</td>
<td>Psychiatric aspects of palliative care: meaning and existential issues</td>
<td>Hall 1A</td>
<td>William Breitbart, Memorial Sloan Kettering Cancer Center, New York, USA</td>
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**Networking, exhibition viewing, poster viewing, Spotlight Theatre and refreshment break**

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<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tr>
<td>10.20</td>
<td>- 10.50</td>
<td>Hall 2</td>
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**10th Conference celebratory talks**

Chaired by Richard Marais, Cancer Research UK Manchester Institute, UK

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<th>Time</th>
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<tbody>
<tr>
<td>10.50</td>
<td>Title TBC</td>
<td>Hall 1A</td>
<td>Mike Richards, Chief Inspector of Hospitals, Care Quality Commission and former National Cancer Director, Department of Health, UK</td>
</tr>
<tr>
<td>11.20</td>
<td>Whither genomics</td>
<td>Hall 1A</td>
<td>Michael Stratton, Wellcome Trust Sanger Institute, Cambridge, UK</td>
</tr>
<tr>
<td>11.50</td>
<td>Whither drug discovery: the genetic basis for cancer therapeutics</td>
<td>Hall 1A</td>
<td>William R Sellers, Novartis Institutes for BioMedical Research (NIBR), Cambridge, USA</td>
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**Networking, exhibition viewing, poster viewing, Spotlight Theatre and lunch**

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<thead>
<tr>
<th>Time</th>
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<tr>
<td>12.20</td>
<td>- 14.10</td>
<td>Hall 2</td>
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**Scientific symposium and Dragon’s Den**

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<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>12.45</td>
<td>Immunotherapy in cancer: a primer</td>
<td>Room 3A</td>
<td>Hosted by Bristol-Myers Squibb</td>
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</table>

Satellite Symposium sponsored by Bristol-Myers Squibb

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12.45 – 14.00
Room 12
The Dragon’s Den: involving consumers in your research
Hosted by NCRI Consumer Liaison Group

Symposia

14.10 – 15.40
Hall 1A
Circulating biomarkers: where have we got to and what's on the horizon?
Hosted by Caroline Dive, Cancer Research UK Manchester Institute, UK

14.10 – 15.40
Room 3A
Inflammation and cancer
Hosted by Fran Balkwill, Queen Mary, University of London, UK

14.10 – 15.40
Room 3B
Prevention
Hosted by Peter Sasieni, Queen Mary, University of London, UK

14.10 – 15.40
Room 11
Stem cells and cancer
Hosted by Axel Behrens, Cancer Research UK London Research Institute, UK

Networking, exhibition viewing, poster viewing and refreshment break

15.40 – 16.00
Hall 2

Parallel sessions and workshops

16.00 – 17.40
Hall 1A
Debate: This house believes that the Cancer Drugs Fund has been good for British cancer patients
Hosted by Malcolm Mason, Cardiff University and Velindre Hospital, UK

16.00 – 17.40
Room 4
Genetically engineered mouse models (GEMM) of cancer: how have they performed?
Hosted by Owen Sansom, Cancer Research UK Beatson Institute, Glasgow, UK

16.00 – 17.40
Room 11
Metabolic adaptations of cancer
Hosted by Eyal Gottlieb, Cancer Research UK Beatson Institute, Glasgow, UK

16.00 – 17.40
Room 3B
Pancreatic cancer: from basic science to clinical implementation
Hosted by Claus Jorgensen, Cancer Research UK Manchester Institute, UK

16.00 – 17.40
Room 3A
Targeting Ras
Hosted by Julian Downward, Cancer Research UK London Research Institute, UK

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Programme at a glance (continued)

16.00 – 17.40  Room 12  Thinking beyond the androgen receptor: a new horizon in castrate-resistant prostate cancer
Hosted by David Waugh, Queen’s University Belfast, UK

16.00 – 17.40  Hall 1B  Workshop: Interventional oncology – state of the art
Hosted by Ricky Sharma, University of Oxford, UK

16.00 – 17.40  Hall 1C  Workshop: Neuro-rehabilitation and palliative care for brain tumours
Hosted by Jane Fleming, University Hospital Waterford, Ireland

Networking and break
17.40 – 18.00  Hall 2

Cancer Research UK Prize ceremony
18.00 – 18.20  Hall 1A  Presented by Nic Jones, Cancer Research UK

Plenary lecture
Chaired by Nic Jones, Chair of the Cancer Research UK Prizes Selection Panel
18.20 – 19.00  Hall 1A  Cancer Research UK Lifetime Achievement Award winner – Challenging nuclear fiction: new roles for old nuclear proteins
Ron Laskey, University of Cambridge, UK

Drinks reception, networking, exhibition viewing and Spotlight Theatre
19.00 – 20.45  Hall 2  Canapés and drinks will be provided

Chairs’ evening (by invitation)
20.00 – 22.00  Room 3A

*Prostate Cancer UK is a registered charity in England and Wales (1005541) and in Scotland (SC039332). Registered company 2653887.

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Plenary abstracts

▶ Quantitative oncology: biologically informed and clinically actionable

09.00 – 09.40
Hall 1A

Peter Kuhn,
University of Southern California, Los Angeles, USA

A biological transition point is the initial, instigating change that occurs when a cancer transitions from local to distant or treatment-sensitive to treatment-resistant; the field is currently limited to treating the corresponding clinical transition point – the time at which this change is first detected due to an amassed population of changed cells. Employing physical science and biological methods we can study the factors that affect biological transition points in order to improve clinical decision making and mitigate the damage caused by delayed clinical detection. Studying the changes occurring within individual tumour cells, within patients’ organ systems, and within populations of patients to chart the dynamic course of cancer evolution, we can better predict and thus better treat this ever-changing disease.

▶ Psychiatric aspects of palliative care: meaning and existential issues in end of life care

09.40 – 10.20
Hall 1A

William Breitbart,
Memorial Sloan Kettering Cancer Center, New York, USA

This plenary lecture provides an overview of existential issues in end of life care, with an emphasis of the important role of ‘meaning’. A novel counselling intervention for patients with advanced cancer, entitled ‘Meaning Centered Psychotherapy (MCP)’, will be described. The basic concepts of MCP will be described. Two forms of MCP have been developed: Meaning Centered Group Psychotherapy and Meaning Centered Psychotherapy. A detailed description of the interventions and the content of each session will be provided. Both interventions are manualised and several randomised controlled trials have been conducted. The results of these studies will be presented which demonstrate that MCP enhances spiritual wellbeing and meaning, improves quality of life, decreases depression, anxiety, hopelessness and desire for hastened death. In addition, adaptations of Meaning Centered Psychotherapy for bereavement, cancer survivors, cancer caregivers, and adolescents with cancer will be described.

Learning objectives:
1. You will become familiar with the concept of spirituality as a construct composed of faith and/or meaning.
2. You will become familiar with the importance of meaning, as a component of spiritual wellbeing, and its relationship to depression, hopelessness and desire for death.
3. You will become familiar with a structured, didactic and experiential eight-session intervention for advanced cancer patients aimed at sustaining or enhancing a sense of meaning in the face of terminal illness.
The cell nucleus plays crucial roles in cell proliferation and cancer, yet research has often been impeded by flawed concepts. Examples will be drawn from cell differentiation, cell proliferation and intracellular transport of proteins and RNA. In each of these areas flawed concepts and models have been challenged by new insights into the roles of known nuclear proteins.

Duplicating the human genome is a logistical challenge. 105 replication initiation events must be coordinated so that all DNA is duplicated exactly once and only once. The cell keeps track of which regions it has already duplicated by a ratchet-like system of ‘replication licensing’ that deploys multiple molecular mechanisms to couple DNA replication to the cell cycle.

Proteins that make up the licence are remarkably powerful markers for improving cancer screening and diagnosis. They include proteins called minichromosome maintenance (MCM) proteins and a small protein called geminin. Together with cyclins they ensure that one round of chromosome duplication is complete before the next can start.

Remarkably geminin also has a novel role in specifying stem cell identity by regulating the expression of the pluripotency factors that programme stem cells. Removal of geminin from mouse embryonic stem cells has two dramatic and independent effects. Predictably they become enormous by synthesising DNA repeatedly without dividing, but they also lose their stem cell identity by differentiating.

An inadequate model also restrained research into how proteins are imported into the nucleus. Overturning it allowed rapid identification of import signals and their receptors (importins). Similarly, models of mRNA export from the nucleus may be too simple. We and others have found examples of nuclear proteins that act as selective mRNA export factors. One of these selectively exports mRNAs that influence gene expression and another enhances export of mRNAs for proteins that repair double stranded breaks in DNA.
10th Conference celebratory talk abstracts

Title TBC

10.50 – 11.20
Hall 1A

Mike Richards,
Chief Inspector of Hospitals, Care Quality Commission and former National Cancer Director, Department of Health, UK

Abstract not received

Whither genomics

11.20 – 11.50
Hall 1A

Michael Stratton,
Wellcome Trust Sanger Institute, Cambridge, UK

Abstract not received

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Whither drug discovery: the genetic basis for cancer therapeutics

11.50 – 12.20
Hall 1A

William R Sellers,
Novartis Institutes for
BioMedical Research
(NIBR), Cambridge, USA

Cancer is largely a disease driven by the acquisition and selection of somatic genetic mutations leading to the gain and loss-of-function of critical oncogenes and tumour suppressors. The elucidation of the first human genome sequence coupled with the advent of Next Generation Sequencing has made it possible to fully elucidate all clonal and many sub-clonal genetic events in large numbers of cancers. In parallel, drug discovery efforts targeting key oncogenes including BCR-ABL, HER2, BRAF, EGFR and KIT, among many others, have led to a new class of therapeutics showing marked clinical activity in diseases previously refractory to standard cytotoxic agents. The full realisation of this paradigm, however, will require solving a number of key problems. Among these are enhancing our ability to drug difficult protein targets, elaborating therapeutics that take advantage of synthetic lethal nodes in tumour suppressor pathways and understanding therapeutic resistance as a starting point for the development of curative combination therapy. In parallel, clinical trials design must advance to allow us to rapidly identify the most effective dose and schedule for new drugs and new drug combinations.
Symposia

Circulating biomarkers: where have we got to and what's on the horizon?
Hosted by Caroline Dive, Cancer Research UK Manchester Institute, UK

14.10 – 14.15
Hall 1A
Introduction by the host

14.15 – 14.40
Hall 1A
Molecular profiling of single circulating tumour cells with diagnostic intention
Christoph Klein, University of Regensburg and Fraunhofer Project Group, Regensburg, Germany

14.40 – 15.05
Hall 1A
Circulating cell-free DNA as a strong multimarker diagnostic, theranostic and prognostic tool for metastatic colorectal cancer patients management care
Alain R Thierry, French Institute of Health and Medical Research (INSERM), Montpellier, France

15.05 – 15.30
Hall 1A
What can we learn from circulating tumour cells in lung cancer – biomarkers, mouse models, drug resistance and heterogeneity
Caroline Dive, Cancer Research UK Manchester Institute, UK

15.30 – 15.40
Discussion

Inflammation and cancer
Hosted by Fran Balkwill, Queen Mary, University of London, UK

14.10 – 14.15
Room 3A
Introduction by the host

14.15 – 14.40
Room 3A
The targets for tumour immunotherapy mediated by the inflammatory properties of vesicular stomatitis virus (VSV)-based antigen presentation depend upon the tumour's anatomical site
Richard Vile, Mayo Clinic, Rochester, USA

14.40 – 15.05
Room 3A
Co-targeting angiogenesis and immunosuppressive cell networks to improve anti-cancer therapy
Michele De Palma, The Swiss Institute for Experimental Cancer Research (ISREC), Swiss Federal Institute of Technology Lausanne (EPFL), Lausanne, Switzerland

15.05 – 15.30
Room 3A
Neutrophil-derived signals promote initiation abilities of cancer stem cells during metastasis
Ilaria Malanchi, Cancer Research UK London Research Institute, UK

15.30 – 15.40
Discussion

Prevention
Hosted by Peter Sasieni, Queen Mary, University of London, UK

14.10 – 14.15
Room 3B
Introduction by the host

14.15 – 14.40
Room 3B
Progress in breast cancer prevention
Jack Cuzick, Queen Mary, University of London, UK

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Symposia (continued)

14.40 – 15.05  Effects of aspirin on cancer incidence and metastasis  
Room 3B  Peter Rothwell, University of Oxford, UK

15.05 – 15.30  Cancer and obesity prevention: finding the causes of the causes  
Room 3B  Tim Lobstein, World Obesity Federation, London, UK and Curtin University, Perth, Australia

15.30 – 15.40  Discussion

Stem cells and cancer
Hosted by Axel Behrens, Cancer Research UK London Research Institute, UK

14.10 – 14.15  Introduction by the host  
Room 11

14.15 – 14.40  Wnt activating mechanisms in colorectal cancer  
Room 11  Vivian Li, Medical Research Council (MRC) National Institute for Medical Research, London, UK

14.40 – 15.05  Tumour-propagating cells in non-small cell lung cancer  
Room 11  Carla Kim, Children's Hospital Boston, USA

15.05 – 15.30  Neutral and biased replacement of intestinal stem cells  
Room 11  Douglas Winton, Cancer Research UK Cambridge Institute, UK

15.30 – 15.40  Discussion
Symposia abstracts

**Circulating biomarkers: where have we got to and what’s on the horizon?**

**14.10 – 14.15**
**Hall 1A**

**Caroline Dive,**
Cancer Research UK
Manchester Institute, UK

**Introduction**
Development of novel minimally invasive biomarkers to facilitate precision medicine delivery edges ever closer to routine application. We have witnessed substantial strides forward in recent years with the detection and analysis of circulating tumour DNA (ctDNA) to monitor patients receiving targeted therapies. Assay sensitivity is continually improving, offering a horizon of ctDNA for earlier detection of disease. Challenges remaining are largely related to standardisation blood processing and ctDNA inclusive trial protocols for multi-centre trial samples. Alain Thierry will discuss ctDNA analysis and his application of ctDNA assays for clinical decision making. What then is the added utility of circulating tumour cells (CTCs)? The major technical hurdle for CTC research is the challenge of CTC heterogeneity and urgent need for robust marker independent technology. These challenges are being met and CTC analysis has much to offer regarding the biology of tumour dissemination, tumour heterogeneity and evolution. Christoph Klein will discuss single CTC analysis with diagnostic precision and the implications for the understanding of cancer evolution and therapy selection. Finally, Caroline Dive will describe the emerging field of CTC explant models that can be used to further characterise tumour biology and to test novel therapies in the setting of small cell lung cancer (SCLC) where CTCs are particularly prevalent.

**14.15 – 14.40**
**Hall 1A**

**Christoph Klein,**
University of Regensburg
and Fraunhofer Project Group, Regensburg, Germany

**Molecular profiling of single circulating tumour cells with diagnostic intention**
Several hundred clinical trials currently explore the role of circulating tumour cell (CTC) analysis for therapy decisions, but assays are lacking for comprehensive molecular characterisation of CTCs with diagnostic precision. We therefore combined a workflow for CTC enrichment and isolation with 100% purity using a non-random whole genome amplification method for single cells. We then developed an assay to predict the outcome of downstream molecular analyses of single CTCs. This assay tested the quality of the whole genome amplification and the genomic integrity of isolated cells and allows identifying CTCs for which more than 90% tested molecular studies were successfully performed, including targeted analysis of point mutations, identification of gene copy number alterations such as ERBB2 amplification or genome wide analyses by aCGH. The selection of high-quality samples enabled us to determine the molecular heterogeneity of single CTCs of metastatic breast cancer patients. We readily identified genomic disparity of potentially high relevance between primary tumours and CTCs. Microheterogeneity analysis among individual CTCs uncovered pre-existing cells resistant to ERBB2-targeted therapies suggesting on going microevolution at late stage disease whose exploration may provide essential information for personalised treatment decisions and shed light on mechanisms of acquired drug resistance.

**Competing interests**
Inventor of presented single cell amplification method.
Circulating cell-free DNA as a strong multimarker diagnostic, theranostic and prognostic tool for metastatic colorectal cancer patients management care

Circulating cell-free DNA (ccfDNA) analysis constitutes a hopeful approach to provide a non-invasive tumour molecular test for cancer patients. We studied tumour-derived ccfDNA by an original approach focusing on its size distribution. Our group was the first to demonstrate that tumour-derived ccfDNA was highly fragmented and mainly composed of <100 bp fragments by Q-PCR and AFM which is smaller than the observed size between 145 and 180 bp reported in the literature. Based upon this discovery, we designed Intplex, an allele specific qPCR based system targeting short sequences of DNA specifically adapted for ccfDNA analysis. With this specific design and our rigorous guidelines for ccfDNA analysis, unprecedented results have been determined and confirmed the powerful biomedical potential of ccfDNA analysis: we validated the detection of KRAS/BRAF point mutation in 106 clinical samples from mCRC patients with 98% of specificity with tumour tissue analysis in a blinded multicenter clinical study. We showed the high diagnostic potential of ccfDNA concentration allowing discrimination between healthy subjects and cancer patients. Moreover, we revealed the prognostic significance of this analysis on a cohort of 106 mCRC patients. Intplex allows the determination of the mutation load which is the proportion of mutant ccfDNA in total ccfDNA reflecting the proportion of specific tumour ccfDNA in total ccfDNA. Finally, ccfDNA analysis made possible the detection of the emergence of RAS and BRAF mutations following anti-EGFR therapy in mCRC patients. The Intplex test can be adapted to all mutations, genes or cancers and enables rapid, highly sensitive, cost effective and repetitive analysis. Our technical approach offers the opportunity to detect quantitative and dynamic mutations and could constitute a non-invasive attractive tool potentially allowing diagnosis, prognosis, theranostics, therapeutic monitoring and follow-up of cancer patients expanding the scope of personalised cancer medicine.

Full authorship
Alain R Thierry1, Safia El Messaoudi1, Cynthia Sanchez1, Brice Pastor1, Caroline Mollevi2, Charles Theillet1, Scott Kopetz3, Muriel Mathonnet4, Denis Pezet5, and Marc Ychou2

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2 Institut du Cancer de Montpellier, Department of Digestive Oncology, 208 Rue des Apothicaires, 34298 Montpellier, France
3 Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas
4 Centre Hospitalier Universitaire, Department of Digestive Surgery, Clinical Investigational Center, CIC-P Inserm 0810, 2 Avenue Martin Luther-King, 87042 Limoges, France
5 CHU Clermont Fd, Department of Digestive Surgery, 1 Place Lucie Aubrac 63003 Clermont Ferrand, France
What can we learn from circulating tumour cells in lung cancer – biomarkers, mouse models, drug resistance and heterogeneity

Two paradigms exist for circulating tumour cells (CTCs) in lung cancer. In small cell lung cancer (SCLC), CTCs detected by the EpCAM dependent CellSearch platform are prevalent, CTC number is prognostic (‘cut off’ >50 CTCs in 7.5ml blood), dynamic range (up to 1000s CTCs in 7.5ml blood) is suitable for use as a pharmacodynamic biomarker and CTC-based predictive biomarker assays are feasible. In non small cell lung cancer (NSCLC), CTCs are more difficult to find, CellSearch detected CTCs are prognostic (‘cut off’ >5 CTCs in 7.5ml blood) but their clinical utility is less clear. Yet marker independent NSCLC CTC enrichment based on size identifies considerably more CTCs and reveals heterogeneity in epithelial-mesenchymal transition (EMT) phenotypes. What CTCs offer is full genome and transcriptome analysis at the single CTC level, cellular protein based biomarkers and the ability to build CTC derived mouse models (that we term CTC derived patient explants [CDX]). We developed 11 CDX where CTCs were enriched at baseline from chemosensitive or chemorefractory SCLC patients and for some patients a second model was derived at patient progression. These are being exploited to search for new drug targets, to test novel drugs and explore drug resistance mechanisms. Notably, we derived a CDX from a NSCLC patient whose CellSearch epithelial CTC count was zero and ~80% CTCs captured on filters were mesenchymal. Current SCLC CTC analysis is focusing on whole genome and exome sequencing of matched longitudinal analysis of baseline and relapse CTC samples to identify genetic changes associated with therapy resistance. Studies underway are aimed at providing mRNA and genomic DNA analysis from the same CTC sample to establish direct linkage between mutational changes and emergent mRNA profiles and pathways to gain insights into mechanisms underpinning treatment responses.

Full authorship
Caroline Dive1, Ged Brady1, Christopher Morrow1, Crispin Miller1 & Fiona Blackhall2,3

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2 Institute of Cancer Sciences, University of Manchester, UK
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Discussion

Inflammation and cancer

Introduction
The links between inflammatory disease and cancer are well-defined: some chronic inflammatory diseases increase the risk of cancer; production of inflammatory mediators is downstream of many oncogenic mutations; cells and mediators of inflammation are present in the tumour microenvironment and inhibition of inflammatory pathways has potential in cancer treatment and prevention.

This session will highlight some recent research on the importance of inflammatory pathways during cancer treatment and relapse.
The targets for tumour immunotherapy mediated by the inflammatory properties of vesicular stomatitis virus (VSV)-based antigen presentation depend upon the tumour’s anatomical site

Although we initially used vesicular stomatitis virus as a direct oncolytic agent, we also observed that it serves as an excellent inflammatory adjuvant, allowing priming of T cell responses against tumour antigens encoded within the virus. As a result, we have shown that VSV engineered to express a cDNA library from human melanoma cells (ASMEL, Altered Self Melanoma Epitope Library) was an effective systemic therapy for subcutaneous (s.c.) murine B16 melanomas (Pulido et al., Nat. Biotech. 2012, 30:337-43). Here we show that the combination of antigens identified from the ASMEL which successfully treated s.c. B16 tumours (VSV-N-RAS/VSV-CYT-C/VSV-TYRP-1) was completely ineffective against intra-cranial (i.c.) B16 tumours. In contrast, a different combination of VSV-expressed antigens isolated from the ASMEL (VSV-HIF-2α/VSV-SOX-10/VSV-C-MYC/VSV-TYRP-1) was highly effective against i.c. B16 tumours, but had no efficacy against s.c B16 tumours. Correspondingly, i.c. B16 tumours expressed a HIF-2αHi, SOX-10Hi, c-mycHi, TYRP1, N-RASlo CYT-Clo antigen profile, which differed significantly from the HIF-2αlo, SOX-10lo, c-myclo, TYRP1, N-RASHi CYT-CHi phenotype of s.c. B16 tumours, and which was imposed upon the tumour cells by CD11b+ cells within the local tumour microenvironment in the brain. By combining T cell co-stimulation with systemic VSV-cDNA treatment, long term cures (>100 days) of over 60% of mice with established i.c. melanomas were achieved, whereas control mice succumbed to tumour within 25-30 days. Our data show that tumours of the same histological type, but growing in different anatomical locations, represent a series of related, but antigenically distinct, ‘quasi-species’ because the site of tumour growth profoundly affects the profile of potential immunogens expressed by the tumour cells. This has important implications for the design of therapies which target the same histological type of tumour growing in different locations.

Co-targeting angiogenesis and immunosuppressive cell networks to improve anti-cancer therapy

We have recently shown that angiopoietin-2 (ANG2/ANGPT2), a proangiogenic factor that promotes endothelial-cell survival and growth by activating the TIE2 receptor, may limit tumour sensitivity to vascular-endothelial growth factor (VEGFA)-targeted therapies. Indeed, combined ANG2/VEGF signalling blockade suppresses tumour angiogenesis and progression in tumours that adaptively up-regulate ANG2 in response to VEGFA blockade (Rigamonti et al., Cell Reports 2014). Although these findings support the clinical rationale for co-targeting ANG2 and VEGFA in tumours that develop resistance to VEGFA inhibition, tumour-associated macrophages (TAMs) represent an important source of pro-angiogenic and immunosuppressive signals that can contribute to abate the efficacy of anti-angiogenic therapy. To address this issue, we are currently developing combination treatments that involve co-targeting angiogenesis and immunosuppressive TAMs, as well as re-stimulating T cells, primarily in mouse models of breast cancer. The results of these studies will be presented at the Conference.

Full authorship
Nicolo’ Rigamonti1, Celine Rmili-Wyser1, Hans-Joachim Mueller2, Carola Ries2, and Michele De Palma1

1 The Swiss Institute for Experimental Cancer Research (ISREC), Swiss Federal Institute of Technology Lausanne (EPFL), Lausanne, Switzerland
2 Roche Diagnostics GmbH, Penzberg, Germany
Neutrophil-derived signals promote initiation abilities of cancer stem cells during metastasis

Collectively our data support the notion that neutrophils sustain fundamental survival and stemness abilities, thereby contributing to metastasis. Targeting the identified neutrophil signals in the context of metastatic disease opens promising opportunities for novel anti-tumour therapeutic strategies.

Introduction

Breast cancer is by far the commonest cancer in women, with an estimated 1.6 million new cases every year, and it is an ideal candidate in which to develop drug therapy for cancer prevention.

Two drugs, tamoxifen and raloxifene, are licensed for preventive therapy in the United States. More recently, two other selective oestrogen receptor modifiers (SERMs), lasofoxifene and arzoxifene, have been investigated in large prevention trials in osteoporotic women. In an individual patient overview of all these drugs, a 55% reduction in ER positive cancer in the five years of active treatment and a further 42% reduction in the next 5 years was seen. However no reduction in ER negative tumours has occurred.

Newer approaches are looking at the role of aromatase inhibitors (AIs). The MAP.3 trial evaluated exemestane and a 65% reduction in invasive tumours after a relatively short 30 months median follow up was seen. More recently the IBIS 2 trial using anastrozole has completed analysis of 3,846 women with a median follow up of 5 years and reported a 53% reduction in all breast cancer, with a larger reduction in ER positive invasive breast cancer. Fracture rates were not significantly increased, and musculoskeletal and vasomotor symptoms were increased, but only by about 10%, with very high rates in the placebo arm.

As both of these classes of drugs (SERMs and AIs) have important side effects, it is important to focus their use among women most likely to benefit. Models have been developed to aid this decision and the Tyrer-Cuzick model appears to be one of the best at the moment. However, newer results have shown that mammographic breast density is an important predictor and a risk score combining the 67 currently identified risk SNPs may also add to predictive accuracy.

Competing interests: Research funding received by AstraZeneca
Symposia abstracts (continued)

14.40 – 15.05  
Room 3B  
Peter Rothwell,  
University of Oxford, UK  

Effects of aspirin on cancer incidence and metastasis

Evidence from observational studies has suggested for several decades now that aspirin might reduce the long-term incidence of some cancers, particularly of the gastrointestinal tract. Long-term follow-up of randomised trials of daily aspirin versus control in prevention of vascular events has recently shown that aspirin does indeed reduce incidence of colorectal cancer after a delay of 8–10 years,\(^1,2\) and that it reduces deaths due to other gastrointestinal cancers and possibly lung cancer.\(^3\)

There is also some evidence that aspirin improves outcome in patients who develop cancer whilst on treatment. The short-term effect of aspirin on deaths due to cancer is larger than the effect on incidence and the effect on mortality occurs too quickly to be reasonably be explained by an effect only on carcinogenesis or early cancer growth.\(^4\) In keeping with evidence that platelets play an important role in blood borne metastasis, in five large randomised trials of aspirin vs control in prevention of vascular events randomisation to aspirin reduced rates of metastasis in participants with a new diagnosis of cancer during follow-up.\(^5\) Consistent evidence of similar effects on distant metastasis and outcome have also been reported in observational studies.\(^6\)

These findings are encouraging, but questions remain. In relation to cancer prevention, for example, most of the randomised trials studied so far included mainly men, although 17-year follow-up in the Womens Health Study did recently show consistent effects in women. Similarly, although evidence of effects of aspirin on risk of gastrointestinal cancers is now substantial, more data are required on other cancers and the optimal dose of aspirin for long-term prevention of cancer remains uncertain. The NON-Vascular outcomes on Aspirin (NOVA) Collaboration has been established to collate all data from previous and ongoing trials of aspirin in order to provide as reliable data as possible on short-term and long-term effects of aspirin.

Cancer and obesity prevention: finding the causes of the causes

The UK has seen an impressive reduction in the prevalence of cancer in the last three decades. But we have seen this decrease is matched by an increase in incidence – we have developed some excellent tools for saving lives and treating the disease, but poor at preventing it. The rise in cancer incidence is matched by a rise in obesity prevalence, and there is good reason to suggest the two are related: low levels of physical activity, high levels of sedentary behaviour and high intakes of fatty and sugary foods and insufficient fruits and vegetables and all major contributors to the risk of cancer obesity and to the risk of cancer. We have a common agenda in prevention.

Let me focus on food and nutrition. It is the leading cause of death and ill-health in the World Health Organisation’s analyses of the Global Burden of Disease. Diet-related NCDs are rapidly becoming the leading causes of early death in lower-income countries. Traditional diets, rich in plant-based foods, vegetables, pulses, grains, are being replaced by foods rich in fats and sugars and salt: tasty and attractive but less protective from ill-health.

There are interested parties in these changes in dietary patterns. Globally, a significant proportion of advertising is devoted to promoting food, fast food outlets, alcohol and tobacco. Further advertising promotes sedentary behaviours. These are large, powerful industries. It can even be argued that the food industry has an embedded investment in fatty tissue: an overweight person needs to consume more just to maintain their core temperature, move around, repair and service their organs. It is perhaps not surprising that food companies are advertising their products globally, and also extending their marketing into remote rural areas of the world.

How do we tackle these big forces? I believe that health professionals have a unique voice and are credited with being relatively free from vested interests. Doctors are taken seriously and given an audience where many others are not, so it is important that researchers, clinicians, practitioners, join with your associations and groups to speak out.

However, there is one caveat. The narrative of blame for obesity is very much a narrative of individual responsibility, of poor choices and stupidity. The media reinforce the message with images and headlines implying blame. More important to us, there are surveys of health practitioners showing that many also have this view of obesity being a result of irresponsibility, and it is important to challenge yourself before speaking out. It is very hard to lose weight once gained, as many of us in this room will acknowledge. We need to be fully on the side of our patients in the wider struggle to prevent poor health.

Discussion
Symposia abstracts (continued)

Stem cells and cancer

Introduction
Every organ harbours adult stem cells which have the potential for long-term replication, together with the capacities of self-renewal and multi-lineage differentiation. These stem cells function in tissue homeostasis and contribute to regeneration in response to injury. In addition, many cancers are caused by transforming mutations occurring in tissue-specific progenitor cells.

Some tumours appear to have a hierarchical cellular organisation similar to normal organs and contain cancer cells that possess characteristics associated with normal stem cells, specifically the ability to give rise to all cell types found in a particular cancer sample.

Wnt activating mechanisms in colorectal cancer
Wnt signalling pathways play essential roles in embryonic development and tissue homeostasis. Aberrant activation of Wnt signalling is the primary cause of colorectal cancer (CRC). Loss of function of adenomatous polyposis coli (APC) is a key step to initiate adenoma formation through constitutive Wnt activation. Despite the crucial role of Wnt/APC in tumour initiation, limited drug targets or inhibitors of Wnt pathway have been developed nowadays due to the unclear mechanism of how APC truncation activates Wnt pathways. We have previously redefined the Wnt activation model in the physiological state, and have further demonstrated the failure of b-catenin ubiquitination in APC-mutated cells as the principal deregulated event upon APC mutation. It still remains unclear how APC mediates b-catenin ubiquitination in the destruction complex. One of our research focuses is to characterise the APC regulatory role in b-catenin ubiquitination to gain better insight of Wnt pathway activation in CRC. We also study the efficacy and efficiency of the current available Wnt inhibitors in CRC cells and organoids by generating specific Crispr-targeted mutations. We aim to identify specific drug targets by understanding the Wnt activating mechanism in CRC.

Tumour-propagating cells in non-small cell lung cancer
Our long-term goal is to elucidate the role of stem cells in lung homeostasis as a prerequisite to the development of therapeutic strategies that can be used to prevent or attenuate lung disease and lung cancer. Our previous experience isolating the first stem cell population from the adult murine lung, termed bronchioalveolar stem cells (BASCs), and our demonstration of a role for these cells in lung cancer, serves as a platform to address these questions. We have recently developed three-dimensional co-culture and subcutaneous co-injection assays that allow us to quantitatively assess the identity and the differentiation potential of lung stem cells. This approach led us to uncover a cross-talk between lung endothelial cells and lung stem cells via a novel signalling axis involving Bmp4, Nfatc1 and Tsp1; this pathway drives BASCs to differentiate into the alveolar epithelial cell lineage. Our work in the intersection of stem cell biology and lung disease has expanded into new insights for understanding metastasis and non-small cell lung cancer (NSCLC). We previously showed the adenocarcinoma Kras/p53 mutant mouse model contains Sca1+ tumour-propagating cells (TPCs), the cells that recapitulate the tumour by transplantation. We recently showed multiple lung tumour sub-populations can give rise to metastatic disease, and that the Sca1+ CD24+ TPCs have the highest metastatic potential. We also showed the Hippo pathway mediators
Yap/Taz are necessary and sufficient for lung cancer progression. Finally, in a new mouse model of lung squamous cancer, the second most common type of NSCLC, we identified a TPC population defined by the markers Sca1 and NGFR. These studies illustrate the utility of stem cell biology approaches to provide new avenues for lung cancer therapeutic targeting.

**Neutral and biased replacement of intestinal stem cells**

The regular anatomy and simple cellular organisation of the intestine provides a powerful model for understanding self-renewal. Our approach is to functionally test the clonogenic potential of populations with different properties and in an agnostic way describe in quantitative terms their net contribution to the stem cell pool as whole. We have previously developed strategies to identify and clonally mark quiescent cells to follow their fate over time. In intestine these are now recognised as committed secretory progenitors but with regenerative potential following injury and are not therefore the steady state stem cells acting to maintain the tissue. In developing methods for lineage tracing that reflects the activity of functional stem cells we have identified that much smaller numbers of stem cells maintain the epithelium before and after transformation than previously suspected. In determining the probabilities of single cells 'winning' in clonal competition with their neighbours we have been able to demonstrate and quantitatively measure the altered probabilities of stem cells carrying defined oncogenic mutations. A continuing challenge is to apply these approaches through the various stages of cancer progression and contexts.
The objectives of this workshop are:
1. to present some of the existing computational tools to perform quantitative image analysis of cancer data sets.
2. to encourage life scientists to develop computational skills to develop their own image analysis algorithms.

The need for image analysis is ever growing in many fields and cancer is not an exception. New and powerful microscopes with automated stages and 3D, 4D and 5D capabilities generate more and more data sets, placing an increased burden in the analysis of those data sets. The development of methods of analysis to extract meaningful and quantitative information from these images is an important part in the search of understanding biological processes. For that purpose many specialised tools, commercial and open-source, are appearing in the market. Sometimes, these tools are normally developed with specific experiments in mind and do not always fit to a particular setting. Some tools present some generic capabilities and it is up to the users to ‘programme’ their own solutions. This may take some time at the beginning, as it takes time to learn how to develop algorithms. However, in the long run, it may be beneficial to develop our own solutions instead of trying to adapt conventional software package.

Our symposium will review the basic principles of tumour immunology, providing a refresher on how the immune system responds to tumour cells and how tumours can escape this. We will also examine clinical applications of immunotherapy and how we might best select patients who would benefit from different immunotherapeutic approaches.

Lunch and refreshments will be available.
The Dragon’s Den: involving consumers in your research

12.45–14.00
Room 12
Hosted by NCRI Consumer Liaison Group

Does your research proposal need some consumer involvement or feedback? Do you need advice on how to tackle tissue donation or help in obtaining approval from an ethics committee or from a funder? Are you facing recruitment challenges in a study that is already open?

Then come and meet our friendly dragons for some free and expert consumer involvement and advice!

Who are the friendly dragons?
Groups of patients and carers who are experienced in cancer research, including NCRI Consumer Liaison Group members who sit on Clinical Studies Groups, CTRad and other NCRI initiatives, members of Independent Cancer Patients’ Voice (ICPV), and consumers who sit on funding committees.

What will happen at the Dragon’s Den session?
The dragons will review your proposal, offer you feedback, and address any specific problems or questions that you may have.

All the discussions will be in small groups in an informal setting, and you can arrange for follow-up contacts if you wish.

Lunch and refreshments will be available.

Join us next year: 1–4 November 2015
conference.ncri.org.uk
Parallel sessions and workshops

- **Debate: This house believes that the Cancer Drugs Fund has been good for British cancer patients**
  
  Hosted by Malcolm Mason, Cardiff University and Velindre Hospital, UK
  
  **16.00 – 17.40**
  
  **Hall 1A**
  
  **Debate panel:**
  
  Peter Clark, NHS England, UK
  
  David Cameron, Edinburgh Cancer Research Centre, Scotland, UK
  
  Tom Crosby, Velindre NHS Trust, Wales, UK
  
  Martin Eatock, Northern Ireland Cancer Network, Northern Ireland, UK

- **Genetically engineered mouse models (GEMM) of cancer: how have they performed?**
  
  Hosted by Owen Sansom, Cancer Research UK Beatson Institute, Glasgow, UK
  
  **16.00 – 16.05**
  
  **Room 4**
  
  **Introduction by the host**
  
  **16.05 – 16.30**
  
  **Room 4**
  
  Inhibiting TGF-beta signalling in cancer models
  
  Gareth Inman, University of Dundee, UK
  
  **16.30 – 16.45**
  
  **Room 4**
  
  Proffered paper: Developing integrin alpha-v beta-6 as a therapeutic target for high-risk breast cancer
  
  John F Marshall, Barts Cancer Institute, London, UK
  
  **16.45 – 17.10**
  
  **Room 4**
  
  Title TBC
  
  Ian Tomlinson, University of Oxford, UK
  
  **17.10 – 17.35**
  
  **Room 4**
  
  Fly approach to cancer therapeutics
  
  Ross L Cagan, Icahn School of Medicine at Mount Sinai, New York, USA
  
  **17.35 – 17.40**
  
  Discussion

- **Metabolic adaptations of cancer**
  
  Hosted by Eyal Gottlieb, Cancer Research UK Beatson Institute, Glasgow, UK
  
  **16.00 – 16.05**
  
  **Room 11**
  
  Introduction by the host
  
  **16.05 – 16.30**
  
  **Room 11**
  
  Fumarate induces redox-dependent senescence by modifying glutathione metabolism
  
  Eyal Gottlieb, Cancer Research UK Beatson Institute, Glasgow, UK
  
  **16.30 – 16.45**
  
  **Room 11**
  
  Proffered paper: Fatty acid binding protein 4 – a point of convergence for angiogenic and metabolic signalling pathways in endothelial cells
  
  Ulrike Harjes, Weatherall Institute of Molecular Medicine, University of Oxford, UK
Metabolic transformation of fumarate hydratase-deficient cancer cells  
**Christian Frezza,** University of Cambridge, UK

Title TBC  
**Robert Bachoo,** UT Southwestern Medical Center, Dallas, USA

Discussion

### Pancreatic cancer: from basic science to clinical implementation

**Hosted by Claus Jorgensen,** Cancer Research UK Manchester Institute, UK

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<tr>
<td>16.05 – 16.30</td>
<td>Room 3B</td>
<td>Using mouse models to explore stromal composition and function</td>
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<td><strong>Ben Z Stanger,</strong> Perelman School of Medicine at the University of Pennsylvania, USA</td>
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<td><strong>Tobias Janowitz,</strong> Cancer Research UK Cambridge Institute, UK</td>
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<td>Reciprocal tumour-stroma signalling in pancreatic ductal adenocarcinoma</td>
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<td><strong>Claus Jorgensen,</strong> Cancer Research UK Manchester Institute, UK</td>
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<td>Room 3B</td>
<td>Clinical relevance of genomic aberrations in pancreatic cancer</td>
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<td><strong>Andrew Biankin,</strong> Wolfson Wohl Cancer Research Centre, University of Glasgow, UK</td>
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### Targeting Ras

**Hosted by Julian Downward,** Cancer Research UK London Research Institute, UK

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<td>Renewed efforts to target Ras directly: the NCI Ras Program</td>
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<td><strong>Dominic Esposito,</strong> Frederick National Laboratory for Cancer Research, Frederick, USA</td>
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<td>16.30 – 16.45</td>
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<td>Proffered paper: A phase 1, dose escalation study of paclitaxel with GSK1120212 (trametinib) for the treatment of advanced melanoma</td>
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<td><strong>Nicholas Coupe,</strong> Oxford University Hospitals NHS Trust, UK</td>
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| 16.45 – 17.10 | Chemical biological modulation of Ras signalling  
Room 3A  
**Herbert Waldmann**, Max Planck Institute of Molecular Physiology, Dortmund, Germany |
| 17.10 – 17.35 | Searching for novel therapeutic approaches to RAS, the commonest and least tractable oncogene  
Room 3A  
**Julian Downward**, Cancer Research UK London Research Institute, UK |
| 17.35 – 17.40 | Discussion |

#### Thinking beyond the androgen receptor: a new horizon in castrate-resistant prostate cancer

Hosted by **David Waugh**, Queen’s University Belfast, UK

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| 16.00 – 16.05 | Introduction by the host  
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| 16.05 – 16.30 | Targeting DNA repair and transcriptional interplay in prostate cancer: mechanisms and implications for disease progression  
Room 12  
**Karen E Knudsen**, Thomas Jefferson University, Philadelphia, USA |
Room 12  
**Kevin Prise**, Queen’s University Belfast, UK |
| 16.45 – 17.10 | Tracking genomic aberrations of the androgen receptor (AR) in castrate-resistant prostate cancer (CRPCa)  
Room 12  
**Gerhardt Attard**, The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK |
| 17.10 – 17.35 | Molecular profiling of castration-resistant prostate cancer  
Room 12  
**Tapio Visakorpi**, University of Tampere, Finland |
| 17.35 – 17.40 | Discussion |

#### Workshops

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| 16.00 – 17.40 | Interventional oncology: State of the art  
Hosted by **Ricky Sharma**, University of Oxford, UK |
| 16.00 – 17.40 | Neuro-rehabilitation and palliative care for brain tumours  
Hosted by **Jane Fleming**, University Hospital Waterford, Ireland |

Download the app for the latest updates
Parallel session and workshop abstracts

Debate: This house believes that the Cancer Drugs Fund has been good for British cancer patients

Introduction
The Cancer Drugs Fund was introduced in the NHS in England at a time when healthcare policy was becoming increasingly divergent across the home nations, and at a time of increasing cost constraints. The intention was to improve access to cancer drugs in England. Senior clinicians from all four nations come together to debate the impact of the fund on cancer treatment in the UK.

Panel
Peter Clark, NHS England, UK
David Cameron, Edinburgh Cancer Research Centre, Scotland, UK
Tom Crosby, Velindre NHS Trust, Wales, UK
Martin Eatock, Northern Ireland Cancer Network, Northern Ireland, UK

Genetically engineered mouse models (GEMM) of cancer: how have they performed?

Introduction
With the drive for stratified medicine based, GEMM mouse models offer an excellent platform to assess genotype specific therapies, actionable mutations and robustly validate novel targets. At one of the earliest NCRI Cancer Conferences, Tyler Jacks offered $100,000 for someone to cure his KRAS P53 lung cancer GEMM model. Reuben Shaw has gone one better and cured KRAS LKB1 lung cancer which is an even more aggressive model with single agent metformin. But how relevant and predictive are these models? Mouse hospitals have arisen but as yet not led to a successful clinical trial. This session will discuss these issues and highlight new avenues and opportunities for GEMM models e.g. immunotherapy and immunomodulation.

Inhibiting TGF-beta signalling in cancer models

Join us next year: 1–4 November 2015
conference.ncri.org.uk
**Proffered paper: Developing integrin alpha-v beta-6 as a therapeutic target for high-risk breast cancer**

**Background**
The integrin αvβ6 is not expressed by most normal tissues but is upregulated during tissue remodelling processes including cancer, where it can promote migration, invasion and survival of cancer cells. High expression of αvβ6 is associated with poor survival in several cancers (colon, lung, cervix) but its role in breast cancer has not been established.

**Method**
We screened over 2000 breast cancer samples for protein expression using immunohistochemistry and another 2000 (METABRIC dataset) for β6 mRNA (ITGB6) expression. Functional tests (migration, invasion, organotypic invasion) supported therapeutic αvβ6-blocking antibody (264RAD) studies in mice.

**Results**
Immunohistochemistry revealed that high expression of the integrin subunit beta6 (β6) is associated with very poor survival (HR=1.99, P=2.9x10^-6) and increased metastases to distant sites (P=0·02). Bioinformatic analysis of the 2000 women in the METABRIC cohort confirmed these results. Furthermore, both analyses showed that co-expression of HER2 gave a significantly worse prognosis (HR=3.43, P=4x10^-12). This was investigated further.

In vitro studies showed that HER2-driven invasion was mediated by αvβ6. In xenograft studies αvβ6-blocking antibody 264RAD intraperitoneally suppressed growth of BT-474 and MCF-7/HER2-18 human breast cancer xenografts similarly to Trastuzumab, the therapeutic HER2-blocking antibody (P<0.001) (both 10mg/kg, bi-weekly). However when 264RAD was combined with Trastuzumab it almost eradicated 100mm3 BT-474 tumours (p<0.0001), stopped the growth of 100mm3 MCF-7/HER2-18 tumours (p<0.0001) and completely eliminated small (10-20mm3) MCF-7/HER2-18 tumours (p<0.0001). Immunohistochemistry revealed residual tumours expressed significantly reduced αvβ6, HER2, Ki67, αSMA and increased Caspase 3 (BT474 only). Western blotting confirmed these results and additionally showed loss of downstream signalling molecules including Akt2 and Smad2. Overall analysis of residual tumours suggested they were of a much lower ‘grade’ tumour.

**Conclusion**
70% of women treated with trastuzumab have, or develop resistance. We suggest targeting both αvβ6 and HER2 could provide an important novel therapy for these women.

**Acknowledgements**
This work was funded by grants from Breast Cancer Campaign and MRC.
**Fly approach to cancer therapeutics**

Cancer has proven a difficult disease to treat in part due to its genetic complexity. This robust cancer network has resisted most long-term treatments including targeted therapies. My laboratory has developed complex Drosophila cancer platforms based on patient sequencing. In general, we find that the greater genetic complexity leads to increased resistance to standard therapeutics.

We have used our fly models to explore cancer mechanisms and, combined with computational and medicinal chemistry, to develop novel drugs based on ‘rational polypharmacology’. Through these efforts we have developed novel drugs, improved old drugs, and have established a Center to bring these and related tools to patient care.

**Discussion**

**Metabolic adaptations of cancer**

**Introduction**

Despite the vast accumulation of knowledge on the molecular bases of cancer, it remains a major cause of death in the developed world. Hence, more effective approaches for cancer treatment are needed. The search for new vulnerabilities of tumours revived an interest in understanding metabolic reprogramming of cancer, from energy metabolism to anabolism. It is now clear that most tumour suppressors and oncogenes regulate metabolic reactions, such that tumour-promoting mutations elicit alterations of metabolic activities and dependencies. In addition, advanced technology in analytical chemistry (metabolomics) facilitated the transformation of cancer metabolism field to the heart of cancer research and cancer drug discovery.

**De novo purine biosynthesis dictates glutamine dependency of glioblastoma cells**

L-glutamine has the unique physiological function of balancing carbon and nitrogen requirements of tissues. It has been proposed that cancer cells undergoing aerobic glycolysis require glutamine carbons to replenish the tricarboxylic acid (TCA) cycle and sustain accelerated anabolism (anaplerosis). Yet we showed that, in glioblastoma (GBM) cells, about half of the glutamine-derived glutamate is secreted out of the cells and does not enter the TCA cycle. In the absence of glutamine, replenishment of the TCA cycle is insufficient to restore cell proliferation. In contrast, cataplerotic reactions culminating with the conversion of glutamate to glutamine by glutamine synthetase (GS) are sufficient to sustain growth in the absence of glutamine. GS is expressed in ~80% of human GBM tumours, and 13C-glucose tracing showed that GS utilises TCA cycle-derived carbons to produce glutamine in patients. GS-derived glutamine provides the amide nitrogen for de novo biosynthesis of nucleotides and thereby dictates GBM dependency on glutamine.
Parallel session and workshop abstracts
(continued)

16.30 – 16.45
Room 11

Ulrike Harjes,
Weatherall Institute of 
Molecular Medicine,
University of Oxford, UK

Proffered paper: Fatty acid binding protein 4 – a point of convergence 
for angiogenic and metabolic signalling pathways in endothelial cells

Background
Fatty acid binding protein 4 (FABP4) is an intracellular fatty acid chaperone and 
implicated in cancer progression. In endothelial cells, FABP4 is induced by VEGFA and 
inhibition of FABP4 blocks most of the VEGFA effects. DLL4-NOTCH signalling limits tumour 
angiogenesis induced by VEGFA, and its upregulation is indicated in tumour angiogenesis 
and tumour therapy resistance. We investigated the DLL4-NOTCH-dependent regulation of 
FABP4 in endothelial cells.

Method
We used gene/protein expression and interaction analyses following inhibitor treatment 
and RNA interference to investigate the regulation of FABP4 human umbilical vein 
endothelial cells (HUVECs).

Results
We found that FABP4 is directly induced by NOTCH. Stimulation of NOTCH signalling 
with human recombinant DLL4 led to FABP4 induction, independently of VEGFA. FABP4 
induction by VEGFA was reduced by blockade of DLL4 binding to NOTCH, or inhibition 
of NOTCH signal transduction. Chromatin immunoprecipitation of NOTCH intracellular 
domain showed increased binding to two specific regions in the FABP4 promoter. The 
induction of FABP4 gene expression was dependent on the transcription factor FOXO1, 
which was essential for basal expression of FABP4, and FABP4 upregulation following 
stimulation of the VEGFA and/or the NOTCH pathway.

Conclusion
We show that the DLL4-NOTCH pathway mediates endothelial FABP4 expression. 
This indicates that induction of the angiogenesis-restricting DLL4-NOTCH can have 
pro-angiogenic effects via this pathway. It also provides a link between DLL4-NOTCH 
and FOXO1-mediated regulation of endothelial gene transcription, and shows that 
DLL4-NOTCH is a nodal point in the integration of pro-angiogenic and metabolic 
signalling in endothelial cells. In light of recent advances in tumour metabolism 
research, this mechanism may be crucial for targeting angiogenesis in the tumour 
environment, and may be a potential mechanism of tumour therapy resistance.

Acknowledgements
This work was funded by Cancer Research UK, Breast Cancer Research Foundation 
and National Health Service Biomedical Research Centre.

16.45 – 17.10
Room 11

Christian Frezza,
University of Cambridge, 
UK

Metabolic transformation of fumarate hydratase-deficient cancer cells
Fumarate hydratase (FH) is an enzyme of the tricarboxylic acid cycle (TCA cycle) that 
catalyses the reversible hydration of fumarate into malate. Germline mutations of FH 
are responsible for Hereditary Leiomyomatosis and Renal-Cell Cancer (HLRCC). We have 
combined analytical chemistry and metabolic computational modelling to investigate 
the metabolic consequences of the loss of FH in immortalised and primary mouse kidney 
cells. We demonstrated that the accumulation of fumarate caused by the inactivation 
of FH leads the formation of succinicGSH, a covalent adduct between fumarate and 
glutathione. Chronic succination of GSH, caused by the loss of FH, or by exogenous
fumarate, leads to persistent oxidative stress that results in cellular senescence in vitro and in vivo. The ablation of p21, a key mediator of senescence, in Fh1-deficient mice resulted in the transformation of benign renal cysts into kidney carcinomas, suggesting that fumarate-induced senescence is a tumour suppressive mechanism that must be bypassed for the initiation of renal cancers.

17.00 – 17.35
Room 11

Robert Bachoo, UT
Southwestern Medical Center, Dallas, USA

Title TBC
Abstract not received.

17.35 – 17.40

Discussion

Pancreatic cancer: from basic science to clinical implementation

16.00 – 16.05
Room 3B

Claus Jorgensen, Cancer Research UK
Manchester Institute, UK

Introduction
Pancreatic ductal adenocarcinoma (PDAC) is the fourth most lethal cancer with an overall 5-year survival below 5%, which has remained almost unchanged for 50 years. New understanding into the development of PDAC alongside technological advances is critical to facilitate early detection, identification and validation of therapeutic targets and subsequent clinical implementation. This session will cover aspects of recent insights into PDAC from basic science to clinical translation.

16.05 – 16.30
Room 3B

Ben Z Stanger, Perelman School of Medicine at the University of Pennsylvania, USA

Using mouse models to explore stromal composition and function
Pancreatic ductal adenocarcinoma (PDA) has the lowest survival rate of any major cancer killer, with an average survival from time of diagnosis of approximately 6 months. One reason for this poor outcome is the proclivity of PDA cells to spread, with the majority of patients having widely disseminated disease at the time of diagnosis. Epithelial-mesenchymal transition (EMT) is believed to be one mechanism underlying the ability of this epithelial tumour type to escape its primary site in the pancreas. Within the context of a well-defined mouse model of PDA, we have introduced a lineage tracer which allows us to distinguish all epithelially-derived cells within the pancreas, thereby providing a unique window into the dynamic changes in phenotype that accompany tumour progression. I will discuss our latest findings using this lineage tracing tool to understand metastasis and the role of the microenvironment in tumour behaviour.
Proffered paper: CXCL12 expression by FAP+ stromal cells is associated with a paucity of CD3+ T cells in human pancreatic adenocarcinoma and may offer a target for drug treatment

Background
To date, human pancreatic ductal adenocarcinoma (PDAC) has been resistant to T cell checkpoint antagonist treatment in clinical trials. The mechanism of this resistance is not understood. Identification of the mechanism may suggest treatments that are synergistic to T cell checkpoint antagonists.

Method
Human samples were investigated in concordance with institutional and national policies. Paraffin sections of confirmed PDAC tumours from the University of Cambridge Addenbrooke’s Hospital tissue bank were immunohistochemically assessed for FAP, p53, CXCL12 and CD3 pattern. These pattern were also investigated in PDAC tumour samples from LSL-KrasG12D/+;LSL- Tp53R172H/+;Pdx-1-Cre (KPC) mice to correlate murine and human results prior to testing potential interventions. AMD3100, a specific CXCR4 inhibitor, was administered to KPC mice by osmotic pump at 90mg/ml and tumour volume and p53+ cancer cell counts were assessed to quantify treatment response.

Results
In treatment naïve human tumours p53+ PDAC cells are surrounded by FAP+ cancer associated fibroblasts (CAFs). CD3+ T cells localise mainly to the tumour stroma. These results were also observed in PDAC tumours from KPC mice. FAP+ CAFs show high staining CXCL12 expression. Tumour growth in KPC mice was slowed by AMD3100. Treatment causes T cells to accumulate in the proximity of cancer cells. Counts of p53+ cells were significantly diminished in AMD3100 treated mice compared to PBS treated controls. The effect was synergistic with anti-PD-L1 administration.

Conclusion
T cell exclusion from PDAC tumours in human and the KPC PDAC mouse model is mediated by FAP+ CAFs and involves CXCL12 expression by these cells. Direct inhibition of the CXCL12 receptor, CXCR4, by administration of AMD3100 leads to improved tumour control in mice. This mechanism of tumoural immune-suppression and the pharmacological intervention to overcome it may be relevant to treatment of human PDAC and other cancers. Clinical trials are planned to demonstrate the clinical relevance of the findings described.

Acknowledgements
Tobias Janowitz has been supported by a Wellcome Trust Translational Medicine and Therapeutics academic clinical lectureship.
**Reciprocal tumour-stroma signalling in pancreatic ductal adenocarcinoma**

Pancreatic ductal adenocarcinomas (PDAC) are genetically and histologically heterogeneous with an extensive extracellular matrix deposition and widespread infiltration and activation of stromal cells. This creates an environment which supports resistance to therapeutic intervention. There is only a limited understanding of how signals that emerge from the tumour cells recruit and activate stromal cells and conversely how stromal cells influence tumour cell specific signalling.

We are focusing on identifying and characterising exchanged signals between tumour and stromal cells to provide a detailed understanding of the complex relationship between tumour and host. To address some of these issues we conducted a comprehensive proteomics analysis of PDA that was integrated with a systematic profiling of secreted signalling factors from pancreatic cancer cells. To determine the phenotypic effect of deregulated soluble growth factors and cytokines on pancreatic fibroblasts, we developed and used a high content image-based assay to quantify the impact on myofibroblast activation. Moreover, to derive a better understanding of tumour cell-dependent signalling in associated fibroblasts, we compared global proteomics changes in naïve and activated fibroblasts, which revealed an extensive re-wiring of their signalling capacity. Importantly, we observed that several extracellular matrix components, growth factors and cytokines were released from activated fibroblasts. Finally, to capture the multicellular environment and the composite nature of the exchanged signals, we have conducted extensive cell-specific analysis of reciprocal signalling in co-culture. Interestingly, this revealed that signals originating specifically from tumour cells are ‘translated’ by neighbouring stromal cells to rewire tumour cell signalling in a non-cell autonomous manner.

**Clinical relevance of genomic aberrations in pancreatic cancer**

Our increasing appreciation of the genomic heterogeneity of cancer suggests that the failure of definitive clinical trials to demonstrate efficacy in many instances is due to the low proportion of responsive phenotypes. Developing genotype-guided approaches to therapy may improve outcomes for pancreatic cancer and many other molecularly heterogeneous malignancies with poor survival rates.

We performed whole genome sequencing and CNV analysis of 100 pancreatic ductal adenocarcinomas. Chromosomal rearrangements leading to gene inactivation were prevalent, affecting genes known to be important in pancreatic cancer (TP53, SMAD4, CDKN2A, ARID1A, ROBO2), and novel candidate drivers of pancreatic carcinogenesis (KDM6A and PREX2). Structural variation classified PDAC into 4 subtypes: stable, locally rearranged, scattered and unstable. A significant proportion had focal amplifications of known oncogenes, and many of which contained therapeutic targets for existing or emerging therapies (ERBB2, MET, FGFR1, CDK6, PIK3R3, and PIK3CA), but at low individual prevalence. Although genomic aberrations that represented actionable target segments for existing therapies were present in small proportions, collectively they accounted for over 40% of PDAC. Genomic instability co-segregated with inactivation of genes important in DNA damage repair (BRCA1, BRCA2 or PALB2), and a mutational signature characteristic of defective DNA maintenance by the BRCA pathway. Patients within this subgroup exhibited significant and sometimes exceptional responses to platinum-based chemotherapy.
Renewed efforts to target Ras directly: the NCI Ras Program

Ras proteins play a major role in human cancers, but to date we have been unsuccessful in targeting Ras for therapeutic attack. It has long been believed that Ras was an ‘undruggable’ target based on decade-old failures due in part to incomplete knowledge of Ras biology, particularly Ras protein-protein interactions and signal transduction. Very little structural or biophysical knowledge of key Ras interacting partners is available, and the biochemical differences between Ras oncogenic mutants and how they affect signalling is still poorly understood. One major goal of the NCI Ras program is to find new methods to target KRas directly by developing tools and methods to improve our understanding of basic KRas biology and KRas signalling. Combining efforts in biochemistry, biophysics, structural biology, and assay development, we aim to develop a better understanding of how KRas interacts with key partners and effectors with the goal of identifying novel druggable targets in the pathway. Areas of focus in the Ras program include cataloguing the different biochemical and biophysical properties of KRas mutants, generating and characterising fully processed KRas protein, determining high resolution structures of Ras and Ras protein complexes, and developing novel assays for high-throughput drug screening. We will discuss our ongoing work in these areas highlighting some of our initial data on novel ways to target this challenging protein.

Proffered paper: A phase 1, dose escalation study of paclitaxel with GSK1120212 (trametinib) for the treatment of advanced melanoma

Background
Treatment options are limited for patients with BRAF wildtype and NRAS mutant metastatic melanoma. Paclitaxel has modest activity as monotherapy in melanoma. ERK is constitutively activated in melanoma regardless of BRAF mutational status resulting in degradation of pro-apoptotic proteins, hypothetically causing resistance to paclitaxel. Trametinib is a highly selective allosteric MEK inhibitor that effectively suppresses ERK. Trametinib in combination with paclitaxel is therefore potentially synergistic and explored in this phase 1 trial.
Chemical biological modulation of Ras signalling

The Ras-proteins are lipidated membrane-bound GTPases that function as molecular switches, translating growth factor-derived signals into cell growth and differentiation. Mutations in Ras are found in around 20-30% of all human tumours, making this oncogene product one of the most relevant targets for the development of anti-cancer drugs. However, despite intense worldwide efforts direct interference with signalling by the Ras proteins has not led to clinically useful drugs yet.

In this talk, the systems biology-based identification of counterintuitive lipidation-dependent mechanisms which orchestrate Ras localisation and signalling will be presented. This research included the development of methods for the synthesis of tailor-made Ras proteins, the development of small molecule inhibitors of Ras palmitoylation and shuttling, and their application in live cell imaging.

The most potent compounds inhibit oncogenic signalling in cells by alteration of Ras localisation and suppress proliferation of human pancreatic ductal adenocarcinoma cells in vitro and in vivo. These findings may inspire novel drug discovery efforts aimed at the development of anti-cancer drugs targeting tumours with mutations in Ras.

Searching for novel therapeutic approaches to RAS, the commonest and least tractable oncogene

RAS oncogenes are the most commonly activated in human cancer, with over a million deaths a year caused by cancers driven by mutationally activated RAS. However, despite RAS proteins being exceptionally well-validated cancer targets, little progress has been made in targeting them in the clinic. This is now beginning to change with a number of advances being made recently in the development of protein-protein interaction inhibitors that block RAS interaction with effector enzymes and also renewed approaches to targeting the post-translational processing of RAS.

My laboratory has concentrated on targeting downstream effectors of RAS, such as RAF protein kinases and type I phosphoinositide 3-kinases (PI3Ks). Disruption of the interaction of PI3K p110α with oncogenic mutant KRAS has been shown to prevent tumour development in a mouse model of KRAS driven lung cancer and also to cause partial regression of established tumours. Additional inhibition of the RAF/ERK pathway with MEK inhibitors causes improved tumour regression in these models, but may prove unacceptably toxic.

Another means of targeting this critical oncogene is the identification of unique dependencies of RAS mutant tumour cells through the use of functional genomic screens, or a synthetic lethal approach. We have identified signalling networks that are essential for RAS mutant cells, but not cells with wild type RAS, including a transcriptional programme controlled by the GATA2 transcription factor which involves the proteasome, NF-κB and Rho signalling. Several synthetic KRAS synthetic lethal screens have been carried out, with rather variable results. However, the one constant feature that has emerged across multiple screens is the proteasome, suggesting that it would be worth re-examining proteasome inhibition in KRAS mutant tumours, especially since a large number of new and less toxic proteasome inhibitors are now in late stage clinical development.

Thinking beyond the androgen receptor: a new horizon in castrate-resistant prostate cancer

Introduction

Targeting of androgen receptor signalling is a mainstream of therapy for advanced disease. However, despite a wave of clinical development and drug approvals, the survival benefit from androgen-deprivation therapies remains sub-optimal. Speakers in the session will focus on addressing recent advances in our understanding of androgen signalling, using pre-clinical evidence conducted in relevant genetic backgrounds to highlight potential modes that underpin progression on therapy and new opportunities for combinatorial therapy.
**Targeting DNA repair and transcriptional interplay in prostate cancer: mechanisms and implications for disease progression**

Recent development of abiraterone, enzalutamide, alpharadin, cabazitaxel and sipuleucel-T has improved outcome, but metastatic prostate cancer (PCa) remains a uniformly fatal disease. Moreover, while molecular subtyping has afforded therapeutic benefit and improved patient survival in other tumour types, no such advances have been gained in PCa. At present, all patients with metastatic PCa are treated identically, without selection of appropriate therapeutic regimens based on tumour profiling. Emerging data from our laboratory and others strongly support the concept that alterations in DNA damage repair (DDR) pathways are more common than previously thought in sporadic PCa, and alterations in these pathways may accord new, more effective means of therapeutic intervention. First, alterations in genes whose functions are key for DNA repair are observed and increase in frequency as a function of disease progression. Second, and new findings indicate that the androgen receptor (AR) is a critical effector of DNA repair competence that alters the response to genotoxic insult in advanced PCa. This function of AR is manifest through the ability of AR to regulate expression and activity of DNAPK, a dual function kinase that facilitates both double-strand DNA break repair and transcriptional activation. Third, emerging data from clinical trials reveal that therapeutic agents which target the DDR pathway are contextually effective in treating advanced prostate cancer, consistent with the postulate that a significant subset of advanced tumours have altered DDR programmes. Findings to be discussed strongly support a model wherein selected DDR pathways can be developed as therapeutic targets to tailor treatment for prostate cancer and improve outcome for advanced disease.

**Proffered paper: Optimal radiation targeting of PTEN deficiency in castrate-resistant prostate cancer in combination with modulators of DNA damage and repair**

**Background**

Radical radiotherapy, often in combination with hormone ablation, is safe and effective in treating the majority of patients with organ-confined prostate cancer (PCa); however, it is associated with a biochemical failure rate of 30%. Improving radiotherapy response is clinically important since patients exhibiting biochemical failure develop castrate-resistant metastatic disease for which there is no curative therapy and median survival is 8-18 months. PTEN is a tumour suppressor whose loss of function through deletion of alleles, promoter methylation or mutation is prevalent in early and advanced PCa and is associated with castrate-resistance. Loss of PTEN function has been reported to confer resistance to radiation treatment.

**Method**

A tetracycline inducible PTEN model in PC3 prostate tumour cells was used to test the efficacy of combined treatments of radiation +/- the ATM inhibitor KU60019 in vitro and in vivo (as a xenograft model in male Fox Chase SCID mice (Charles River Laboratories)). Animals were administered an oral suspension of this drug [100 mg/kg] for 5 consecutive days. PTEN-induction by daily doxycycline gavaging was performed for 48 hours prior to commencing ATMi treatment and was continued until removal of the animal from the experiment. Anti-tumour efficacy was determined by tumour growth delay with a 4-fold increase in tumour size as an endpoint.
Parallel session and workshop abstracts (continued)

Results
Significant reduction of tumour growth in ATMi treated PTEN deficient tumours was observed, with low toxicity and synergistic efficacy in combination with 2 Gy irradiation. These findings were supported by western blot analysis of resected tumours which showed targeted inhibition of phosphorylated ATM and its downstream target Histone H2AX. Additional immunofluorescence staining of FFPE tumours confirmed PTEN induction.

Conclusion
Combination treatments of ionising radiation +/- ATMi in prostate tumours with different PTEN status has potential for future validation.

Acknowledgements
This work was supported by Prostate Cancer UK [S10-08].

Tracking genomic aberrations of the androgen receptor (AR) in castration-resistant prostate cancer (CRPCa)

Next-generation sequencing of circulating plasma DNA from castration-resistant prostate cancer (CRPCa) offers an opportunity to monitor tumour genomic aberrations over the course of the disease. These studies have identified multiple independent clones with distinct genomic patterns showing complex dynamics over the lethal course of prostate cancer, partially related to treatment selection pressure. Clones harbouring resistance-conferring AR mutations emerge in approximately 20% of patients treated with abiraterone and exogenous corticosteroids. These mutations are activated by ligands that persist in abiraterone-treated patients, including by prednisolone or dexamethasone at clinically relevant doses, and confer a survival advantage. Often sub-clones with alternative genomic aberrations, including AR amplification, are also present suggesting multiple mechanisms co-exist that lead to re-activation of AR signalling. These data introduce a management paradigm requiring sequential monitoring of advanced prostate cancer patients with plasma and tumour biopsies to ensure early discontinuation of agents when they become potential disease drivers and identify therapeutic targets that will allow selection of the next best treatment.

Molecular profiling of castration-resistant prostate cancer

The emergence of castration resistance is one of the most challenging clinical problems in treating prostate cancer (PCa). We have utilised several genome-wide methods to identify genetic and epigenetic alterations underlying the development of castration-resistant PCa (CRPCa). First, comparative genomic hybridisation (CGH) revealed amplification of androgen receptor (AR) gene in one third of CRPCAs. Subsequently, it was shown that CRPCa cells commonly over-express AR, sensitising the receptor to low levels of androgens. Recently, we have deep-sequenced CRPCAs for genomic, transcriptomic and DNA methylation alterations. PCa and CRPCa tumours showed a distinct signature on all levels of characterisation. AR, TGF-beta and EMT signalling pathways as well as chromatin modifiers were recurrently aberrated in PCa whereas CRPCa-specific aberrations mainly affected AR signalling. Dual genomic hits (i.e. mutations and amplifications) to AR were also found in some CRPCa cases. Alternative AR transcripts were also common in CRPCa cells but rare in hormone-naïve PCa cells.
Interventional oncology: state of the art

Advances in imaging and interventional radiology have resulted in the emergence of a new medical specialty at the interface between Clinical Oncology and Radiology, termed ‘interventional oncology’. It encompasses a broad range of diagnostic, supportive and therapeutic procedures, including complex drainage procedures, thermal ablation, local delivery of chemotherapy or embolics and interventional administration of radiopharmaceuticals. Interventional oncology is a growth area for Cancer Centres and referring oncologists need to be aware of the treatments. This session will demonstrate how interventional oncology is changing clinical practice, with an emphasis on patient selection, clinical governance and specialist follow-up as a team approach.

Speakers:

New frontiers in the treatment of liver cancer
Valérie Vilgrain, Beaujon Hospital, Clichy and Universite Paris Diderot, Sorbonne Paris Cite, France
This talk will deal with imaging underpinning interventional oncology. Prof Vilgrain will use liver imaging as an example of how state-of-the-art imaging is essential to successful radiological procedures. Finally, she will address the important issue of the how new techniques in Interventional Oncology can be incorporated into head-to-head clinical trials such as SARAH.

Interventional oncology: the next oncological discipline
Andy Adam, King’s College London, UK
This talk will deal with the PRINCIPLES underpinning interventional oncology. Prof Adam will discuss emerging data on the combined use of interventional radiological procedures and radiotherapy or chemotherapy. Finally, he will address the important issue of the partnership between Radiology and Clinical Oncology to optimise care for patient.

Future clinical trials of interventional oncology: What we can learn from surgical trials
Graeme Poston, Liverpool University, UK
This talk will deal with DESIGN OF CLINICAL TRIALS in interventional oncology. Prof Poston will use surgical oncology trials to illustrate learning points relevant to future trials of new radiological procedures. Finally, he will address the important issue of the how we should design clinical trials to change clinical practice in the future.
Parallel session and workshop abstracts
(continued)

16.00 – 17.40
Hall 1C
Hosted by Jane Fleming, University Hospital Waterford, Ireland

Neuro-rehabilitation and palliative care for brain tumours
This workshop is aimed at bringing together professionals in the fields of supportive care, quality of life, neuro-rehabilitation, and palliative care to plan transition points in care and foster collaborations in research.

Following diagnosis and treatment of a brain tumour, patients will have different trajectories, which may be predicted, ranging across recovery, stability or progression. For improved survivorship, close collaboration is required between clinicians involved with neuro-rehabilitation, supportive care and palliative care. This requires coordination of different specialties and expertise from supportive care to end-of-life care. It is imperative that improvement in prognosis is associated with improvement in the quality of survivorship.

Speakers:
Introduction
Jane Fleming, University Hospital Waterford, UK
Seizure management for primary brain tumour patients
Andrew Nicolson, The Walton Centre, Liverpool, UK
Rehabilitation for patients with neurological tumours
Alasdair Fitzgerald, Astley Ainslie Hospital, Edinburgh, UK
The patient perspective
Debbie Keatley, NCRI Brain CSG
Palliative care and rehabilitation – two sides of the same coin?
Faye Gishen, Marie Curie Hospice Hampstead, London, UK
Searching for a safety net on the brain tumour roller coaster – the carer and family perspective
Kathy Oliver, International Brain Tumour Alliance (IBTA)
Improving patient outcomes – the Neuro-Oncology rehab hub
Helen Bulbeck, Brainstrust – the brain cancer people, UK
Spotlight Theatre

10.30 – 10.45

Simon R Lord,
University of Oxford, UK

ACP McElwain Prize: A neoadjuvant window study of metformin’s effects on breast cancer metabolism

There are now over 50 clinical trials worldwide examining the potential of metformin as an anticancer drug. However most metformin biomarker studies to date have solely investigated serum metabolic markers of the insulin axis and immunohistochemical markers of proliferation, apoptosis and the AMPK axis. This single arm clinical study in a neoadjuvant breast cancer population, investigated the intratumoral breast cancer metabolic response as determined by dynamic 18F-FDG PET-CT with changes in metabolic serum markers, whole cancer mRNA genome sequencing (RNASeq), tumour metabolomic profiling using mass spectrometry techniques, and intratumoral changes in markers of the AMPK axis determined by immunohistochemistry. In total 41 patients were recruited and underwent pharmacodynamic tests pre- and post- 2 weeks of metformin. Preliminary RNASeq data demonstrates striking changes in the expression of genes encoding for the units of the mitochondrial electron transport chain (including complex 1) and the regulatory enzymes of glycolysis, glutaminolysis and fatty acid oxidation consistent with a direct metabolic effect on breast cancer cells by metformin. Also serum C-peptide was lowered by metformin (0.56 ± 0.04 nmol/L vs 0.48 ± 0.02 nmol/L, pre- and post-metformin, respectively (paired t-test, p = 0.003)) in this cohort of non-diabetic breast cancer patients, suggesting that downregulation of the host’s insulin axis may also play a role. Kinetic modelling of the early dynamic PET-CT data suggested a trend toward a decrease in efflux of 18F-FDG from the tumour subsequent to metformin treatment. In summary, this is the first study in the clinical setting to offer strong evidence that metformin may directly affect mitochondrial function in cancer cells resulting in an energy stress that subsequently upregulates glucose and glutamine metabolism.

Full authorship

Lord SR1,2, Patel N3, Liu D3, Fenwick J3, Gleeson F3, Haider S1,2, Buffa F1,2, Harris AL1,2.

1 Department of Oncology, University of Oxford, UK
2 The Weatherall Institute of Molecular Medicine, University of Oxford, UK
3 Oxford Cancer Imaging Centre, Churchill Hospital, Oxford, UK

12.30 – 13.00

British Association of Surgical Oncology (BASO) Surgery Prize and Cancer Research Excellence through Surgical Trials (CREST) Award

Lynda Wyld (BASO Vice President) will present the BASO Surgery Prize to the winner, Sumit Nandi. Richard Shaw (NIHR CRN: Cancer, Associate Director and National Specialty Lead for Surgical Oncology) will present the CREST award to the winning surgical team.

There will also be a presentation from the BASO Surgery Prize winner:

Gemcitabine-loaded and antibody-tagged superparamagnetic iron oxide nanoparticles as targeted drug vehicles in pancreatic cancer cell lines

Sumit Nandi, University of Liverpool, UK

Background

Pancreatic cancer is a devastating malignancy. Despite advances in the surgical management and adjuvant chemotherapy, pancreatic cancer still has a very poor prognosis. Nanotechnology provides a novel approach for targeted drug delivery, possibly reducing the offset effects of systemic chemotherapy. Superparamagnetic iron oxide nanoparticles (SPIONs) are inorganic particles that can be functionalised as targeted drug
vehicles with a stealth polymer coating and a specific antibody tag to recognise certain antigen expressing cells. Our aim is to develop and investigate the effects of SPIONs capable of targeted cell death of pancreatic cells by release of its chemotherapy payload.

**Method**
Micellar SPIONs, incorporating a gemcitabine pro-drug, conjugated to anti-CA19.9 antibodies (NP:CA19.9) were manufactured using self assembly methodology. Cellular uptake was assessed using transmission electron and co-localisation fluorescent microscopy. Antigen expression of cell lines was determined using indirect immunofluorescence. Antibody targeting was assessed using EZ4U cytotoxicity assay in BxPC-3 (Ca-19-9 +ve) and MiaPaCa-2 (Ca-19-9 -ve) cell lines.

**Results**
Endocytosis of the SPIONs was demonstrated by their presence in endosomes and corroborated by colocalisation analysis (Manders coefficient = 0.92). The IC50 of NP:CA19.9 was significantly improved with specific antibody targeting in BxPC-3 cells (354nM vs 1,175nM) but absent in MiaPaCa-2 cells (3,510nM vs 3,090nM).

**Conclusion**
We have developed a novel nanohybrid to target antigen expressing pancreatic cancer cells using a specific antibody tag. When loaded with modified gemcitabine, these SPIONs act as pH-triggered delivery vehicles capable of intracellular drug release. This could reduce off target effects leading to increased chemotherapy agent efficacy and offer the prospect for new treatments in pancreatic cancer.

**BACR AstraZeneca Young Scientist Frank Rose Award: Genome analysis of clonally transmissible cancers in dogs and Tasmanian devils**

Tasmanian devil facial tumour disease (DFTD) and canine transmissible venereal tumour (CTVT) are the only two known naturally occurring clonally transmissible cancers. These are cancers that can be transmitted between individuals by the physical transfer of living cancer cells. Thus DFTD and CTVT are long-lived somatic cell lineages that each first originated once as cancers in single individuals but that have now ‘metastasised’ through their respective host populations as parasitic clonal cell lineages. DFTD is spread by biting and is threatening its host species, the Tasmanian devil, with extinction. CTVT is a sexually transmitted cancer that affects dogs and has spread around the world together with its host. The genome sequences of DFTD and CTVT have revealed features of the individuals that first spawned these two lineages as well as patterns of mutation and selection that have driven the evolution and characterised the emergence and spread of these two unusual long-lived cancers.
ACP McElwain Prize: RORyt+ innate lymphoid tissue inducer cells promote lymphatic invasion in triple negative breast cancers

Inflammation and infiltration of the tumour tissue by host immune cells have been shown to support tumour growth, invasion and metastasis. Here, we describe the novel identification of innate lymphoid tissue inducer (LTi) cells within breast cancer tumour microenvironments; and their role in promoting tumorigenesis via activation of the RANKL/RANK axis.

Results
We analysed the expression of LTi-associated chemokine/chemokine receptor genes (CXCL13/CXCR5, CCL19/CCL21/CCR7) within the METABRIC Tissue Bank. An unsupervised hierarchical cluster analysis revealed co-expression of these genes, categorising breast tumours as relatively high/low expressors. Tumours exhibiting relatively high expression of these genes were found to be enriched for ‘basal-like’ breast cancers. Immunofluorescence of the primary tumour sections identified cells that were comparable in phenotype to LTi cells. Higher LTi counts were found to correlate with an increased lymphatic vessel density, lymphatic tumour cell invasion with greater risk for involving >4 lymph nodes within the basal-like breast cancers. We also report on the dynamic nature of LTi cell recruitment into the primary tumours within a triple negative breast cancer (4T1.2) mouse model. These changes were associated with change in the serum levels of LTi-associated chemokines and RANKL (a key regulator of LTi cell function). Our in vitro and in vivo work demonstrated: i) recruitment of intratumoural LTi cells was dependent primarily on CCL21; ii) the close interaction between the tumoural LTi and stromal cells was dependent on CXCL13; and iii) an inhibitory effect of chemokine blockade on tumour cell migration/metastasis into the draining lymph node via RANK-RANKL axis.

Conclusion
We report for the first time, the identification of LTi cells within the human breast cancer tumour microenvironment and propose a pivotal role for these cells, through stromal cell interactions in the tumour microenvironment, in facilitating lymphatic invasion of tumour cells through modulation of the local lymphoid chemokine profile.

Full authorship
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10 UCL Cancer Institute, Paul O’Gorman Building, University College London, London WC1E 6DD, UK

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Spotlight Theatre (continued)

17.45 – 17.55

Routes from diagnosis for patients diagnosed with breast cancer in England in 2014

Julie Flynn, Macmillan Cancer Support

Background
Routes from diagnosis (RfD) performs retrospective analysis of almost 85,000 breast, lung, prostate and brain/CNS cancer patients’ interactions with the NHS in England over seven years – the richest picture yet of cancer survivorship. It reveals significant variation in outcomes, survival and cost within and between cancer types. It allows us to understand just how many people affected by cancer are living with serious long-term conditions.

Methods
After removing patients with invalid records, no inpatient records or evidence of any prior tumours, 26,926 patients diagnosed with breast cancer in England in 2004 were included in the detailed survivorship outcome framework for breast cancer.

Results
Limited survival:
6.5% of patients had 0-12 months survival
13.8% of patients had 1-5 years survival with cancer complications

Limited to moderate survival:
5.5% of patients had 1-7 year survival with other inpatient diagnoses
0.9% of patients had 1-7 years survival with no inpatient diagnoses
4.5% of patients had 5-7 years survival with cancer complications

On-going survival:
19.2% of patients had 7+ years survival with cancer complications
29.1% of patients had 7+ years survival with other inpatient diagnoses
20.5% of patients had 7+ years survival with no other inpatient diagnoses

19.9% of the cohort experienced metastatic disease. Of those patients identified, 14.7% of patients aged 25-64 had already developed metastases at the time of their breast cancer diagnosis. This proportion was higher for each of the older age brackets; 65-69 (19.9%), 70-74 (22.3%) and 75+ (25.9%). 54.7% of patients aged 65-69 who presented with metastases at diagnosis lived to one year, whilst one year survival for patients of this age who developed metastases after diagnosis was 95.5%. Five-year survival was 19.7% and 32.1% respectively.

Conclusions
While it is already known that the majority of breast cancer patients survive, we now know that more than two thirds of patients surviving seven years or more experience either cancer complications or other inpatient morbidities. This tells us that the health journey for breast cancer patients can be long-term and complex.

Late diagnosis disproportionately affects older and more deprived populations, earlier diagnosis is essential to enabling the UK to meet the best cancer outcomes in Europe.

19.30 – 20.00

Trends in Pathology and The Royal College of Pathologists prize

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Programme at a glance

Workshops

08.00 – 08.45
Room 11
BACR educational workshop: Epigenome-wide association studies (EWAS) in cancer – converging on a consensus approach

08.00 – 08.45
Room 3B
A beginner’s guide to cancer immunotherapy
Hosted by Elaine Vickers, Science Communicated Ltd, Sheffield, UK

08.00 – 08.45
Room 12
Nutrition in cancer research: the UK National Strategic Research Initiative in Nutrition and Cancer
Hosted by Southampton Biomedical Research Centre with NOCRI

08.00 – 08.45
Room 4
Biobanking to enable research
Hosted by Bridget Wilkins, NCRI Confederation of Cancer Biobanks and St Thomas’ Hospital, London, UK

Clinical Trials Showcase part 1

Hosted by Matt Seymour, NIHR Clinical Research Network: Cancer, Leeds, UK

09.00 – 09.20
Hall 1A
ARTemis: A randomised trial of bevacizumab with neo-adjuvant chemotherapy (NACT) for patients with HER2-negative early breast cancer: primary endpoint – pathological complete response (pCR)
Helena Earl, University of Cambridge and NIHR Cambridge Biomedical Research Centre, UK

09.20 – 09.40
Hall 1A
REST- A Dutch/UK randomised phase III trial on the use of thoracic radiotherapy in extensive stage small-cell lung cancer
Corinne Faivre-Finn, The Christie NHS Foundation Trust, Manchester, UK

Plenary lecture

Chaired by Owen Sansom, Cancer Research UK Beatson Institute, Glasgow, UK

09.40 – 10.20
Hall 1A
Mouse models of malignant glioblastoma multiforme: cancer stem cells and beyond
Luis Parada, University of Texas Southwestern Medical Center, USA

Networking, exhibition viewing, poster viewing, Spotlight Theatre and refreshment break

10.20 – 10.50
Hall 2

10th Conference celebratory talks

Chaired by Richard Marais, Cancer Research UK Manchester Institute, UK

10.50 – 11.20
Hall 1A
Whither clinical trial design
Speaker TBC

11.20 – 11.50
Hall 1A
Whither metabolomics
Karen H Vousden, Cancer Research UK Beatson Institute, Glasgow, UK

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11.50 – 12.20
Hall 1A
Whither localised therapies
Tim Maughan, Cancer Research UK and Medical Research Council
Oxford Institute for Radiation Oncology, UK

Networking, exhibition viewing, poster viewing, Spotlight Theatre and lunch

12.20 – 14.10
Hall 2

Scientific symposia

12.45 – 14.00
Room 11
Do biomarkers matter in gastrointestinal and colorectal cancers?
Hosted by Amgen
Amgen Oncology has provided sponsorship for this conference. Amgen Oncology has a stand at the conference and a symposium but has had no input into the main programme, topics or awards.

12.45 – 14.00
Room 3A
The good, the bad and the experts: exploring research, diagnosis and management in pancreatic ductal adenocarcinoma (PDAC)
Hosted by Celgene

Symposia

14.10 – 15.40
Hall 1A
Cancer evolution
Hosted by Charles Swanton, Cancer Research UK London Research Institute and University College London Cancer Institute, UK

14.10 – 15.40
Room 11
Cancer immunotherapy 2014: a new paradigm
Hosted by James Larkin, The Royal Marsden NHS Foundation Trust, London, UK

14.10 – 15.40
Room 3B
High precision radiation therapy
Hosted by Diana Tait, The Royal Marsden NHS Foundation Trust and The Royal College of Radiologists, London, UK

14.10 – 15.40
Room 3A
Optimising care for those living with and beyond cancer – where does primary care fit in?
Hosted by Ella Watson, Oxford Brookes University, UK and Clare Wilkinson, Bangor University, UK

Networking, exhibition viewing, poster viewing and refreshment break

15.40 – 16.00
Hall 2

Parallel sessions and workshops

16.00 – 17.40
Room 3B
Biology of the radiation response
Hosted by W Gillies McKenna, Cancer Research UK and Medical Research Council Oxford Institute for Radiation Oncology, UK

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Programme at a glance (continued)

16.00 – 17.40  DNA repair in cancer biology and treatment  
   Hall 1A  Hosted by Chris Lord, The Institute of Cancer Research, London, UK

16.00 – 17.40  Integration between oncology and palliative care  
   Room 4  Hosted by Irene Higginson, King’s College London, UK

16.00 – 17.40  Melanoma  
   Room 3A  Hosted by Pippa Corrie, Addenbrooke’s Hospital, UK

16.00 – 17.40  Molecular pathology – the genomic basis of cancer  
   Room 11  Hosted by Manuel Salto-Tellez, Queen’s University Belfast, UK

16.00 – 17.40  Molecular profiling of childhood cancers  
   Room 12  Hosted by Christine Harrison, Northern Institute for Cancer Research and Royal Victoria Infirmary, Newcastle, UK

16.00 – 17.40  Workshop: Imaging as a biomarker for cancer management  
   Hall 1B  Hosted by Gina Brown, The Royal Marsden NHS Foundation Trust, London, UK and Fiona Gilbert, University of Cambridge, UK

16.00 – 17.40  Workshop: Helping doctors to suspect cancer promptly when patients present with symptoms: from clinical audit to novel point-of-care testing  
   Hall 1C  Hosted by Georgios Lyratzopoulos, University of Cambridge, UK and Greg Rubin, Durham University, UK

Networking and break Registration area and Galleria

17.40 – 18.00  Registration area and Galleria

Clinical Trials Showcase part 2
Hosted by Matt Seymour, NIHR Clinical Research Network: Cancer, Leeds, UK

18.00 – 18.20  ET: A randomised, multicentre, phase III trial to evaluate ERCC1 as a predictive biomarker for comparing platinum with nonplatinum chemotherapy, in patients with advanced/metastatic non-small cell lung cancer (NSCLC)  
   Allan Hackshaw, University College London, UK

18.20 – 18.40  Prospective, multi-centre, case-control study to evaluate a novel Cytosponge™-TFF3 test for diagnosing Barrett’s oesophagus  
   Rebecca Fitzgerald, MRC Cancer Unit, Hutchison/MRC Research Centre, Cambridge, UK

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Plenary lecture
Chaired by Caroline Dive, Cancer Research UK Manchester Institute, UK

18.40 – 19.20
Hall 1A
BACR Tom Connors lecture – Targeting and imaging cancer phenotypes: Focal Adhesion Kinase as a critical regulator of tumour cells and the host immune response
Margaret Frame, University of Edinburgh, UK

Conference dinner and party (ticketed event)

20.00 onwards
The Echo Arena, BT Convention Centre
Limited tickets are available for this event. Please go to the onsite payment desk to reserve your place no later than noon, Tuesday 4 November. Only ticket holders will be admitted.
Glioblastoma multiforme (GBM) is an incurable cancer with a rapid progression and a prognosis of months from the time of diagnosis. Given the resistance to all known therapies, new paradigms to understand this disease and identify novel therapeutic targets are sorely needed. We have used genetically engineered models to ablate GBM relevant tumour suppressors in brain cells. Our fully penetrant mouse models indicate that adult stem cells and progenitors are preferential sites of tumour initiation. As such, further study of these cells, and how they transform may provide unique insights into tumour development and progression. Our efforts to understand whether additional cell types can give rise to GBM indicate that fully differentiated brain cells are considerably more resistant to tumour suppressor mediated transformation than are stem cells, but in contrast, OPC progenitor cells are also able to give rise to GBM that, while pathologically similar to stem cell derived tumours, also have unique growth and molecular properties that distinguish them clearly. I will discuss the state of understanding of these tumours and the implications for cancer stem cells and therapeutic opportunities.

Lay abstract

Traditional concepts of how solid tumours form and grow involved equivalent cell division. That is, all cells of the tumour are essentially equivalent and each has the property of dividing to give the ‘equivalent’ tumour cells. The corollary is that therapeutic shrinking of the tumour by, for example, 70% represents a 70% effectiveness of the therapy. If we instead consider that some tumours may develop in a hierarchical manner, with stem-like cells at the apex of the hierarchy giving rise to cells that lose their stemness and can only divide for a limited number of cycles, then shrinkage of the tumour is a poor measure of therapeutic effectiveness. In this model, therapeutic effectiveness can only be measured by the loss of the stem-like cells – the cancer stem cells.
selective autophagic targeting of Src (and other oncogenic tyrosine kinases) is an adaptive mechanism to maintain viability, identifying a cancer cell vulnerability that provides a new therapeutic opportunity.

We have also found a novel function for FAK in generating an immunosuppressive and pro-tumorigenic microenvironment. Specifically, FAK activity in cancer cells drives recruitment and/or differentiation of CD4+CD25+FoxP3+ regulatory T cells, likely through altered transcription of the genes encoding the intratumoral cytokines Interleukin-2 (IL-2), Interleukin-10 (IL-10), and Transforming Growth Factor-beta (TGFβ). This suppresses the anti-tumour activity of antigen-primed cytotoxic CD8+ T cells and permits survival, and growth, of FAK-expressing tumours in immune competent hosts. Importantly, cancer cell immune evasion depends on FAK’s catalytic activity, and VS-4718, a small molecule FAK kinase inhibitor that is in clinical development, suppresses regulatory T cells, increases cytotoxic CD8+ T cells and promotes tumour regression and clearance in mice. This identifies an additional mechanism, namely immunomodulation, through which FAK kinase inhibitors may impart anti-tumour efficacy.

Full authorship
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**Clinical Trials Showcase**

▶ **ARTemis: A randomised trial of bevacizumab with neo-adjuvant chemotherapy (NACT) for patients with HER2-negative early breast cancer: primary endpoint – pathological complete response (pCR)**

**Background**

Bevacizumab (bev) has been used with NACT in breast cancer trials. Geparquinto reported benefit for bev in triple negative (neg) patients (pts) (pCR 36.4% vs 27.8% p=0.02), as did CALGB-40603 (pCR 52% vs 44%, p=0.057), although NSABP-B40 showed benefit in ER positive (pos) pts (pCR 23.3% vs 15.2%, p=0.008).

**Method**

ARTemis is a randomised phase 3 trial adding bev to NACT (docetaxel (D)-FEC). Pts with HER2-neg invasive breast cancer were eligible. Stratification was by age, ER status (neg:weak pos:strong pos), tumour size (T2:T3/4), clinical involvement of axillary nodes and inflammatory/locally advanced disease. Pts were randomised (1:1) to bev+D-FEC or D-FEC. The primary endpoint was pCR, defined as no residual invasive cancer in the breast or axillary lymph nodes after NACT. 800 pts were required to detect 10% differences in pCR rates; 85% power, 5% alpha level.

**Results**

800 pts were randomised from 66 UK centres (May2009-Jan2013). 68% were <50 years old, 19% had inflammatory and/or locally advanced disease, 79% of tumours <50mm, 52% clinical node pos and 33% ER-neg. A 2-reader independent review of pathology reports showed significantly more pts on bev+D-FEC had a pCR (22% (95%CI 18-27%) vs 17% (13-21%); p=0.03 [adjusted for stratification factors]). pCR rates differed significantly across ER (neg 38%, weak pos 39%, strong pos 7%; p<0.0001) and differences in bev effect across ER were observed ((bev+D-FEC:D-FEC pCR rates) ER neg (44%:32%), weak pos (52%:26%), strong pos (6%:7%)). Treatment effect remained significant after adjustment for ER (p=0.03).

**Conclusion**

ARTemis showed a significant improvement in pCR with the addition of bev to D-FEC. ER-neg and ER-weak pos / HER2-neg breast cancer pts appeared to benefit most from bev, whilst pCR rates in ER-strong pos pts were lower and did not appear to benefit from bev. Our results are similar to those reported in Geparquinto and CALGB-40603.

Helena Earl1,2, Louise Hiller3, Janet Dunn3, Clare Blenkinsop3, Louise Grybowicz4, Anne-Laure Vallier4, Jean Abraham1,5, Jeremy Thomas6, Elena Provenzano2,5, Luke Hughes-Davies5, Karen McAdam7, Stephen Chan8, Rizvana Ahmad9, Tamas Hickish10, Stephen Houston11, Daniel Rea12, John Bartlett13,14, Carlos Caldas1,15, David Cameron14, Larry Hayward6

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REST – A Dutch/UK randomised phase III trial on the use of thoracic radiotherapy in extensive stage small-cell lung cancer

09.20 – 09.40
Hall 1A

Corinne Faivre-Finn,
The Christie NHS Foundation Trust, Manchester, UK

Background
A majority of patients with extensive stage small-cell lung cancer (ES-SCLC) who undergo chemotherapy and prophylactic cranial irradiation (PCI), have persistent intrathoracic disease. This randomised study, evaluated the role thoracic radiotherapy (TRT) in this patient group.

Method
Patients (WHO 0-2) with confirmed ES-SCLC with a response after 4-6 cycles of standard chemotherapy were randomised to receive TRT (30 Gy/10fractions) or no TRT. All received PCI. Primary study endpoint was overall survival. Acute toxicity was graded using CTCAE v3.0. The study had 80% power to detect a hazard ratio of 0.76 at 1 year. Accounting for 5% dropout before treatment, 483 patients had to be randomised. Analysis was based on intent to treat.

Results
Between Feb’09 and Dec’12, 498 patients were enrolled; Median follow-up was 24 months. 88% had residual intrathoracic disease. Baseline characteristics were well balanced. Mean age was 63 year (36-85), 89% had WHO 0-1; 11% WHO2. Mean interval between start of chemotherapy and randomisation was 16 weeks. In the TRT arm, 5 patients did not receive TRT due to progression or refusal. No severe toxicities were observed. At the time of analysis (Dec’13), 76 patients were still alive. Progression-free survival was longer in the TRT-arm (HR=0.73, CI 0.61-0.87; p=0.001). Curves for overall survival overlapped during the first 9 months and then diverged in favour of the TRT-arm. The survival difference at 1 year was not statistically significant (33% vs 28%; HR=0.84, CI 0.69-1.01; p=0.066). Survival at 2 years was 13% (CI 9-19) for the TRT and 3% (CI 2-8%) for the control arm (P=0.004).

Conclusion
TRT improves progression-free survival. Although TRT did not influence the risk of death in the first year, it led to a significant increase in 2-year survival. In addition to PCI, TRT should be considered in all patients who respond to chemotherapy.

Acknowledgements
This study was supported by grants from the Dutch Cancer Society (CKTO, endorsed by Cancer Research UK, supported by the Dutch Lung Cancer Research Group, Manchester Academic Health Science Centre Trials Co-ordination Unit and the UK National Cancer Research Network.
Clinical Trials Showcase (continued)

Corinne Faivre-Finn1, Matthew Hatton2, Michael Snee3, Pooja Jain4, Paula Wilson5, Rhona McMenemin6, Clive Peedell7, Andrew Bates8, Angel Garcia9, Janet Ironside10, Sally Falk1, Harm van Tinteren11, Astrid Keijser12, Ben Slotman13

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ET: A randomised, multicentre, phase III trial to evaluate ERCC1 as a predictive biomarker for comparing platinum with nonplatinum chemotherapy, in patients with advanced/metastatic non-small cell lung cancer (NSCLC)

18.00 – 18.20
Hall 1A

Allan Hackshaw,
University College
London, UK

Background
Increased expression of excision repair cross-complementing-group-1 (ERCC1) protein is associated with platinum resistance in NSCLC based on retrospective findings. We conducted the first prospective phase III trial to evaluate ERCC1 as a predictive biomarker: to assess whether non-platinum therapy is superior to platinum for ERCC1-positive and non-inferior for ERCC1-negative tumours.

Method
Chemo-naive patients with stage IIIB/IV NSCLC were randomised to receive either platinum-based or non-platinum doublet chemotherapy, after ERCC1 stratification using a recommended monoclonal antibody (clone 8F1) assessed centrally. Patients with squamous histology had cisplatin/gemcitabine or paclitaxel/gemcitabine; non-squamous patients had cisplatin/pemetrexed or paclitaxel/pemetrexed, every 3 weeks for up to 6 cycles. Primary endpoint was overall survival (OS). From 2012, we concurrently used another antibody (clone 3F2) specific for XPF/ERCC1 protein complex.

Results
648 patients (squamous=177; non-squamous=471) were randomised. Recruitment stopped in 2012 for squamous patients because paclitaxel/gemcitabine OS was inferior to cisplatin/gemcitabine, regardless of ERCC1 status: median OS 7.7 vs 11.2 months, HR=1.54 (95% CI 1.05-2.26, P=0.03). Accrual terminated in 2013 when the main trial objectives could not be met for non-squamous patients: preliminary OS HR for ERCC1-positive 1.08 (95%CI 0.75-1.54, P=0.68), median OS 9.7 (paclitaxel/pemetrexed) vs 10.9 (cisplatin/pemetrexed) months. For ERCC1-negative, HR 0.94 (0.62-1.43, P=0.79), median OS 9.5 (paclitaxel/pemetrexed) vs 8.4 (cisplatin/pemetrexed) months. HRs using XPF antibody were ERCC1+ve 1.10 (0.76-1.61, p=0.61), and ERCC1-ve 1.21 (0.65-2.24, p=0.54). Findings for progression-free survival were similar. ERCC1 positive rate in non-squamous patients was 54% (8F1) or 71% (XPF); but 28% of patients had discordant ERCC1 status. Grade 3/4 haematological toxicities were less common with non-platinum therapy: 31% (cisplatin/gemcitabine) vs 17% (paclitaxel/gemcitabine), and
22% (cisplatin/pemetrexed) vs 17% (paclitaxel/pemetrexed).

**Conclusion**

ERCC1 was not a predictive biomarker in advanced NSCLC, in contrast to retrospective and meta-analysis findings[1], but supported recent concerns[2]. Key issues arose over using predictive biomarkers in prospective trials, and their reliability.

**References**


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### Prospective, multi-centre, case-control study to evaluate a novel Cytosponge™ – TFF3 test for diagnosing Barrett’s oesophagus

**18.20 – 18.40**

**Hall 1A**

**Rebecca Fitzgerald,**
Hutchison/MRC Research Centre, Cambridge, UK

**Background**

Barrett’s oesophagus (BE) is a common condition which is often undiagnosed and predisposes to oesophageal adenocarcinoma. A minimally-invasive cell sampling device, the Cytosponge™, coupled with an immunohistochemical marker, trefoil factor 3 (TFF3), has shown promise as a diagnostic tool.

**Method**

A multicentre, prospective study was performed to evaluate the safety, acceptability and accuracy of the Cytosponge™-TFF3 test in patients with reflux and dyspepsia symptoms without BE (controls) and cases with BE (≥ 1 cm circumferential BE or ≥3 cm tongues). The data were compared with endoscopy.

**Results**

1,110 individuals took part comprising 463 controls (median age 56 years (interquartile
range (IQR 44-66), Male:Female ratio 1.0:1.3) and 647 cases (median age 66 years (IQR 58-73), Male:Female ratio 4.0:1.0). 1,042 (93.9%) patients successfully swallowed the Cytosponge™ and no serious adverse events were attributed to the device. Using a visual analogue scale, the Cytosponge™ was rated favourably compared with endoscopy (p=0.0003) and patients who were not sedated for endoscopy were more likely to rate the Cytosponge™ higher than endoscopy (Mann-Whitney test, p<0.001). The overall sensitivity of the test was 79.9% (95% confidence interval (CI) 76.4-83.0%) increasing to 87.2% (95%CI 83.0-90.6%) for BE segments with ≥3 cm of circumferential BE. There was no loss of sensitivity in patients with dysplasia. The specificity for diagnosing BE was 92.4% (95%CI 89.5-94.7%).

Conclusion
The Cytosponge™-TFF3 test is safe, acceptable and has very good accuracy for diagnosing BE. This test warrants consideration as an alternative to endoscopy for diagnosing BE with potential applicability to screening in primary care.

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The control of metabolism is a fundamental requirement for all life, with perturbations of metabolic homeostasis underpinning numerous pathologies. While altered metabolism in tumour cells was described almost a century ago, recent work is beginning to reveal how these changes help to support the growth and survival of cancer cells in stressful microenvironments. These metabolic alterations help to promote tumorigenesis, but may also provide targetable vulnerabilities in cancer compared to normal cells that could be exploited for therapy. One challenge facing cancer cells is fluctuating nutrient availability and recent work has highlighted the importance of serine uptake to support one-carbon metabolism via the THF cycle. We have found that the tumour suppressor p53 can help to support the adaptation of cancer cells to serine starvation by facilitating the switch to the de novo serine synthesis pathway (SSP). The activation of p53 in response to serine depletion leads to a transient cell cycle arrest, allowing the cells to channel metabolites into glutathione synthesis and survive increased oxidative stress. Interestingly, many transformed cells are highly dependent on the uptake of exogenous serine and dietary depletion of serine in vivo reduces cancer growth without impacting general health. Surprisingly, despite being interconvertible with serine, glycine cannot substitute for serine in supporting tumour cell growth and our analyses indicate that this is due to a depletion of one-carbon pools in glycine-fed cells, supporting previous data showing excess glycine can be detrimental to tumour growth. De novo serine synthesis involves the diversion of glycolytic intermediates into the SSP, resulting in a greater dependence on OXPHOS to provide energy. As predicted, we have also shown a synergy between serine depletion and inhibitors of OXPHOS and we are testing some of these combinations in experimental tumour therapy. Other metabolic pathways, for example the control of lipid synthesis, are also beginning to reveal new therapeutic targets as well as the potential of repurposing drugs designed to treat other metabolic diseases for cancer therapy.

Funded by CRUK, ERC and MRC.
Localised therapies (surgery and radiotherapy) are the main curative modalities in cancer treatment. Only 11% of cancers are cured by systemic therapy alone. Definition of routes of invasion, meticulous surgical technique, multidisciplinary management and treatment in high volume centres has improved surgical outcomes in many cancers. Minimally invasive surgery has further reduced surgical complications and accelerated return to normal health. In the future the use of robotic surgery and novel image guidance may further reduce morbidity and improve complete resection rates. Biomarkers predicting response to non-surgical therapy will enable avoidance of surgery in those with sensitive disease and prioritisation of surgery in those with predicted resistant disease.

Radiotherapy (RT) has become dramatically more anatomically precise in its delivery in the last 30 years based on increasingly sophisticated imaging, computerised planning and linear accelerator engineering. This has led to reduction in morbidity and created the potential for dose escalation to increase cure. The introduction of proton beam therapy in 2017 will deliver a further reduction in unwanted dose to normal tissues with reduction in morbidity and second cancer risk, making this the RT treatment of choice for cancers in children and young adults and potentially many other patient groups.

The next phase of RT development will be biologically driven. The efficacy of RT treatment varies with differences in the tumour microenvironment, notably hypoxia, metabolism and immune response, and the DNA damage response. Defining this variability using functional imaging, immune and genetic biomarkers and selecting the appropriate way to modulate treatment using novel targeted therapies or differences in dose delivery to deliver biologically optimised treatment will be at the heart of RT research in the next decade. This biologically based stratification added to the anatomical precision of modern radiotherapy carries great promise in improving outcomes in the next decade.
Symposia

Cancer evolution
Hosted by Charles Swanton, Cancer Research UK London Research Institute, UK

14.10 – 14.15
Introduction by the host

14.15 – 14.40
Making sense of intratumour heterogeneity: evidence of a ‘Big Bang’ tumour expansion
Andrea Sottoriva, The Institute of Cancer Research, London, UK

14.40 – 15.05
Unravelling the complexity of lung cancer evolution
Nicholas McGranahan, Cancer Research UK London Research Institute, UK

15.05 – 15.30
Computational dissection of intratumour genetic heterogeneity and applications to the study of cancer treatment, evolution and metastasis
Scott Carter, Broad Institute of MIT-Harvard, Cambridge, USA, Dana-Farber Cancer Institute, Boston, USA and Massachusetts General Hospital, Boston, USA

15.30 – 15.40
Discussion

Cancer immunotherapy 2014: a new paradigm
Hosted by James Larkin, The Royal Marsden NHS Foundation Trust, London, UK

14.10 – 14.15
Introduction by the host

14.15 – 14.40
T cell checkpoint blockade in melanoma: from mouse to man and back
Christian Blank, The Netherlands Cancer Institute, Amsterdam, The Netherlands

14.40 – 15.05
Targeting immune checkpoints in cancer: new mechanistic insights
Sergio A Quezada, UCL Cancer Institute, University College London, UK

15.05 – 15.30
T cell immunosurveillance of healthy and transformed epithelia
Adrian Hayday, King’s College London, UK

15.30 – 15.40
Discussion
### High precision radiation therapy

Hosted by **Diana Tait**, The Royal Marsden NHS Foundation Trust, London, UK and The Royal College of Radiologists

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<td><strong>Uwe Oelfke</strong>, The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK</td>
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### Optimising care for those living with and beyond cancer – where does primary care fit in?

Hosted by **Eila Watson**, Oxford Brookes University, UK and **Clare Wilkinson**, Bangor University, UK

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<td>Models for delivery of follow-up care – what does the evidence tell us thus far?</td>
<td><strong>Jon Emery</strong>, University of Melbourne, Australia</td>
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<td>Optimising care beyond breast cancer – perspectives from the front line</td>
<td><strong>Alastair Thompson</strong>, University of Texas, MD Anderson Cancer Center, Houston, USA and <strong>Maggie Wilcox</strong>, Independent Cancer Patients’ Voice, UK</td>
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Symposia abstracts

Cancer evolution

Introduction
This session is aimed at translational and basic scientists together with clinical, medical and surgical oncologists. A multidisciplinary approach is essential to decipher and manage intra-tumour heterogeneity solid and haematological malignancies, a disease with excessive genomic instability and mutational diversity. Speakers will review the genetic diversity within individual cancer subtypes and novel scientific, medical and informatics approaches to monitor genomic changes over space and time. The impact of our improving knowledge on clinical trial design and deciphering drug resistance mechanisms will be a central focus of this session.

Making sense of intratumour heterogeneity: evidence of a ‘Big Bang’ tumour expansion
Recent cancer genomic studies have revealed an unexpected level of complexity and variation between and within patients. In particular, intratumour heterogeneity is an important issue with critical implications for personalised medicine. However, the lack of a quantitative model of reference with which to make sense to the tsunami of genomic data makes such variation hard to interpret. Here we present a ‘Big Bang’ model, whereby a tumour grows predominantly as a single expansion producing numerous intermixed sub-clones. In this model, not just public (clonal) mutations, but also the majority of detectable private (sub-clonal) mutations arise during the earliest phase of tumour growth. We validated this model by genomic profiling of 349 individual glands from 15 colorectal tumours and show that intratumour heterogeneity patterns naturally follow from the Big Bang. We also demonstrate that most detectable intratumour heterogeneity originates from private alterations acquired early during growth, and not from the later expansion of selected sub-clones. This finding exposes the profile of the primordial tumour, well before it became clinically detectable. This model has important implications in understanding the origins of intratumour heterogeneity and in designing personalised treatment strategies.

Unravelling the complexity of lung cancer evolution
Spatial and temporal dissection of the genomic changes occurring during the evolution of human non-small cell lung cancer (NSCLC) may help elucidate the basis for its dismal prognosis. We sequenced 25 spatially distinct tumour regions from seven operable NSCLCs and found evidence of branched tumour evolution in all cases, with driver mutations arising before and after subclonal diversification. There was pronounced intratumour heterogeneity in copy number alterations, translocations, and mutations associated with APOBEC cytidine deaminase activity. Despite maintained carcinogen exposure, tumours from smokers showed a relative decrease in smoking-related mutations over time, accompanied by an increase in APOBEC-associated mutations. In tumours from ex-smokers, genome-doubling occurred within a smoking-signature context before subclonal diversification, suggesting that a long period of tumour latency may have preceded clinical detection. The presence of regionally separated driver mutations, coupled with the relentless and heterogeneous nature of the genome instability processes are likely to confound treatment success in NSCLC.
Computational dissection of intratumour genetic heterogeneity and applications to the study of cancer treatment, evolution and metastasis

Starting from a normal cell, cancers evolve via multiple rounds of mutation, selection, and expansion. Continued application of this process to the growing cancer cell population results in branched genetic variegation, whereby multiple cancer subclones relate to each other in a tree-like fashion. Consequently, cancer tissues are substantially heterogeneous both across different anatomical regions and within single cancer biopsies. Here we give an overview of a suite of computational tools for dissecting intra-tumour heterogeneity using whole-exome sequencing data. We describe how high-quality copy-number profiles can be generated and integrated with germline SNP and somatic mutation data to resolve the subclonal structure of individual tumour samples. We then describe methods for reconstructing the phylogeny of multiple related tumour samples, taking subclonal structure into account. We then describe the application of these techniques to the analysis of cancer evolution and metastasis, with examples from chronic lymphocytic leukaemia, small cell lung cancer models, brain metastases, and Barrett’s oesophagus.

Introduction

This session is aimed at all those interested in novel immunotherapies to treat cancer. The approval of the anti-CTLA4 agent ipilimumab to treat advanced melanoma in 2011 was a landmark, whilst 2014 has seen the first approvals of anti-PD1 therapy in the US and Japan; further approvals are anticipated in 2015 and non-randomised trials have shown evidence of safety and efficacy in multiple solid tumour types. In this session the background for the development of T cell checkpoint inhibitors will be reviewed and the latest clinical and scientific data discussed, alongside consideration of the T cell surveillance of healthy and transformed epithelia.

Discussion

15.05 – 15.30
Hall 1A
Scott Carter, Broad Institute of MIT-Harvard, Cambridge, USA, Dana-Farber Cancer Institute, Boston, USA and Massachusetts General Hospital, Boston, USA

15.30 – 15.40
Discussion

Cancer immunotherapy 2014: a new paradigm

14.10 – 14.15
Room 11
James Larkin, The Royal Marsden NHS Foundation Trust, London, UK

14.15 – 14.40
Room 11
Christian Blank, The Netherlands Cancer Institute, Amsterdam, The Netherlands

Introduction

This session is aimed at all those interested in novel immunotherapies to treat cancer. The approval of the anti-CTLA4 agent ipilimumab to treat advanced melanoma in 2011 was a landmark, whilst 2014 has seen the first approvals of anti-PD1 therapy in the US and Japan; further approvals are anticipated in 2015 and non-randomised trials have shown evidence of safety and efficacy in multiple solid tumour types. In this session the background for the development of T cell checkpoint inhibitors will be reviewed and the latest clinical and scientific data discussed, alongside consideration of the T cell surveillance of healthy and transformed epithelia.

T cell checkpoint blockade in melanoma: from mouse to man and back

After decades of failure to improve the prognosis of metastatic melanoma patients, the treatment has progressed markedly in recent years due to the development of targeted therapies directed against (mutated) signalling proteins and immunotherapies like monoclonal antibodies (mAb) targeting T cell checkpoint blockade. Melanoma has been always considered one of the most immunogenic tumours, but only the recent improvement in understanding how T cell responses are modulated and which of these mechanisms are used by tumours to escape the immune response have allowed us to achieve clinically meaningful outcomes.

Anti-CTLA4 is the first mAb targeting co-inhibition that has received approval from FDA and EMA for the treatment of stage IV melanomas based on the improvement of overall survival in phase III trials.

More recently, blockade of PD1/PDL1 interactions has shown even higher objective clinical responses in early phase clinical trials. While CTLA-4 is thought to inhibit the early
expansion phase, the PD-1/PD-L1 signal alters the effector phase of T cell responses. This is reflected in the response characteristics of CTLA-4 blockade inducing responses late after treatment initiation, while PD-1/PD-L1 blockade can induce early responses. In case of response, both can induce long-term melanoma control or even cure.

Identification of patients benefiting from these promising therapies (biomarker development) and of combinations that increase the response rates (either combinations of different T cell checkpoint modulators or combinations with targeted therapies) will be the challenge for the nearby future.

**Competing interests**
Research grant from Novartis. Consultancy for Roche, BMS, MSD, Novartis, and GSK.

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**Targeting immune checkpoints in cancer: new mechanistic insights**

The continual interplay between the immune system and cancerous cells is thought to result in the establishment of a dynamic state of equilibrium. This equilibrium depends on the balance between subsets of effector and regulatory lymphocytes. Whereas the overall mechanisms underpinning the establishment and maintenance of the intratumour balance between Teff and Treg cells remain unknown, in many solid cancers it is characterised by the dominant infiltration of regulatory T cells over effector T cells resulting in a low Teff/Treg ratio. Furthermore, different subtypes of regulatory cells and inhibitory molecules such as CTLA-4 tightly control the few effector T lymphocytes that manage to infiltrate the tumour. The outcome of this balance is critical to survival, and while in a few cases the equilibrium resolves in the elimination of the tumour by the immune system, in many other cases the tumour manages to escape immune control.

Remarkably, antibodies against CTLA-4, a key immune modulatory receptor expressed on T cells, efficiently modify this balance, driving effector T cell expansion and increasing the ratio of Teff/Treg within the tumour. Whilst the high Teff/Treg ratio driven by anti-CTLA-4 directly correlates with tumour destruction in mice and humans, the mechanisms underpinning this phenomenon remain unknown.

By focusing in the study of effector and regulatory tumour-reactive CD4+ T cells my group is interested in the mechanism underpinning the activity of different immune-modulatory antibodies within the tumour microenvironment, and the potential positive and negative impact that the tumour microenvironment may have in the recruitment, survival and function of different T cell subsets. In this context and using a murine model of melanoma we have recently demonstrated that both the change in the Teff/Treg balance as well as tumour rejection depend on the selective depletion of tumour-infiltrating Treg cells expressing high levels of surface CTLA-4. Regulatory T cell depletion is mediated by ADCC and completely depends on the expression of Fc gamma RIV on tumour infiltrating CD11b+ myeloid cells. These results reveal novel and unexpected mechanistic insight into the activity of anti-CTLA-4-based cancer immunotherapy, and illustrate the importance of specific features of the tumour microenvironment on the final outcome of antibody-based immune-modulatory therapies.
**T cell immunosurveillance of healthy and transformed epithelia**

T cell infiltrates are common in carcinomas, and correlate with a good prognosis. Hence, there is considerable therapeutic interest in promoting the activity of these cells and in reducing the local immunosuppressive environment of the tumour. In this regard, we investigate the regulation of tumour infiltrating lymphocytes (TILs) from the perspective of intraepithelial T lymphocytes (IEL), a very large but poorly understood T cell compartment, ordinarily resident in healthy tissues. In particular we have sought to understand how novel, locally expressed members of the ‘B-7 supergene family’ regulate the activities of IEL. Such genes, expressed in a tissue-specific fashion may likewise regulate TILs in specific tumour-types, and may make better targets for clinical intervention than the checkpoints that also regulate systemic T cells. We have characterised one such local B-7-like regulator expressed exclusively in the thymus and suprabasal keratinocytes that regulates mouse epidermal T cells, conferring on them a unique, rapid response mode to the types of tissue dysregulation that characterise the early stages of cell transformation. This is consistent with the increased susceptibility to cutaneous carcinomas of mice lacking intraepidermal T cells. We have now identified T cells in human skin with a very similar response mode, and propose that their regulation and enhancement is an appropriate clinical target for immunotherapy. Moreover, we have recently identified another B-7 related gene that is expressed specifically in the small intestinal epithelium, and which is critical to the regulation of intestinal IEL. We shall present these findings, and consider their possible relationship to biological and clinical aspects of tissue immunosurveillance.

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**High precision radiation therapy**

**Introduction**

The application of new technologies to radiotherapy planning and treatment delivery has spawned a new generation of treatment options, known by the term ‘advanced radiotherapy techniques’. The basis of these is increased geometric and anatomical certainty permitting highly targeted approaches and consequently to lead to potential biological enhancement. This session consists of three outstanding international speakers covering three different aspects of this technical revolution. The session opens with Professor Robert Timmerman giving the George Edelstyn lecture on Stereotactic Radiotherapy (SABR). His presentation will cover the evolution of this technique and its potential settings in clinical practice, particularly its application alongside systemic therapies.

The session will then focus on proton therapy, a technique available in many parts of the world and which is planned to be operational in two UK centres by 2018. Professor Tony Lomax who has worked with protons at the Paul Scherrer Institute in Switzerland, will share his experiences and his vision for the development of proton therapy.

All precision radiotherapy techniques rely on high quality image guided approaches. Professor Uwe Oelfke, from The Institute of Cancer Research will conclude the session with his thoughts on the development of this approach and the potential for utilising...
Symposia abstracts (continued)

Stereotactic ablative radiotherapy (SABR): a local therapy poised to fight metastatic cancer
Highly focused, accurate and image-guided radiation delivery to very potent dose can be safely delivered using the techniques and technologies employed with stereotactic ablative radiotherapy (SABR). SABR is fundamentally different from conventionally fractionated radiotherapy in its approach, conduct, techniques, and biology. Trials in early stage lung cancer have demonstrated targeted tumour control similar to surgery with tolerance in even non-surgical patients. In these clinical models, the treatment has been optimised with impressive clinical results that have justified making SABR a standard option for several patient populations. Initial use in advanced and metastatic cancer have centered primarily around oligometastatic presentations similar to surgical indications. However, more recent clinical trials have identified patient populations with even more extensive dissemination that might benefit. Considering the difficulty in controlling gross disease with systemic therapy, a non-invasive local therapy could allow longer progression free intervals and, perhaps, improved survival. SABR integrates seamlessly with systemic therapies and could prove to be synergistic. Within this clinical model of metastatic patients in need of better therapy, SABR is being tested hoping to allow improved tumour control while maintaining high levels of quality life.

Proton therapy: pushing the frontiers of radiotherapy
Proton therapy is a rapidly expanding modality for cancer treatments, with many new facilities being built around the world. Indeed, two such facilities will be installed in the next few years in the NHS, providing the capability of advanced proton therapy for a select number of patients.

The main advantage of protons for radiotherapy is the localised deposition of energy (dose) in the so-called Bragg peak. This ‘focus’ of high dose can be considered a spot of radiation, which can be painted over the tumour, such as to conform the high doses to the tumour more effectively than conventional radiotherapy using photons. Current state-of-the-art proton therapy is based on the Pencil Beam Scanning (PBS) approach (pioneered and developed at the Paul Scherrer Institut in Switzerland), which provides the flexibility and efficiency of modern radiotherapy techniques such as IMRT. However, only now are reports based on meaningful numbers of patients beginning to emerge, with encouraging results.

In this presentation, the basics of PBS proton therapy will be presented and its potential advantages demonstrated. In addition, an overview of the first clinical results from our own, and other clinics, will be discussed. Given its dose sparing advantages, we will show that proton therapy brings significant advantages in the treatment of children and young adults, but also in the treatment of geometrically complex and large tumours over a whole spectrum of indications. The installation of two such facilities in the UK will thus be an important addition to the NHS armoury in the fight against cancer.
Image guided radiation therapy

Image guided radiation therapy (IGRT) was the key technological development in modern radiation oncology practice within the last decade. The commercial introduction of cone-beam computer tomography (CBCT) images in 2004, led to a step change in nearly all radiation therapy procedures, ranging from the definition of margins on pre-treatment images to on-line reconstruction of delivered doses and automated quality assurance procedures. Central theme of all our efforts in the development of IGRT is to treat the anatomy of the patient observed at time of treatment.

The clinical exploitation of volumetric radiographic imaging at time of the treatment is still a major area of research, especially for anatomical areas that are subject to deformations on a day to day basis. Plan of the day concepts or online re-planning scenarios are under development for many clinical indications and their impact on clinical outcomes is still under evaluation. However, despite the major impact and success of radiographic based IGRT, there are still two major problems to be solved: i) the limited image quality of CBCT images for many treatment sites, especially for tumours in the pelvic area; and ii) the constraints imposed by image acquisition speed and additional imaging dose for the monitoring of intra-fraction organ motion.

Both of these problems are very well addressed with the development of image guided radiation therapy based on magnetic resonance imaging (MRI). MRI guided radiation therapy (MRigRT) technology offers the next technologically driven step change of our field. The lecture will include: i) selected IGRT projects pursued at ICR/RMH; ii) a report on the status and potential of MRI-guided RT; iii) discuss the plans of MRigRT at RMH/ICR; iv) a personal view of the further impact of MRigRT on the way we may deliver radiation therapy in the future.

Discussion
Symposia abstracts (continued)

Optimising care for those living with and beyond cancer – where does primary care fit in?

14.10 – 14.15
Room 3A

Introduction
This symposium will highlight the key issues facing patients and their families following the end of initial treatment, and will consider different models for providing follow-up care. In particular, speakers will focus on the role of primary care in optimising survivorship care, and the interface between primary and secondary care.

The session will be relevant for surgeons, oncologists, nurses, GPs, researchers, patients and carers.

14.15 – 14.35
Room 3A

Primary care views on optimising care for those living with and beyond cancer: findings from a systematic review and GP survey

Primary care practitioners (PCPs), with their generalist approach and experience of prevention and chronic disease management, have a key role to play in caring for people living with and beyond cancer. Furthermore, a recent UK survey showed that cancer survivors have increased rates of consultations in primary care. However, while the Quality Outcomes Framework targets require PCPs to keep a register of patients diagnosed with cancer and review them within 3 months of diagnosis, there are no other primary care targets or guidelines relating to long-term consequences of cancer treatment and quality of care for co-morbid disease among people living with and beyond cancer.

PCP views on optimising care for those living with and beyond cancer will be discussed, with reference to findings from two recent studies we have conducted. The first is a systematic review of studies indexed on five electronic databases before March 2014 that included PCP views on caring for adult patients living beyond a diagnosis of cancer and who had completed active treatment. Twenty-one studies have been included. The results will be presented in five categories: current practice, views of the primary/secondary care interface, knowledge and educational needs, barriers such as time and access to specialist services, and preferences for optimising care. The second is a web-based survey of GP attitudes and experiences of follow-up care for people living with and beyond cancer, with a particular focus on cardiovascular health after cancer. GP views on current and optimal management of people who have recently completed their active cancer treatment, awareness and management of possible late effects following cancer treatment, and relevant training needs, will be presented.

In conclusion, there will be a brief overview of two ongoing pilot UK trials of primary care-based interventions to address the unmet needs of men following prostate cancer treatment.

14.35 – 15.00
Room 3A

Models for delivery of follow-up care – what does the evidence tell us thus far?

Improvements in cancer detection, treatment and an ageing population mean that there are an increasing number of people living with and beyond cancer. Current hospital-centred models of cancer follow-up have tended to focus on detection of cancer recurrence which may result in significant unmet needs, particularly psychosocial needs.
This presentation will first present the findings of a rapid review focused on the role of primary care in cancer follow-up. Several trials have assessed alternative models of cancer follow-up care involving primary care, with most assessing the period of survivorship relatively soon after treatment completion. Many of these studies have involved either a shared model of follow-up care between the oncology specialist and primary care provider or a direct transfer of follow-up care to the primary care provider, with the majority of studies focusing on detecting recurrence or managing adverse effects of chemotherapy. Several randomised controlled trials have shown primary care-led follow-up care to be equivalent to hospital-led care in terms of patient wellbeing, recurrence rates and survival, and might be less costly. Successful primary care-led follow-up requires appropriate guidelines, clear communication and accessible specialist care if required.

The second aspect of this presentation will report findings from the ProCare Trial, a multi-centre phase II RCT of shared care for prostate cancer conducted in Australia. The intervention is a shared care model of follow-up visits in the first 12 months after completing treatment for prostate cancer with the following specific components: a survivorship care plan, GP management guidelines, register and recall systems, screening for distress and unmet needs and patient information resources. Data will be presented on psychosocial outcomes, unmet needs and clinical process measures and key issues learnt about the feasibility of this novel model of shared care will be discussed.

**Optimising care beyond breast cancer – perspectives from the front line**

The success of the treatments for breast cancer has resulted in 10 year survival for some 80% of women in the UK, with millions of women worldwide living with the consequences of treatment.

Three areas which particularly impact the experience of breast cancer survivors – and primary care – include the surgical pathway and follow up regimens, the consequences of endocrine therapy and impacts on upper limb function.

There are contrasts and cultural differences across the globe between the processes a patient may go through having surgery and in follow up. Short stay surgery requires planning and excellent post-operative care in the community; trials for women with breast cancer have demonstrated the benefits of early discharge to primary care with a drain in place. Determining the frequency and modalities of follow up radiologically (such as in the Mammo50 trial) and clinically (primary care follow up, nurse/allied health professional-led follow up in primary or secondary care) present opportunities to improve patient experiences.

Managing the consequences of (extended) adjuvant endocrine therapy balanced with adherence to therapy is a key issue for women surviving oestrogen receptor positive breast cancer. These individuals remain at long term risk of recurrent or new breast cancers mitigated by the use of tamoxifen or aromatase inhibitors (AIs) for 5 years and more. Yet effective management of symptoms or interventions for adherence remain elusive.

Reducing upper limb complications through less axillary surgery (including sentinel node biopsy, the Z0011, SNAC1 trial results and the POSNOC trial now underway) and rehabilitating the upper limb (the future PROSPER trial) present clear opportunities.
Symposia abstracts (continued)

Differences between health care systems present further challenges and opportunities to optimise life after breast cancer. For those in the front line, living beyond breast cancer acknowledges the inheritance from treatments and requires a multidisciplinary interface between primary and secondary care.

15.30 – 15.40 Discussion
Workshops and scientific symposia

BACR educational workshop: Epigenome-wide association studies (EWAS) in cancer – converging on a consensus approach

08.00 – 08.45
Room 11

Speakers:

James Flanagan,
Imperial College
London, UK

Jonathan Mill,
University of Exeter, UK

Robert Lowe,
Queen Mary, University
London, UK

Just as genome-wide association studies (GWAS) grew from the field of genetic epidemiology, so too do epigenome-wide association studies (EWAS) derive from the burgeoning field of epigenetic epidemiology, with both aiming to understand the molecular basis for disease risk and other disease outcomes. While genetics is currently unmodifiable, there is hope that epigenetic biomarkers may be reversible and/or modifiable. The vast majority of EWAS thus far have used blood DNA methylation using the 450K Illumina beadchip arrays, and there have been numerous diseases, exposures and lifestyle factors investigated, with several significant associations now identified. This provides a strong justification that this approach may prove fruitful in many cancer types. Crucially, we have begun to understand the many technical, biological and environmental factors that influence data analysis. This workshop aims to provide the current consensus approaches for study design, data processing, biostatistical approaches, accounting for various confounding factors, data presentation and experimental validation. Lastly, much like the GWAS studies, EWAS are likely to require large international consortium-based approaches to reach the numbers of subjects, and statistical and scientific rigor, required for robust findings, and several consortia will be discussed.

A beginner’s guide to cancer immunotherapy

08.00 – 08.45
Room 3B

Hosted by Elaine Vickers,
Science Communicated Ltd,
Sheffield, UK

This workshop is designed to help you understand the basics of cancer immunotherapy: what it means, how it works, and why everyone is so excited about it.

Elaine will describe what we mean when we talk about cancer immunotherapy, and she will explain various approaches being tried, such as genetically-modified dendritic cells, re-programmed cytotoxic T cells, and antigen vaccines.

She will also explain the current craze for ‘immunomodulators’. CTLA-4, PD-1, and PD-L1 have been the buzz-words of recent cancer conferences. Elaine will explain what these proteins are, the treatments that target them, and the excitement these treatments are causing.

This workshop is geared towards non-scientists, such as doctors, nurses, trials staff and patients who would like to get the most out of this year’s Conference.

Join us next year: 1–4 November 2015 conference.ncri.org.uk
Workshops (continued)

Nutrition in cancer research: the UK National Strategic Research Initiative in Nutrition and Cancer

08.00 – 08.45
Room 12
Hosted by Southampton Biomedical Research Centre with NOCRI

The numbers of incident cancers in the UK are projected to increase, mainly due to greater numbers of people living to older ages, but also associated with imprudent lifestyle choices. A greater proportion of these cancers are estimated to be attributable to nutritional factors (diet, body composition, physical inactivity) as smoking prevalence declines and rates of obesity continue to increase. Currently between a quarter and a third of all cancers in the UK are estimated to be attributable to these nutrition-related factors.

While a role for nutrition in cancer development is established, the underpinning cellular and molecular mechanisms are less clear. Equally while increasing observational data link nutrition to outcome after cancer diagnosis, the precise causal factors have not been characterised systematically. It seems likely that at least some of the variation in prognosis (whether due to cancer phenotype or response to therapy) may be the result of nutritional factors.

The UK has internationally competitive research both in cancer and in nutrition. However these individual strengths have not been systematically combined.

The National Institute for Health Research has launched an initiative led by its Southampton Biomedical Research Centre to promote interdisciplinary translational research by better exploiting existing resources, and improving effectiveness by bringing a coherent strategic framework to address the area.

This workshop:
- will describe the processes and structures established to oversee the project
- will update on progress including an initial mapping exercise
- invites all interested bodies, institutions and individuals to engage with this initiative, with a view to forming communities of practice as basis for interdisciplinary work.

Tea, coffee and pastries will be served.

Biobanking to enable research

08.00 – 08.45
Room 4
Hosted by Bridget Wilkins, NCRI Confederation of Cancer Biobanks and St Thomas’ Hospital, London, UK

With the increase of ‘omics’-focused research and the requirement for large cohorts of patient samples, biobanks are positioned to play a critical role in catalysing translational and precision medicine. The aim of this workshop is to showcase how biobanks are being used to enable research studies that would otherwise not have been possible and to accelerate the translation of research discoveries into clinical practice. Three different perspectives will be given on this topic:
- a funder’s
- a biobank’s
- a researcher’s.

Tea, coffee and pastries will be served.
Amgen scientific symposium: Do biomarkers matter in gastrointestinal and colorectal cancers?

12.45 – 14.00
Room 11
Hosted by Amgen

Speakers:
Nick Maisey, Guy’s and St Thomas’ NHS Foundation Trust, London, UK
Phil Quirke, Leeds Institute of Cancer and Pathology, UK

Professor Quirke will discuss the emerging role of personalised medicine in oncology, focusing on biomarkers involved with malignancies of the gastrointestinal tract, including C-Met, Ras and Braf. This rapidly expanding area needs careful forward planning to facilitate its effective implementation. Dr Nick Maisey will present a series of case studies to illustrate the role of personalised medicine in gastric and colorectal cancers.

Amgen Oncology has provided sponsorship for this conference. Amgen Oncology has a stand at the conference and a symposium but has had no input into the main programme, topics or awards.

Celgene scientific symposium: The good, the bad and the experts: exploring research, diagnosis and management in pancreatic ductal adenocarcinoma (PDAC)

12.45 – 14.00
Room 3A
Hosted by Celgene

Our understanding of pancreatic ductal adenocarcinoma (PDAC) and our ability to treat this deadly malignancy is advancing rapidly. Indeed, a new publication on pancreatic cancer is posted on PubMed every two hours. This interactive forum, hosted by Celgene, uses several innovative approaches to bring together the clinical and research communities to place the most important recent advances into context and highlight the next steps in research, diagnosis and management.

Each of our faculty will discuss one advance they feel will strongly change how we think about PDAC. In particular, the faculty will consider how basic and clinical research can inform clinical practice – and vice versa.

The faculty will then have a full and frank discussion of controversies and conundrums in PDAC. The faculty's expertise allows them to offer different perspectives on the same theme and the audience will be encouraged to participate fully. This session will illustrate the importance of interactions and collaboration between researchers and clinicians.

Finally, we would encourage you to come prepared to ‘quiz the expert’ and ask our expert faculty your unanswered questions on any aspect of PDAC. Ask anything from basic biology, to clinical phenotype, to treatment, to service structure. This is more than a Q&A session: we aim to identify opportunities for further research and unanswered questions.

We hope the meeting will help researchers and clinicians map new avenues into the understanding, diagnosis and treatment of PDAC.
Learning objectives
By attending this meeting, delegates will:
· Appreciate important current trends and advances in PDAC research and their relevance to clinical practice.
· Identify areas where further research is needed and outstanding issues.
· Have an understanding of the challenges in PDAC and the translation of treatments from ‘bench to bedside’.
· Have a better appreciation of the perspectives of the research and clinical communities involved in advancing the management of PDAC.

Speakers include:
· Harpreet Wasan (Chairman), Imperial College London, Hammersmith Hospital, London, UK
· Jordan Berlin, Vanderbilt-Ingram Cancer Center, Nashville, USA
· Jeff Evans, Beatson West of Scotland Cancer Centre, Glasgow, UK
· Sheela Rao, The Royal Marsden NHS Foundation Trust, London, UK
· Paul Ross, Guy’s Hospital, Guy’s and St Thomas’ NHS Foundation Trust, London, UK

Lunch and refreshments will be available.
Parallel sessions and workshops

**Biology of the radiation response**
Hosted by W Gillies McKenna, Cancer Research UK and Medical Research Council Oxford Institute, UK

16.00 – 16.05
Introduction by the host

16.05 – 16.30
A modern interpretation of the 5 Rs of radiobiology and their impact on clinical practice
Kevin Harrington, The Institute of Cancer Research, London, UK

16.30 – 16.45
The Royal College of Radiologists Ross Prize winner: selected from RCR proffered paper session in the Spotlight Theatre, 12.45 – 13.45

16.45 – 17.10
Combining radiotherapy with DNA repair inhibitors in the lab and the clinic
Anthony Chalmers, University of Glasgow, UK

17.10 – 17.35
Genetic screens exploring tumour radiosensitivity
Geoff Higgins, Cancer Research UK and Medical Research Council Oxford Institute for Radiation Oncology, UK

17.35 – 17.40
Discussion

**DNA repair in cancer biology and treatment**
Hosted by Chris Lord, The Institute of Cancer Research, London, UK

16.00 – 16.05
Introduction by the host

16.05 – 16.30
Break-induced replication mediates repair of collapsed DNA replication forks and tandem duplications in cancer cells
Thanos D Halazonetis, University of Geneva, Switzerland

16.30 – 16.45
Proffered paper: PET imaging of DNA damage using 89Zr-labelled anti-γH2AX-TAT immunoconjugates
James Knight, University of Oxford, UK

16.45 – 17.10
APOBEC3B mutagenesis in cancer: basic mechanisms and clinical implications
Reuben S Harris, University of Minnesota, Minneapolis, USA

17.10 – 17.35
DNA repair defects, PARP inhibitors and metastatic prostate cancer
Johann de Bono, The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK

17.35 – 17.40
Discussion

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Parallel sessions and workshops (continued)

Integration between oncology and palliative care
Hosted by Irene Higginson, King’s College London, UK

16.00 – 16.05  Room 4  Introduction by the host

16.05 – 16.30  Room 4  A patient viewpoint: integrate oncology and palliative care
Roger Wilson, NCRI Consumer Liaison Group, London, UK; Sarcoma UK, London, UK; and Sarcoma Patients Euronet, Munich, Germany

16.30 – 16.45  Room 4  Proffered paper: 'battle' or 'journey'? A large-scale study of metaphors for cancer
Veronika Koller, Lancaster University, UK

16.45 – 17.10  Room 4  Integrating palliative care into oncology – improving the palliative care of cancer patients in the care pathway
Tiina Saarto, Helsinki University and Helsinki University Central Hospital, Finland

17.10 – 17.35  Room 4  A phase II mixed-methods study on early integration of palliative care in advanced respiratory and gastrointestinal cancer patients
Massimo Costantini, Hospital of Santa Maria Nuova, Florence, Italy

17.35 – 17.40  Discussion

Melanoma
Hosted by Pippa Corrie, Addenbrooke’s Hospital, Cambridge, UK

16.00 – 16.05  Room 3A  Introduction by the host

16.05 – 16.30  Room 3A  In vivo RNAi screening for novel therapeutic cancer targets
Daniel Peeper, Netherlands Cancer Institute, Amsterdam, The Netherlands

16.30 – 16.45  Room 3A  Proffered paper: G12DNRAS and kinase-dead BRAF cooperate to drive naevogenesis and melanomagenesis
Malin Pedersen, The Institute of Cancer Research, London, UK

16.45 – 17.10  Room 3A  The ageing microenvironment promotes metastasis and therapy resistance
Ashani T Weeraratna, Melanoma Research Center, The Wistar Institute, Philadelphia, USA

17.10 – 17.35  Room 3A  Tumour heterogeneity and co-operative behaviour in melanoma
Claudia Wellbrock, Manchester Cancer Research Centre, University of Manchester, UK

17.35 – 17.40  Discussion
Molecular pathology – the genomic basis of cancer
Hosted by Manuel Salto-Téllez, Queen’s University Belfast, UK

16.00 - 16.05
Introduction by the host
Room 11

16.05 - 16.40
MSK-IMPACT: clinical implementation of next generation sequencing to enable personalised oncology and targeted therapies
Marc Ladanyi, Memorial Sloan Kettering Cancer Center, New York, USA
Room 11

16.40 - 16.55
Proffered paper: Epidermal growth factor receptor copy number gain (EGFR CNG) and response to gefitinib in oesophageal cancer (OC): Results of a biomarker analysis of a phase III trial of gefitinib versus placebo (TRANS-COG)
Russell Petty, University of Aberdeen and NHS Grampian, Aberdeen, UK
Room 11

16.55 - 17.20
Molecular pathology: the genomic basis of cancer
Reinhard Buettner, Cologne University Hospital and Center for Integrated Oncology (CIO), Cologne, Germany
Room 11

17.20 - 17.35
Genomics, integromics and the role of molecular pathology
Manuel Salto-Téllez, Queen’s University Belfast, UK
Room 11

17.35 - 17.40
Discussion

Molecular profiling of childhood cancers
Hosted by Christine Harrison, Northern Institute for Cancer Research and Royal Victoria Infirmary, Newcastle, UK

16.00 - 16.05
Introduction by the host
Room 12

16.05 - 16.30
Exploiting biological heterogeneity to improve outcomes in childhood medulloblastoma
Steven C Clifford, Northern Institute for Cancer Research, Newcastle University, UK
Room 12

16.30 - 16.45
Children’s Cancer and Leukaemia Group (CCLG) McElwain Award winner – Routine molecular subgrouping of medulloblastoma: bridging the divide between research and the clinic using low-cost DNA methylomics
Edward Schwalbe, Northern Institute for Cancer Research, Newcastle University and Northumbria University, UK
Room 12

16.45 - 17.10
Using next generation sequencing to characterise in detail the biological mechanisms that underpin genomic instability in ETV6-RUNX1 ALL and identify recurrent drivers associated with leukaemic transformation
Elli Papaemmanuil, Wellcome Trust Sanger Institute, Cambridge, UK
Room 12

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Parallel sessions and workshops (continued)

17.10 – 17.35
Room 12
Development of precision medicine trials for Philadelphia chromosome-like acute lymphoblastic leukaemia
Stephen P Hunger, University of Colorado School of Medicine and Children’s Hospital Colorado, Aurora, USA

17.35 – 17.40
Discussion

Workshops

16.00 – 17.40
Hall 1B
Imaging as a biomarker for cancer management
Hosted by Gina Brown, The Royal Marsden NHS Foundation Trust, London, UK and Fiona Gilbert, University of Cambridge, UK

16:00 – 17:40
Hall 1C
Helping doctors to suspect cancer promptly when patients present with symptoms: from clinical audit to novel point-of-care testing
Hosted by Georgios Lyratzopoulos, University of Cambridge, UK and Greg Rubin, Durham University, UK

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Parallel session and workshop abstracts

Biology of the radiation response

16.00 – 16.05
Room 3B

W Gillies McKenna,
Cancer Research
UK and Medical
Research Council
Oxford Institute for
Radiation Oncology, UK

Introduction
Radiation was first used to treat cancer within a year of Roentgen’s discovery of the X-ray, and within ten years it was clear radiation could cure cancer, but after the invention of chemotherapy many people thought this would replace radiation as a cancer treatment. Yet, more than 100 years after the discovery of the X-ray and sixty years after the discovery of chemotherapy, surgery and radiotherapy remain the mainstays of curative cancer treatment, and have in fact continued to improve the outcomes for patients with cancer by moving towards less toxic combined modality applications. Now we recognise that cancer is a genetic disease. This has recently led to an explosion of research into, and the application of novel agents targeting the mutations present in the cancer, but the results of applying these novel agents as single agents have also been disappointing, and they have also not succeeded in supplanting radiation as a cancer treatment. A major change in cancer treatments and outcomes could be achieved by introducing molecularly targeted agents in patients with early stage disease by combining them with surgery and radiation.

Research is now focused on ways to use molecular agents in ways that could make radiation more effective as a cancer treatment. We now believe we can use our knowledge of the mutations present in cancer cells to find ‘Achilles heels’ to make the cancer more sensitive to radiation as a cancer treatment. We believe we should study patients by genomic characterisation and molecular and functional imaging, and should on the basis of this information devise personalised treatment plans that would use molecularly targeted agents in combination with the full gamut of minimally invasive surgical and radiotherapy modalities. The three talks in this session will explore how we can use our knowledge of the biology of the radiation response to devise methods for increasing the efficacy of radiation treatment, expanding the usefulness of this indispensable modality.

16.05 – 16.30
Room 3B

Kevin Harrington,
The Institute of Cancer Research, London, UK

A modern interpretation of the 5 Rs of radiobiology and their impact on clinical practice

The 4 Rs of radiobiology were initially described to provide a means of understanding the success or failure of localised radiotherapy. Differential repair of tumour and normal cells between treatment fractions, redistribution of cells into more or less radiosensitive phases of the cell cycle, repopulation of tumour cells between fractions and reoxygenation of tumour cells during treatment were all invoked to explain the overall outcome of a course of radiotherapy. Later, intrinsic radiosensitivity was added as the 5th R of radiobiology. At the time, this represented an admission of our inability to explain, at the mechanistic level, the different radiocurabilities of diseases like seminoma, lymphoma, glioma and melanoma.

Nonetheless, the 5 Rs have been extremely important as a framework within which to examine new therapeutic strategies from the point of view of both tumour and normal cells. Each of the Rs can be viewed as a twin-edged sword, such that changes can occur in either direction to increase or decrease the net therapeutic effect. For example, tumour cells with defects in their DNA repair pathway are more likely than adjacent normal cells to die following a dose of radiation. However, the aberrant DNA repair pathway may already have allowed the tumour cell to accumulate non-lethal mutations in other important genes that allow it to tolerate unrepaired DNA damage (or to repair it in an
inaccurate fashion that enhances genetic instability). In similar fashion, the enhanced tumour cell division that occurs during a course of radiotherapy is usually seen as the driving force behind accelerated repopulation, but it may also make a tumour cell more susceptible to radiation-induced death by driving it into mitosis with potentially lethal unrepaired DNA damage.

Insights into the molecular biology of cancer now allow us to reinterpret the classical 5 Rs of radiobiology in terms of their underlying mechanisms. The particular strength of this approach is that it leads naturally into a discussion of potential new targeted therapies that may favourably modulate the tumour response and increase the therapeutic index. Specific examples of how knowledge of the molecular biological basis of the radiation response has shaped our current approach to cancer treatment will be discussed. In addition, future directions will be explored.

Combining radiotherapy with DNA repair inhibitors in the lab and the clinic
Radiotherapy kills cancer cells by damaging their DNA, so the ability to repair radiation-induced DNA damage is fundamental to treatment resistance. Increasing understanding of the DNA damage response and the availability of specific inhibitors of components of this response is enabling the development of therapeutic strategies with potential to enhance radiation sensitivity in a tumour specific manner. Inhibitors of poly (ADP-ribose) polymerase (PARP) are currently being studied in combination with radiotherapy in phase I studies in a number of tumour sites.

The emergence of the cancer stem cell hypothesis has added another layer to this field of research, with certain tumour stem cells exhibiting radiation resistance through upregulation of the DNA damage response. Targeting S-phase and G2/M checkpoint activation through ATR or Chk1 generates moderate radiation resistance that is mitigated by the enhanced DNA repair capacity of the cancer stem cells. Dual targeting of both cell cycle checkpoints and DNA repair appears to generate optimum radiosensitisation in these populations and is a promising therapeutic strategy.

Genetic screens exploring tumour radiosensitivity
Although some key DNA damage repair proteins and signal transduction pathways such as PARP and EGFR are recognised as playing an important role in tumour radiosensitivity, the detailed molecular processes that determine intrinsic radiosensitivity remain largely unclear.

In order to identify novel proteins that regulate tumour radiosensitivity and may hence represent new, clinically useful drug targets, we have undertaken large scale radiosensitivity screens using a druggable genome library of siRNAs targeted against approximately 8,000 genes.

This work has identified genes that would not necessarily be expected to play a role in intrinsic radiosensitivity, such as genes involved in vitamin B metabolism.
In addition we have identified genes such as POLQ (DNA polymerase theta), which is overexpressed in multiple different tumour types, and is associated with poor clinical outcomes. Importantly, POLQ is not present in most normal tissues. POLQ knockdown induces tumour cell radiosensitisation without affecting normal tissue cells. If compounds can be developed to successfully inhibit these targets, they may be used clinically to increase the efficacy of radiotherapy without exacerbating normal tissue reactions.

**Discussion**

**DNA repair in cancer biology and treatment**

**16.00 – 16.05**
Hall 1A

Chris Lord, The Institute of Cancer Research, London, UK

**Introduction**
Genomic instability is one of the most pervasive characteristics of tumour cells and is probably the combined effect of DNA damage and tumour-specific DNA repair defects. Although these processes drive genomic instability and ultimately the disease process, they also provide therapeutic opportunities.

In this session, we aim to discuss not only the precise molecular processes involved in DNA repair, but also how these systems shape the mutational spectrum of cancers. Finally, we will discuss how our growing understanding of DNA repair processes is informing the development of therapeutic approaches to the disease.

**16.05 – 16.30**
Hall 1A

Thanos D Halazonetis, University of Geneva, Switzerland

**Break-induced replication mediates repair of collapsed DNA replication forks and tandem duplications in cancer cells**

Break-induced replication (BIR) is a specialised form of homologous recombination that repairs one-ended DNA double-strand breaks (DSBs). In budding yeast, Pol32, the non-essential subunit of DNA polymerase delta, is required for BIR. BIR has also been implicated in repair of damaged replication forks, based on the observation that tandem duplications arising under conditions of DNA replication stress are dependent on Pol32. BIR has not been characterised in mammalian cells. However, since replication stress and tandem duplications are prevalent in human cancers, we wondered whether damaged forks in cancer cells are repaired by a BIR-like mechanism. Indeed, in a cyclin E-induced model of DNA replication stress, POLD3, the human ortholog of yeast POL32, was required for cell cycle progression and processive DNA synthesis, when cyclin E was overexpressed. In the same cell system, cyclin E overexpression led to tandem duplications with microhomology junctions and knockdown of POLD3 suppressed the emergence of these duplications. Depletion of POLD3 also compromised the repair of DNA DSBs in irradiated human cells. Further, in a GFP-based DSB repair assay designed to monitor BIR, depletion of POLD3 reduced the efficiency of repair, whereas repair by synthesis-dependent strand annealing/gene conversion or single-strand annealing were unaffected. We propose that BIR is relevant in human cancer for repairing damaged DNA replication forks and for the high frequency of tandem duplications with microhomology junctions.
Parallel session and workshop abstracts (continued)

16.30 – 16.45
Hall 1A
James Knight,
University of Oxford, UK

Proffered paper: PET imaging of DNA damage using $^{89}$Zr-labelled anti-γH2AX-TAT immunoconjugates

Background
The efficacy of most anti-cancer treatments, including ionising radiation (IR) and many cytotoxic drugs, depends on an ability to cause DNA damage. Previously, we showed that quantification of intratumoral DNA damage is possible, for example to predict early response to treatment. Using an $^{111}$In-labelled construct targeting DNA damage signalling protein via anti-γH2AX antibodies, linked to the cell-penetrating peptide, TAT, we demonstrated that SPECT imaging allows dose-dependent measurement of DNA double strand-breaks (1). Given the increasing availability of PET imaging in the clinic, we have now prepared a PET imaging agent, based on the same construct, radiolabelled with the positron-emitting isotope, $^{89}$Zr.

Method
Anti-γH2AX-TAT was synthesised using EDC/NHS chemistry for TAT-peptide linkage, as previously described. TAT-peptide conjugation confers cell-penetrating and nuclear localisation properties. Conjugation of pSCN-benzyl-desferrioxamine (DFO) allowed radiolabelling with $^{89}$Zr. Since $^{89}$Zr also emits beta-particles, and 909 keV gamma rays, some radiobiological measurements were included to ensure the compound itself does not cause any additional DNA damage.

Results
$^{89}$Zr-anti-γH2AX-TAT was taken up by MDA-MB-468 breast cancer cells, similar to $^{111}$In-anti-γH2AX-TAT. Retention of the $^{89}$Zr-labelled compound was 8-fold longer in irradiated cells, compared to non-irradiated cells, or compared to non-specific control compound. PET imaging revealed significantly higher uptake of $^{89}$Zr-anti-γH2AX-TAT in irradiated xenograft tumours in mice, compared to non-irradiated control or non-specific control compound (12.1±1.6 vs. 5.2±1.9 and 5.1±0.8 %ID/g, respectively; P<0.0001). Monte Carlo simulation of radiation dose deposition within a 1 nm range, showed only little difference between $^{89}$Zr or $^{111}$In nuclei. In vitro analysis showed that exposure of naïve or irradiated cells to $^{89}$Zr-anti-γH2AX-TAT did not significantly change either the number of observable γH2AX foci or clonogenic survival.

Conclusion
$^{89}$Zr-anti-γH2AX-TAT allows PET imaging of DNA double strand break damage in a tumour xenograft mouse model.

References

16.45 – 17.10
Hall 1A
Reuben S Harris,
University of Minnesota, Minneapolis, USA

APOBEC3B mutagenesis in cancer: basic mechanisms and clinical implications

Cancer genomic DNA sequences enable identification of all mutations and suggest targets for precision medicine. The identities and patterns of the mutations themselves also provide critical information for deducing the originating DNA damaging agents, causal molecular mechanisms, and thus additional therapeutic targets. A classic example is
ultraviolet light, which crosslinks adjacent pyrimidines and causes C-to-T transitions. A new example is the DNA cytosine deaminase APOBEC3B, which was identified recently as a source of DNA damage and mutagenesis in breast and several additional cancer types. This enzyme is normally an effector protein in the innate immune response to virus infection but its upregulation in breast cancer causes elevated levels of genomic C-to-U deamination events, which manifest as C-to-T transitions and C-to-G transversions within distinct DNA trinucleotide contexts (preferentially 5’-TCA and 5’-TCG). Genomic C-to-U deamination events within the same trinucleotide contexts also lead to cytosine mutation clusters (kataegis), and may precipitate visible chromosomal aberrations such as translocations. Clinical studies indicate that APOBEC3B upregulation correlates with poorer outcomes for oestrogen receptor positive breast cancer patients including shorter durations of disease free survival and overall survival after surgery. APOBEC3B may therefore have both diagnostic and prognostic potential. APOBEC3B may also be a candidate for therapeutic targeting because inhibition of this non-essential enzyme is predicted to decrease tumour mutation rates and diminish the likelihood of undesirable mutation-dependent outcomes such as recurrence, metastasis, and the development of therapy resistant tumours.

Selected literature

DNA repair defects, PARP inhibitors and metastatic prostate cancer
Many cancers have DNA repair defects and these can be utilised in synthetic therapeutic lethal strategies to impart patient benefit. Preclinical and clinical studies have shown that PARP inhibitors have anti-tumour activity against tumours with defects in high fidelity homologous DNA repair. PARP inhibitors have impressive anti-tumour activity against cancers in BRCA carriers with evidence for clinical benefit to patients with ovarian, breast and advanced prostate cancer. Anti-tumour activity with PARP inhibitors has also been demonstrated against sporadic cancers with loss of HR DNA repair due to somatic cell genomic aberrations or repair gene promoter methylation. Data will be presented on the anti-tumour activity of PARP inhibitors against prostate cancer, with a particular focus on anti-tumour activity in sporadic castration resistant prostate cancer (CRPCa). Data from the investigator-initiated TO-Parp trial will be presented; this adaptive design is focused on identifying a biomarker panel that identifies PARP inhibitor sensitivity in this population. All the patients on the TO-Parp trial received olaparib at 400mg bid (tablets), had fresh CRPCa biopsies pre-trial participation as well as after 2-4 weeks of olaparib. All patient fresh samples have undergone exome and transcriptome sequencing in efforts to elucidate which sporadic CRPCa patients respond to PRP inhibition.
Parallel session and workshop abstracts

(continued)

17.35 - 17.40 | Discussion

Integration between oncology and palliative care

16.00 – 16.05
Room 4

**Irene Higginson**, King’s College London, UK

**Introduction**

Earliest models for palliative care and oncology integration had these as separate entities. When a person was seen as having a terminal diagnosis, and potentially curative treatment ended, then they could be referred to palliative care. This approach saw palliative care and oncology as separate rectangles in the illness journey. Gradually over the course of many years this model has changed, at least in much contemporary palliative care, and we now see palliative care and oncology needing to be more integrated. The level of integration should be orientated to the needs of the person, not some medically defined boundaries.

Patients have symptoms and complex problems earlier in the course of illness, where palliative care can help, but then perhaps withdraw until symptoms recur. The advances in cancer treatments and care, and the demographic changes in our society, also demand this. There is empirical evidence to support this approach, including randomised trials, showing benefit on patient outcomes including symptoms, quality of life and possibly also survival. So the question is now not whether palliative care and oncology should integrate, but how it is best achieved. This session considers the latest developments and evidence about palliative care and oncology integration, from different viewpoints.

16.05 – 16.30
Room 4

**Roger Wilson**, NCRI Consumer Liaison Group, London, UK; Sarcoma UK, London, UK; and Sarcoma Patients Euronet, Munich, Germany

**A patient viewpoint: integrate oncology and palliative care**

Most cancer research using patients is not centred on patients. Research relies on methodologies to assess an intervention. These do not handle qualitative data very well, are flawed in rare diseases, use endpoints which patients do not relate to, and result in un-nuanced simplistic conclusions. Current debates about limiting costly treatments by age are a good illustration of such simplicity in practice. It can also be argued that cancer patients are challenged by the system as much as they are by disease and its treatment. There is a need for medical care which is truly personalised, taking account of the whole needs of the patient. The integration of palliative and oncology care would be a positive move. A focus from the moment of diagnosis on the real needs of the whole patient, rather than the disease which the patient hosts, would benefit all patients. This kind of integrated care is relevant to survivorship as much as it is to end of life. A secondary issue is that this approach would challenge research. Qualitative and probabilistic methodologies more sensitive to the real needs of patients would be needed.

16.30 – 16.45
Room 4

**Veronika Koller**, Lancaster University, UK

**Proffered paper: A ‘battle’ or a ‘journey’? A large-scale study of metaphors for cancer**

**Background**

Violence metaphors for cancer (including ‘battle’, ‘fight’, ‘war’) are used conventionally in English, but have been criticised for their potentially harmful consequences for patients. In recent policy documents in the UK (e.g. the NHS 2007 Cancer Reform Strategy), they have been avoided in favour of the notion of cancer as a ‘journey’ with clinical ‘pathways’ delineated as models of care.
Method
The ESRC-funded project ‘Metaphor in End-of-Life Care’ at Lancaster University combined manual qualitative analysis with quantitative computer-aided methods to investigate metaphor use in 1.5 million-words of interviews and online forum contributions by terminally ill cancer patients, family carers and health professionals. The frequencies and functions of metaphors for cancer experiences (Did you find your journey a battle or a [...] trudge?). There is evidence that Violence metaphors can express and reinforce negative feelings, especially about the self. However, they can also have a positive, empowering function (e.g. expressing personal determination and mutual solidarity), while Journey metaphors are sometimes used to express feelings of distress and disempowerment (e.g. patients describing themselves as ‘passengers’ on the cancer ‘journey’).

Results
Both Violence and Journey metaphors are regularly used by all three groups. In particular, patients use a variety of these to talk about a wide range of aspects of their illness experiences (Did you find your journey a battle or a [...] trudge?). There is evidence that Violence metaphors can express and reinforce negative feelings, especially about the self. However, they can also have a positive, empowering function (e.g. expressing personal determination and mutual solidarity), while Journey metaphors are sometimes used to express feelings of distress and disempowerment (e.g. patients describing themselves as ‘passengers’ on the cancer ‘journey’).

Conclusion
The variety of attitudes, emotions and needs that are expressed by patients' Violence and Journey metaphors need to be addressed in the provision of healthcare. A blanket rejection of Violence metaphors would deprive some patients of the potential positive functions of these metaphors, just like an uncritical promotion of Journey metaphors overlooks the disempowering ways in which they can be used. Greater awareness of patients’ own metaphor use can lead to more effective approaches to communication about the experience of cancer.

Acknowledgements
The research presented in this paper was supported by the UK’s Economic and Social Research Council (ESRC grant number: ES/J007927/1).

Integrating palliative care into oncology – improving the palliative care of cancer patients in the care pathway
Cancer care is based on multidisciplinary teamwork with medical oncologists, radiotherapists, surgeons, pathologists, radiologists, but recently also with palliative care specialists. The palliative needs of cancer patients are various: prevention and treatment of treatment-related toxicity; rehabilitation; nutritional support; symptom control; psychosocial and spiritual counselling; and finally, end of life care. As stated by the World Health Organisation (WHO), palliative care should be introduced in oncology early in the course of illness in conjunction with anticancer therapies that are intended to prolong life to better understand and manage distressing clinical complications and symptoms. Palliative care will enhance quality of life, helping patients live as actively as possible until death and helping the family cope during the patient’s illness and in their own bereavement. It may also positively influence the course of illness.

How can we manage the integration? Palliative care specialists should be responsible for advanced palliative care, but every oncologist should have basic skills. In the Cancer Center of Helsinki University Hospital, registrars specialising in oncology have three months’ mandatory training in the palliative care unit, which has proved very helpful and well-liked. Consequently 13% (7/53) of oncologists working in the Cancer Center...
A phase II mixed-methods study on early integration of palliative care in advanced respiratory and gastrointestinal cancer patients

Aims
Assessing feasibility, acceptability, and perceived efficacy of early palliative care integration for newly diagnosed advanced respiratory and digestive cancer patients.

Methods
Oncologists and pneumologists of two outpatient clinics were asked to offer to 40 consecutive newly diagnosed eligible patients the early palliative care (PC) intervention together with standard oncological care. Eligibility criteria were: diagnosis within 8 weeks of advanced lung, pleural, stomach and pancreas cancer, PS of 0-2, and having not started chemotherapy yet. The intervention was provided by a specialised hospital based PC team (PCT) through at least monthly (or more frequent) consultations until death, referral to community teams, refusal, or other reasons. A semi-structured interview was administered to six patients, six family caregivers and six physicians to explore perceived efficacy, strengths and weaknesses of the intervention. Transcripts were analysed using content analysis.

Results
Fifty-seven of 136 consecutive newly diagnosed cancer patients were eligible. Physicians proposed the intervention to 44 patients (77.2%). Reasons for not proposal were staff error (n=2), a competitive trial (n=1), patient living out of place (n=2), and patient needing to start chemotherapy immediately (n=8). Only 4 out of the 44 patients (9.1%) refused the PC intervention. Thirty-nine patients attended the first visit with the PCT (one retired the consent). Preliminary results from qualitative analysis showed that all patients and most relatives referred on the usefulness of the PC intervention with reference to its main focus, i.e. symptom management, information, and support to strategies employed to cope with illness. Physicians highlighted their difficulty in informing eligible patients on the PC intervention, and in sharing information and coordinating care with colleagues of the PCT.

Conclusion
Early integration of palliative care in oncology seems to be both feasible and well accepted by patients, relatives and physicians, although some difficulties emerged concerning patient information and inter-professional communication.
Melanoma

16.00 – 16.05
Room 3A
Pippa Corrie,
Addenbrooke’s Hospital,
Cambridge, UK

Introduction
In the last four years, five new drugs, representing four different classes of agents with unique mechanisms of action have been licensed for the treatment of metastatic melanoma, each representing step changes in improving outcomes from this deadly disease. These remarkable clinical benefits arise from extensive preclinical research unravelling the mechanisms of normal and abnormal melanoma cell proliferation. Key challenges in terms of innate and acquired resistance have yet to be overcome. In this session, the use of melanoma models to better understand the microenvironment and tumour heterogeneity will be discussed.

16.05 – 16.30
Room 3A
Daniel Peeper,
Netherlands Cancer Institute, Amsterdam,
The Netherlands

In vivo RNAi screening for novel therapeutic cancer targets
Melanoma is the most aggressive type of skin cancer and its incidence is steadily increasing. Melanomas tend to spread rapidly, which is associated with a grim prognosis. Until recently, most advanced stage melanomas were refractory to the available therapeutic options, but there are recent developments offering better perspectives. For example, new therapeutic approaches have become available, which target genetic vulnerabilities within the melanomas. A primary example of such a dependency is the common BRAFV600E mutation, which is essential for proliferation and survival of melanoma cells. In the clinic, the mutant BRAF oncogene product can be targeted by specific inhibitors, including vemurafenib, which cause unprecedented melanoma regression. However, relapse eventually occurs around six months due to a variety of resistance mechanisms, both MAP kinase-dependent and independent. Therefore, in spite of these new perspectives, there is a dire need to identify additional targets amenable to therapeutic intervention, to be used in combination with vemurafenib or other specific inhibitors to overcome or prevent drug resistance and achieve more durable responses. To achieve this, we set out to identify melanoma factors that are required for proliferation and survival specifically in an in vivo setting. Thus, we performed negative selection RNAi screens parallel in vitro and in vivo and focused on the hits that were preferentially depleted in tumours relative to the corresponding cells in culture. The results from these screens will be discussed.

16.30 – 16.45
Room 3A
Malin Pedersen,
The Institute of Cancer Research, London, UK

Proffered paper: G12DNRAS and kinase-dead BRAF cooperate to drive naevogenesis and melanomagenesis

Background
Melanoma is the most deadly form of skin cancer and is a disease that is rising in incidence. Q61 mutant NRAS and V600 mutant BRAF, the most common mutations in melanoma, are mutually exclusive unless the tumours are placed under the selective pressure of BRAF drugs, whereas some of the rare NRAS and BRAF mutants are coincident even without drug selection. Notably, where mutant RAS and BRAF are coincident, it involves codons G12 and G13 of NRAS, and codons such as G466, G469, D594 and G596 of BRAF, all of which impair or kill BRAF kinase activity.

Method
We used Cre-recombinase / LoxP technology to express G12DNRAS and kinase-dead BRAF (D594ABRAF) at physiological levels in adult mouse melanocytes.
Parallel session and workshop abstracts (continued)

Results
We here show that G12DNRAS and kinase-dead BRAF (D594ABRAF) cooperate to drive melanocyte proliferation, producing lesions of lightly pigmented dendritic melanocytes in the superficial reticular dermis and heavily pigmented epithelioid/ovoid melanocytes in the deep reticular dermis. The superficial paucicellular lesions resemble naevus of Ota, and the highly cellular deeper lesions resemble dermal melanocytosis with scattered foci of blue naevi. G12DNRAS and D594ABRAF also drive the development of hypo-pigmented melanomas composed of undifferentiated atypical spindle melanocytes extending from the upper dermis to the subcutaneous layers, and hyper-pigmented melanomas of predominantly heavily pigmented pleomorphic epithelioid melanocytes in the deep reticular dermis which resemble animal-type melanoma in humans. All lesions stain positive for melanoma markers and for Ki67, pERK and pAKT.

Conclusion
A small number of human melanomas harbour G12/G13 NRAS mutations that are coincident with inactivating mutations in BRAF. We express G12DNRAS and kinase-dead BRAF in mouse melanocytes and show that they cooperate to drive naevogenesis and melanomagenesis, producing lesions that resemble human melanoma with distinct histopathological characteristics. Thus, we have developed a tractable model to study human melanoma initiation and progression.

The ageing microenvironment promotes metastasis and therapy resistance
The incidence of the vast majority of cancers is higher in populations over the age of 50. The effects of an aged microenvironment on tumour progression, prognosis and clinical outcome have been largely unexplored, and no age-based biomarkers or protein signatures for monitoring therapeutic response have been defined. Here, we perform a molecular analysis of how normally ageing cells can affect tumour progression, using melanoma as a model. Individuals over the age of 50 have a much poorer prognosis for melanomas of equal grade and stage, compared to younger individuals. To date, the molecular underpinnings of this disparity have not been identified. Using transgenic mouse models of melanoma, as well the generation of artificial skin with human tumour cells and fibroblasts, we explored how the changes in ageing affect tumour progression. Our results show that changes in the ageing microenvironment drive metastasis and therapy resistance via mechanisms that involve Wnt signalling and response to ROS. These data suggest that the prognosis and treatment of cancer in ageing individuals cannot be guided by recent advances and guidelines. Instead, new efforts must be made to understand and treat cancers in an age-appropriate manner.

Tumour heterogeneity and co-operative behaviour in melanoma
Tumour heterogeneity triggers intra-tumour signalling, which can contribute to cancer progression and impact on the efficacy of cancer drugs. With increasing evidence of genetic and phenotypic heterogeneity within tumours, signalling between individual cancer cell subpopulations is therefore an important factor in cancer biology and therapy.

Melanoma frequently displays heterogeneity with regard to different melanoma cell subpopulations displaying different MITF expression levels. MITF is a transcription factor that controls a melanoma-specific nuclear programme, which is thought to define
Molecular pathology – the genomic basis of cancer

16.00 – 16.05
Room 11
Manuel Salto-Tellez, Queen’s University Belfast, UK

Introduction
In 1999, the then director of the National Cancer Institute challenged “the scientific community to harness the power of comprehensive molecular analysis technologies to make the classification of tumours vastly more informative.” This challenge aimed to change “the basis of tumour classification from morphological to molecular characteristics” (NIH guide, 2008). Almost 20 years down the road, this session will include talks by pathologists who have used high-throughput genomic approaches to create a new taxonomy of cancer based on genomic profiles.

This is a general session aimed to all scientists, pathologists and clinicians with an interest in genomic oncology, and in particular cancers of lung, soft tissue and gastrointestinal origin. In addition, it is tailored for those aiming to apply high-throughput technologies in routine molecular diagnostics.

In summary, our data identified a striking co-operativity between melanoma cell subpopulations that not only impacts on drug response, but also preserves heterogeneity and drives melanoma progression without the need for clonal selection or nuclear reprogramming.

‘MITF-heterogeneity’ is also instrumental during melanoma progression. Using a zebrafish xenograft model, we analysed the interaction between MITF<sup>hi</sup> and MITF<sup>lo</sup> subpopulations during early steps of melanoma dissemination. We found that in a heterogeneous setting MITF<sup>hi</sup> inherently-invasive cells co-invade with subpopulations of MITF<sup>lo</sup> poorly-invasive cells, a phenomenon we term ‘co-operative invasion’. During co-operative invasion, the MITF<sup>hi</sup> invasive cells provide protease activity and deposit extracellular matrix (ECM), and the MITF<sup>lo</sup> poorly invasive cells benefit from this heterogeneous situation. On the other hand, the MITF<sup>hi</sup> cells modify the mode of invasion of both subpopulations and, as a consequence, heterogeneous tumours invade more efficiently. Importantly, we did not observe ‘clonal selection’ for a particular melanoma cell subpopulation or changes in the MITF-driven ‘EMT’ expression programme during co-operative invasion.

'epithelial' or 'mesenchymal'-like melanoma phenotypes. We have previously shown that high MITF expression (MITF<sup>hi</sup>) confers cell autonomous resistance to MAP-kinase pathway targeting therapy in melanoma. We have now discovered that in heterogeneous melanomas, MITF<sup>hi</sup> therapy-resistant cells could directly protect MITF<sup>lo</sup> sensitive cells from BRAF inhibitor-induced cell death through intra-tumour signalling.
Parallel session and workshop abstracts (continued)

**16.05 – 16.40**

Room 11

**Marc Ladanyi,** Memorial Sloan Kettering Cancer Center, New York, USA

**MSK-IMPACT: clinical implementation of next generation sequencing to enable personalised oncology and targeted therapies**

**16.40 – 16.55**

Room 11

**Russell Petty,** University of Aberdeen and NHS Grampian, Aberdeen, UK

**Proffered paper: Epidermal growth factor receptor copy number gain (EGFR CNG) and response to gefitinib in oesophageal cancer (OC): results of a biomarker analysis of a phase III trial of gefitinib versus placebo (TRANS-COG)**

**Background**
Cancer Oesophagus Gefitinib (COG) trial randomised 450 patients (pts) with advanced OC progressing after chemotherapy to gefitinib (G) or placebo (P). Improved disease control rates (DCR), patient reported outcomes, and progression free survival (PFS) were seen with G-indicative of rapid and durable responses that were observed in a subgroup. We hypothesised that EGFR CNG in OCs would identify the subgroup responsive to G.

**Method**
EGFR CNG was determined by FISH. Disomy, low and high trisomy and low polysomy were classified as negative (No CNG) and high polysomy and amplification as positive (CNG). Primary endpoint was Overall Survival (OS) for G versus P in EGFR CNG and no CNG groups. Secondary endpoints were PFS, DCR and outcomes in EGFR amplified patients only.

**Results**
EGFR FISH results were available for 295 patients. Clinical features were not different from the COG trial. EGFR CNG was found in 48/295 (16.3%). There was no significant correlation with EGFR CNG and any clinical features which were also balanced in G and P groups. In EGFR CNG Pts OS was improved with G compared to P (HR=0.52 95% CI 0.28, 0.96 p=0.033), with survival for GvsP 79 vs 64%, 38 vs 14%, 27 vs 5% and 13 vs 0% at 3, 6, 9, and 12 months respectively. There was no difference in OS for G vs P in EGFR No CNG pts (HR=0.90 95% CI 0.69,1.17 p=0.429). For PFS EGFR CNG pts, HR=0.55, 95% CI 0.3, 1.10 p=0.051 for GvsP and HR=0.84 95% CI 0.65, 1.09, p=0.192 for EGFR No CNG pts. DCR was improved for G in EGFR CNG pts (39 vs 14%, p=0.054).

EGFR amplification (6%) pts gained greatest benefit from G (OS, HR=0.19 95% CI 0.05-0.65 p=0.007).

**Conclusion**
EGFR CNG identified a subgroup of OCs who benefit from Gefitinib as a second line treatment and is a useful predictive biomarker for the first stratified treatment approach in this setting.
**Molecular pathology: the genomic basis of cancer**

Traditionally, tumours are classified by histopathological criteria, i.e. based on their specific morphological appearances. Consequently, current therapeutic decisions in oncology are strongly influenced by histology rather than underlying molecular or genomic aberrations. The increase of information on molecular changes however, enabled by the Human Genome Project and the International Cancer Genome Consortium as well as the manifold advances in molecular biology and high-throughput sequencing techniques, inaugurated the integration of genomic information into disease classification. We have therefore introduced multiplex deep sequencing of informative gene sets into routine histopathological diagnostics and molecular pathology. This comprehensive approach integrating morphological and molecular information is currently changing cancer diagnostics in five categories:

1. Somatic genomic or epigenomic alterations acquired during cancerogenesis may be used for disease classification as we show this approach being superior to conventional morphological classifications.
2. A significant portion of solid tumours depend on oncogenic driver lesions, which provide molecular targets for prediction of effective and selective therapies.
3. Genomic alterations in signal transduction cascades and gene expression pattern may be used as prognostic parameters predicting the need and extent of adjuvant therapy.
4. In the case of multiple syn- or metachronous tumours, genomic profiling assists allocation of metastases from tumours with unknown primary (CUP) and correct staging as multiple small primary tumours and systemic metastases are reliable being discriminated.
5. Finally, mutational profiling of circulating tumour DNA may facilitate monitoring the response of tumours to therapy and development of secondary resistance. Taken together, comprehensive molecular tumour pathology paves the way for a new rational and the basis of personalised genomic medicine.

**References**


**Genomics, integromics and the role of molecular pathology**

Fifteen years ago, the director of the US National Cancer Institute challenged “the scientific community to harness the power of comprehensive molecular analysis technologies to make the classification of tumours vastly more informative.” This challenge aimed to change “the basis of tumour classification from morphological to molecular characteristics”. Indeed, in a world where molecular medicine is leading the main scientific discoveries, what is the role of pathology in modern science and modern medicine?

This lecture will argue that molecular pathology is a key element for the development of genomic/molecular medicine. To do so, we will discuss an integrated model for provision...
Parallel session and workshop abstracts

of molecular pathology that makes the most of molecular pathology resources; we will introduce the Pathology Integromics for Cancer (PICan) platform for clinical, pathological and biological integration; we will present examples of this integromics approach to research carried out in prostate cancer (PCa), rectal cancer (RC) and small bowel adenocarcinoma (SBA); and, finally, we will discuss the application of some of these high-throughput technologies in routine diagnostics.

The three cancers stated above are chosen because they represent clear examples in which a careful pathological scrutiny is essential to make the most of genomics information. For instance, the focus on subgroups which are defined by morpho-molecular means in PCa, or the characterisation of post chemo-radiotherapy remnants in the analysis of treatment-related changes (RC).

The work on SBA is the most advanced in our laboratory. This represents the most comprehensive study on SBA to date, which has allowed the detection of known and new therapeutic targets (such as Her2, KIT or KRAS), a taxonomy that recapitulates predisposing disease (immune group) and biology (gastric-like versus colon-like) and a disease-specific biomarker with potential diagnostic/screening implications (CHN2).

17.35 – 17.40 Discussion

Molecular profiling of childhood cancers

16.00 – 16.05
Room 12
Christine Harrison,
Northern Institute for Cancer Research and Royal Victoria Infirmary, Newcastle, UK

Introduction
This session will provide an insight into the application of state-of-the-art genomic technologies in the classification of two significant types of childhood cancer: medulloblastoma and acute lymphoblastic leukaemia. These topics will be covered by expert translational researchers in these fields. These talks will cover how these approaches have identified novel genetic abnormalities within these diseases with improved treatment opportunities. The session will include opinion on how realistically these approaches are being introduced into clinical practice and whether they provide valuable alternatives when conventional therapy fails.

16.05 – 16.30
Room 12
Steven C Clifford,
Northern Institute for Cancer Research, Newcastle University, UK

Exploiting biological heterogeneity to improve outcomes in childhood medulloblastoma
Overall survival rates for medulloblastoma, the most common malignant paediatric brain tumour, now stand at around 70%. However, clinical improvements have plateaued and the majority of survivors suffer life-long side-effects associated with current therapies. Recent advances in genomic and epigenomic profiling are revolutionising our understanding of the biological heterogeneity which underlies medulloblastoma, and these discoveries offer major opportunities to individualise therapy and improve outcomes.

First, how medulloblastoma now represents a paradigm for the molecular sub-classification of cancer and its translational exploitation. Critically, we now understand the
clinical entity ‘medulloblastoma’ as an umbrella term encompassing at least four distinct molecular subgroups (termed WNT, SHH, Group 3 and Group 4), which are characterised by unique genomic, epigenomic and mutational signatures, clinical demographics and outcomes.

Second, how these advances, coupled with the identification and validation of a series of molecular and histopathological biomarkers of favourable- (e.g. WNT subgroup) and poor-risk (e.g. MYC amplification) tumours, allow more accurate outcome prediction. These findings have led to ground-breaking pan-European clinical trials opening in late-2014, which will stratify therapy based on molecular risk biomarkers, with the aim of improving survival rates and reducing side-effects.

Third, how the new molecular pathology is informing the next wave of biological discovery, aimed at the identification of novel disease biomarkers and therapeutic targets. I will particularly focus on emerging data which are providing a first picture of the molecular evolution of medulloblastoma over its disease course, the unique biological characteristics which emerge at relapse, and how these could be targeted therapeutically.

Finally, how complex molecular profiles are being developed into low-cost molecular diagnostics assays for routine clinical application, to support the targeted delivery of individualised therapies in paediatric neuro-oncology across Europe.

**Children’s Cancer and Leukaemia Group (CCLG) McElwain Award winner –**

**Routine molecular subgrouping of medulloblastoma: bridging the divide between research and the clinic using low-cost DNA methylomics**

**Background**

DNA-methylation patterns allow the subclassification of medulloblastoma, the most common childhood malignant brain tumour, into four molecular subgroups (WNT, SHH, MBGrp3 and MBGrp4). These subgroups have distinct molecular and clinico-pathological features, and their distinction is now informing future treatments and risk-stratification.

Whilst microarrays to assign subgroup are suitable for research purposes, they are limited by expense, platform-specificity, sample quality requirements and practicality. Here, we aimed to develop a low-cost, array-independent, robust subgrouping assay suitable for routine quality-controlled subclassification, including scant and poor-quality samples.

**Method**

A minimal, multiply-redundant, 19-locus methylation signature was derived to assign subgroup, using Illumina 450k DNA-methylation array data and subgroup calls from 225 medulloblastomas. A cross-validated machine-learning classifier was developed to assign subgroup using these loci. We next investigated whether bisulfite treatment of DNA could induce methylation-dependent SNPs suitable for multiplexed interrogation of methylation status, using an adaptation of Sequenom's iPLEX assay. Multiplexed primer-mixes were designed and quantitation validated using molar-ratios of bisulfite-treated methylated:unmethylated DNA. Subsequently, the assay was run on 101 DNA extracts from fresh-frozen, FFPE and cytospin (<30,000 nuclei) tumour material, representing all subgroups. Subgroup assignments by Sequenom assay were compared to gold standard 450k array calls.
Parallel session and workshop abstracts
(continued)

Using next generation sequencing to characterise in detail the biological mechanisms that underpin genomic instability in ETV6-RUNX1 acute lymphoblastic leukaemia (ALL) and identify recurrent drivers associated with leukaemic transformation

Current sequencing technologies have delivered the ability to profile cancer genomes with great precision allowing for the characterisation of the complete spectrum of genetic events (single base pair events, small insertions or deletions as well as structural variations) with a base pair resolution.

The ETV6-RUNX1 fusion characterises 25% of B-cell precursor ALL but on its own is not sufficient for overt leukaemia. We surveyed the genomes of 56 leukaemic samples of ETV6-RUNX1 ALL by low-depth genome and high-depth exome sequencing to: 1. Identify critical secondary events to the ETV6-RUNX1 fusion gene necessary for leukaemic transformation; 2. Perform detailed analysis of the composite genomic architecture of ETV6-RUNX1 ALL; 3. Study patterns of mutations (composition, location, chromatin landscape, timing) for insights into potential biological mechanisms of genomic instability.

We confirmed 523 structural variations (average of 11 per case; range of 0-49) in 44 of the samples in the study. We identified 779 somatic substitutions and 16 indels across 715 protein-coding genes and 3. Each sample had on average 14 coding point mutations (range of 1-95), consistent with the low number of acquired somatic mutations reported in hematological cancers and childhood malignancies. A remarkable paucity of recurrent gene mutations was observed. However, 76% of intrachromosomal rearrangements were deletions, and accounted for many of the frequent secondary events in ETV6-RUNX1 ALL.

A striking enrichment of deletion breakpoints adjacent to recombination signal sequence (RSS) sites was observed. RSS sites are conserved sequence motifs recognised by the recombination activating gene (RAG) endonucleases that mediate V(D)J recombination during antibody diversification. Clusters of recurrent gene deletions targeting the same or adjacent nucleotides were observed across samples with evidence of re-iterated events within the same sample. RAG-mediated deletions emerge as the dominant mutational process, characterised by recombination signal sequence motifs near breakpoints, incorporation of non-templated sequence at junctions, ~30-fold enrichment at promoters and enhancers of genes actively transcribed in B cell development and an unexpectedly high ratio of recurrent to non-recurrent structural variants. Single-cell tracking shows that...
Development of precision medicine trials for Philadelphia chromosome-like acute lymphoblastic leukaemia

While the overall survival for paediatric acute lymphoblastic leukaemia (ALL) is now 85-90%, high risk subsets can be identified that have significantly inferior outcomes. Ph-like (or BCR-ABL1-like) ALL is one recently identified high risk ALL subset that is defined by a gene expression profile similar to that of Philadelphia chromosome-positive (Ph+) ALL but without BCR-ABL1 fusion. Our studies in the Children’s Oncology Group (COG) have shown that the frequency of Ph-like ALL increases in age from 10% in children younger than 10 years to 27% in young adults 21-40 years old and that it is associated with a high relapse rate and inferior survival. Genomic studies of Ph-like ALL (as defined by the COG) have shown that about half of cases have chromosome rearrangements leading to over-expression of the cytokine receptor CRLF2, with JAK1/2 point mutations present in about half of CRLF-rearranged cases. Most of the remaining Ph-like ALL cases have chromosome rearrangements, often cryptic, that create ABL1, ABL2, CSF1R, PDGFRB and JAK2 fusion proteins. The ABL1, ABL2, CSF1R, and PDGFRB fusions phenocopy BCR-ABL1 in that they transform factor dependent cell lines and are exquisitely sensitive to the ABL1 class tyrosine kinase inhibitors imatinib and dasatinib in vitro, in animal models, and anecdotally in humans with Ph-like ALL. COG investigators have developed assays to rapidly identify Ph-like ALL cases and characterise the underlying genomic lesions and are preparing to implement a clinical trial that will test addition of dasatinib to chemotherapy in Ph-like ALL cases with ABL1, ABL2, CSF1R, and PDGFRB fusions. Additional studies are being developed to test the JAK2 inhibitor ruxolitinib in cases with JAK1/2 point mutations and JAK2 fusions.
Helping doctors to suspect cancer promptly when patients present with symptoms: From clinical audit to novel point-of-care testing

Most cancer patients first visit a non-specialist doctor (typically a general practitioner), often with non-specific symptoms. Suspecting cancer in these patients in an appropriate and timely fashion is challenging given the poor predictive value of most symptoms and the many patients in whom they relate to benign disease. This workshop will cover:

a) learning from diagnostic errors / significant event audit
b) practice variation in diagnostic use and current initiatives by Cancer Research UK/ the Royal College of General Practitioners
c) how epidemiological variation in post-presentation delay can inform targeting of research and policy efforts
d) the important contribution of novel or emerging point-of-care tests.

Imaging as a biomarker for cancer management

Imaging is central in assessment of cancer and treatment response. This workshop intends to show the breadth of imaging applications towards both the qualitative and quantitative assessment of cancer, and its subsequent utility in determining treatment efficacy.

The workshop will give a general overview of the imaging modalities available, the quantitative nature of imaging, and will give examples from the current cancer trials portfolio. The workshop intends to show the capabilities, but will also highlight the complexities of using imaging as a biomarker and the advantages of early engagement of imaging specialist in designing clinical trials.

16.00 – 17.40

Hosted by Gina Brown, The Royal Marsden NHS Foundation Trust, London, UK and Fiona Gilbert, University of Cambridge, UK

16.00 – 17.40

Hosted by Georgios Lyratzopoulos, University of Cambridge, UK and Greg Rubin, Durham University, UK
Using Macmillan and NCIN’s Local Cancer Intelligence tool to inform regional improvement

In this spotlight session, we’ll be demoing a new tool for NHS commissioners to help build an understanding of the changing nature of cancer at a local population level.

**Local Cancer Intelligence**
Local Cancer Intelligence (LCI) is a website for NHS commissioners and Macmillan’s service development teams. It brings together the information they need on the changing burden of cancer in their local area. It was created by Macmillan and Public Health England’s National Cancer Intelligence Network (NCIN) – the experts on the numbers, needs and experiences of people affected by cancer.

There are two main audiences:
- NHS commissioners with responsibilities for cancer care
- Macmillan’s local Service Development Teams

LCI is designed to help users understand the changing burden of cancer in their area. Users don’t have to be expert data analysts – we’ve presented only the most important stats for each area, displayed in an accessible way.

**Part of the bigger picture**
The purpose of Macmillan’s Cancer Population Evidence Programme is to generate and bring together the evidence Macmillan and the health and social care system need to plan for the future. Local Cancer Intelligence is a part of this work, bringing together evidence on epidemiology, health economics, and patient experiences and outcomes, to enable Macmillan’s regional teams and NHS commissioners to put in place effective service solutions.

**Built in partnership**
Local Cancer Intelligence is a collaboration between Macmillan Cancer Support and Public Health England’s National Cancer Intelligence Network (NCIN), combining the best data and insights from NCIN, Macmillan and other sources to help you understand the local burden of cancer.

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**The Royal College of Radiologists proffered paper presentations**

- **The UK HeartSpare Study (Stage IB): Randomised comparison of the voluntary breath-hold technique and prone treatment in larger-breasted women**
  **Frederick Bartlett**, The Royal Marsden NHS Foundation Trust, London, UK

- **Image-guided radiotherapy in prostate cancer: validation of a dose calculation method based on cone beam CT contours**
  **Hemal Ariyaratne**, Mount Vernon Cancer Centre, London, UK

- **Patterns of relapse following intensity-modulated radiotherapy (IMRT) to the bladder and pelvic nodes in node positive or high risk bladder cancer: Early outcomes from the single-centre phase II prospective Intensity Modulated Pelvic Node and Bladder Radiotherapy (IMPART) trial**
  **Melissa Tan**, The Royal Marsden NHS Foundation Trust, London, UK
Stereotactic body radiotherapy (SBRT) for oligometastatic prostate cancer: can we delay initiation of palliative androgen deprivation therapy?

Daniel Henderson, The Royal Marsden NHS Foundation Trust, London, UK

Accumulated dose-volumes to the rectum are greater than those planned in approximately 80% of patients treated with helical tomotherapy for prostate cancer

Jessica Scaife, Addenbrooke’s Hospital and University of Cambridge, UK
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- Our comprehensive programme of Conferences, Study Days & Short Courses cover site specific cancers, palliative care, haemato-oncology, targeted treatments & cancer therapies, advanced practice masterclasses, procedural skills and non-clinical topics such as leadership & professional development
- We are a centre of excellence in Surgical Training and our portfolio includes key skills & basic surgical training, preparation courses for the MRCS & FRCS examinations and laparoscopic training
- The Maguire Communication Skills Training Unit is an internationally recognised unit dedicated to improving patient experience by developing & teaching communication skills
- The Biological Basis of Cancer Therapy teaching course has been running for over 15 years and examines the science behind all forms of modern cancer treatment covering cancer biology, clinical pharmacology, radiobiology, medical physics and medical statistics
- The Christie FRCR Part 2B Preparation Course is an interactive, practical course specifically focusing on the clinical aspects of the FRCR Part 2B exam
- The Masters of Research in Oncology (MRes) is a joint venture between The Christie and the School of Cancer and Enabling Sciences at The University of Manchester and attracts students from both the UK and abroad looking to expand their training from five to six years to allow a year focused on scientific study
- Our pioneering Complementary Therapy education service offers a combination of courses, diplomas and conferences
- Introducing the Christie Scholars - International Clinical Fellows Programme
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GAS5 Regulates Apoptosis and Responses to Chemotherapeutic Drugs in Breast Cancer Cell Lines

MR Pickard, WH Hudson, EA Orlund & CT Williams

Department of Biochemistry and Worship Cancer Institute, Emory University School of Medicine, Atlanta, Georgia, USA

Background

The expression of the non-protein coding gene, growth arrest-specific 5 (GAS5), is down-regulated in breast cancer and patients with lower expression show reduced response to chemotherapy. GAS5 encodes a small non-coding RNA (IncRNA), while its 3’ terminus give rise to a small RNA. Mature IncRNA plays a critical role in growth arrest and senescence in human papillomavirus 16 (HPV-16) infected cells, but the mechanism by which it regulates cellular responses to chemotherapy is not well understood.

The aims of this study were to investigate the effects of GAS5 expression on cell survival, and whether GAS5 silencing could be used as a strategy to enhance cellular GAS5 levels.

Silencing of GAS5 in MDA-MB-231 cells

The reduced GAS5 expression by co-RTK/IR induction and the associated loss of cell viability directly—related to cellular GAS5 expression—further effects of GAS5 silencing were observed. GAS5-CRISPR/Cas9-mediated GADD45 expression in S. thermophilus induced a remarkable increase in cell viability (data not shown).

GAS5 IncRNA promotes apoptosis

The GAS5-01_01 EST (comprising nucleotides 2-12) promotes UV-C-induced apoptosis. Compared to the control, GAS5 induces a significant increase in the p53/ATF-1 (bottom panel), and the p21/ATF-1 (top panel), thus allowing the p53/ATF-1 (bottom panel), and the p21/ATF-1 (top panel) to be identified as key mediators of the apoptosis-promoting activity of the GAS5 IncRNA. As such, GAS5 IncRNA also stimulates apoptosis in metastatic MDA-MB-231 breast cancer cell lines. These findings provide insights into the role of GAS5 in the regulation of GAS5 expression in response to conventional therapies.

Conclusion

- Down-regulation of GAS5 expression impaired cell survival in breast cancer cell lines.
- GAS5 IncRNA promotes cell survival in a range of breast cancer cell lines.
- GAS5 IncRNA enhances chemotherapeutic drug resistance in breast cancer cell lines.

Funding by the National Institutes of Health.
Programme at a glance

**Prize winners announcement**

09.00 – 09.10  Richard Marais, Chair of the 2014 Scientific Committee  
Hall 1A

**Plenary lecture**

09.10 – 09.50  From symptom to cancer treatment: the vital clinical and political leadership  
Peter Vedsted, Aarhus University, Denmark  
Hall 1A

**Parallel sessions**

10.00 – 11.40  Drug resistance modelling: patients, organoids and mice  
Hosted by David Adams, Wellcome Trust Sanger Institute, Cambridge, UK  
Room 11

10.00 – 11.40  Human papilloma virus (HPV) – positive head and neck cancer  
Hosted by Kevin Harrington, The Institute of Cancer Research, London, UK  
Hall 1B

10.00 – 11.40  Lung cancer and mesothelioma  
Hosted by Marianne Nicolson, Royal Aberdeen Infirmary, UK  
Room 3A

10.00 – 11.40  New methods for tumour functional imaging  
Hosted by Kevin Brindle, University of Cambridge, UK  
Hall 1C

10.00 – 11.40  Toxicities of anti-cancer therapies  
Hosted by Sam Ahmedzai, University of Sheffield, UK  
Room 3B

10.00 – 11.40  What makes a target attractive for cancer drug discovery  
Hosted by Donald Ogilvie, Cancer Research UK Manchester Institute, UK  
Hall 1A

**Networking and refreshment break**

11.40 – 12.00  Registration area and Galleria

**Plenary lecture**

Chaired by Charles Swanton, Cancer Research UK London Research Institute and University College London Cancer Institute, UK

12.00 – 12.40  Cancer genomics: state of the science and clinical translation  
Elaine Mardis, Washington University, USA  
Hall 1A
Closing remarks

12.40 – 12.50  Charles Swanton, Cancer Research UK London Research Institute and University College London Cancer Institute, UK

Hall 1A

Networking and lunch (available to take away)

12.50 – 13.30  Registration area and Galleria

Join us next year: 1–4 November 2015  conference.ncri.org.uk
From symptom to cancer treatment: the vital clinical and political leadership

09.10 – 09.50
Hall 1A

Peter Vedsted, Aarhus University, Denmark

“If I had symptoms I worried about – and it could be cancer – how should my healthcare system take responsibility for my diagnostic pathway?”

The public demand for fast high-quality cancer diagnosis and treatment is evident. Real-life stories confirm that the trust in a healthcare system basically depends on the fulfilment of this demand. Unexplained differences in cancer survival between countries, regions and population groups make us wonder why apparently similar treatment seems to result in different outcomes. A key issue is the interface between primary and secondary care, not least the access to cancer investigations and their efficiency in the use of healthcare resources.

But how do we create a responsible healthcare system? And what would the effect be? Huge international efforts have been made aiming to ensure high-quality cancer care. Yet, an increasing awareness of the insufficiency of the classical cancer diagnosis has evolved in recent years, with the UK in the driver’s seat.

The prevailing idea in many healthcare systems has been that increasing public awareness in itself will promote a rational demand for primary care; the GP will refer relevant patients, on the basis of guidelines, to diagnostic work-up, which will ensure expedited cancer diagnosis.

A responsive primary-care sector is the first step in meeting the patients’ needs. But is general practice always accessible? Do clinicians have sufficient knowledge of cancer risk? Would it be a dangerous idea to give GPs direct access to investigations?

This plenary will present experiences, from a health-services perspective, with the organisation of faster pathways from first symptom to treatment. A particular focus will be set on guideline-based primary cancer diagnosis, access to investigations and the leadership in making the optimal pathways for cancer diagnosis. We will also discuss inefficient use of healthcare resources; waste, duplication and ‘double-gatekeeping’ understood as the lack of integration between primary care and hospitals.
**Cancer genomics: state of the science and clinical translation**

12.00 – 12.40
Hall 1A

**Elaine Mardis,**
The Genome Institute at Washington University
School of Medicine,
St Louis, USA

The increasing application and analysis of next-generation sequencing toward cancer genomes, transcriptomes and epigenomes has resulted in an integrated view of somatic alterations that spans from ‘N of 1’ studies to large cohorts. Recent trends include improved characterisation of heterogeneity and how it changes across progression events or due to clinical treatment, improved monitoring of progression and therapy resistance offered by genotyping circulating nucleic acids or tumour cells, and improved understanding regarding the nature of acquired resistance, to name a few. In the clinic, genotyping of patients to properly assign targeted therapy is increasing in scale and sophistication. Co-opting the immune system is another area of therapeutic intervention being informed by genomics. My lecture will focus on several vignettes that are exemplary of the wide-scale impact of cancer genomics, from foundational knowledge about somatic alterations and continued discovery to translational mechanisms that are beginning to impact patients’ lives.
Parallel sessions

Drug resistance modelling: patients, organoids and mice
Hosted by David Adams, Wellcome Trust Sanger Institute, Cambridge, UK

10.00 – 10.05  Introduction by the host
Room 11

10.05 – 10.30  Analysing response and resistance in circulating DNA
Nitzan Rosenfeld, Cancer Research UK Cambridge Institute, UK
Room 11

10.30 – 10.45  Proffered paper: Olaparib penetrates glioblastoma at therapeutic levels: results of stage 1 of the OPARATIC trial; a phase I study of olaparib in combination with temozolomide in patients with relapsed glioblastoma
Anthony Chalmers, University of Glasgow, UK
Room 11

10.45 – 11.10  Cancer cell models as a therapeutic biomarker discovery platform
Mathew Garnett, Wellcome Trust Sanger Institute, Cambridge, UK
Room 11

11.10 – 11.35  Unravelling therapy resistance in mouse models of human breast cancer
Jos Jonkers, The Netherlands Cancer Institute, Amsterdam, Netherlands
Room 11

11.35 – 11.40  Discussion

Human papilloma virus (HPV) – positive head and neck cancer
Hosted by Kevin Harrington, The Institute of Cancer Research, London, UK

10.00 – 10.05  Introduction by the host
Hall 1B

10.05 – 10.30  Human papillomavirus: the biology of carcinogenesis
Ned Powell, Cardiff University, UK
Hall 1B

10.30 – 10.45  Proffered paper: Clinical trials of MVA-EBNA1/LMP2, a therapeutic cancer vaccine designed to treat Epstein-Barr virus (EBV)-positive nasopharyngeal carcinoma (NPC)
Neil Steven, The University of Birmingham and University Hospital Birmingham NHS Foundation Trust, UK
Hall 1B

10.45 – 11.10  What differences should there be in the way we treat HPV +ve and HPV -ve squamous cell cancer of the head and neck?
Kevin Harrington, The Institute of Cancer Research, London, UK
Hall 1B

11.10 – 11.35  The immune response in HPV-positive oropharyngeal cancer
Gareth Thomas, University of Southampton, UK
Hall 1B

11.35 – 11.40  Discussion

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### Lung cancer and mesothelioma

Hosted by Marianne Nicolson, Royal Aberdeen Infirmary, UK

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### New methods for tumour functional imaging

Hosted by Kevin Brindle, University of Cambridge, UK

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### Toxicities of anti-cancer therapies
Hosted by Sam Ahmedzai, University of Sheffield, UK

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Dorothy Keefe, University of Adelaide and SA Cancer Service, Adelaide, Australia |
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Catharine West, University of Manchester, UK |
| 10.45 – 11.10 | A new era in understanding and managing chronic gastrointestinal (GI) consequences of cancer treatment  
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Jean Klastersky, Jules Bordet Institute, Brussels, Belgium |
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### What makes a target attractive for cancer drug discovery
Hosted by Donald Ogilvie, Cancer Research UK Manchester Institute, UK

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Graeme CM Smith, Oncology IMED, AstraZeneca, Macclesfield, UK |
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Maria Romina Girotti, Cancer Research UK Manchester Institute, UK |
| 10.45 – 11.10 | Drug discovery targets for anti-cancer antibodies  
Martin Glennie, University of Southampton, UK |
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Ian Collins, The Institute of Cancer Research, London, UK |
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Parallel session abstracts

Drug resistance modelling: patients, organoids and mice

10.00 – 10.05
Room 11
David Adams, Wellcome Trust Sanger Institute, Cambridge, UK

Introduction
The aim of this session will be to discuss the problem of cancer drug resistance by the analysis of human samples, the use of organoid culture systems, and also mice. The aim would be to have a state-of-the-art talk about the problem of drug resistance in the clinic and how molecular techniques are being used to understand it. This would be followed by a talk about how patient derived material can be used to screen in vitro for cancer drug sensitivities/resistance, and finally how mouse model systems may help provide mechanistic insights. The latter should bring together PDX models and also engineered mice.

10.05 – 10.30
Room 11
Nitzan Rosenfeld, Cancer Research UK Cambridge Institute, UK

Analysing response and resistance in circulating DNA

10.30 – 10.45
Room 11
Anthony Chalmers, University of Glasgow, UK

Proffered paper: Olaparib penetrates glioblastoma at therapeutic levels: results of stage 1 of the OPA RATIC trial; a phase I study of olaparib in combination with temozolomide in patients with relapsed glioblastoma

Background
Drug delivery is a major problem in the treatment of glioblastoma (GBM). Tumour pharmacokinetics (PK) of small molecule targeted agents have not been widely studied in GBM, and poor activity may result either from lack of biological efficacy or from adverse PK. Olaparib, a small molecule inhibitor of the DNA repair enzyme poly(ADP-ribose) polymerase (PARP), has potential to overcome treatment resistance of GBM [1]. Despite radiological responses in brain metastases [2], GBM penetration by olaparib has not been studied.

Method
Pre-clinically, blood-brain barrier penetration was assessed in vitro by directional transport of [14C]-olaparib across MDCKII cells expressing MDR1 and in vivo by autoradiography of rats and mice treated with [14C]-olaparib. In the clinical setting, eight patients with recurrent resectable GBM were recruited to the OPA RATIC trial and underwent dynamic contrast-enhanced (DCE) MRI at baseline followed by tumour resection after 4 days of oral olaparib (tablet formulation: 100 mg QD, n=5; 200 mg BID, n=3). Olaparib levels were measured in tumour and plasma by LC-MS.

Results
Olaparib was a substrate for MDR1 and efflux was blocked by the MDR1 inhibitor ketoconazole. Radioactivity was not detected in the central nervous systems (CNS) of rats or mice after single dose [14C]-olaparib, but significant levels were measured in subcutaneous HCT-116 tumour xenografts up to 96 hrs. Olaparib was detected in 24/24 resected GBM specimens from 8 patients at concentrations similar to those in previous breast cancer studies in which PARP inhibition and tumour responses were observed.
Pre-treatment DCE-MRI showed increased vascular permeability in tumours, and tumour cellularity parameters correlated with olaparib levels.

**Conclusion**

Olaparib is excluded from the CNS under normal conditions but reliably penetrates recurrent GBM at therapeutic levels and has promise as a chemo- and radio-sensitising agent in GBM. Small molecule PK in GBM are poorly predicted by standard pre-clinical models.

**Acknowledgements**

Sponsored by the Cancer Research UK Drug Development Office and supported by the UK National Cancer Research Network. Thanks to participating centres, local principal investigators, neurosurgeons, neuroradiologists, neuropathologists and research nurses. Particular thanks to the patients who participated in this study, and their families.

**References**


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**Cancer cell models as a therapeutic biomarker discovery platform**

Mathew Garnett, Wellcome Trust Sanger Institute, Cambridge, UK

Alterations in cancer genomes strongly influence clinical responses to anti-cancer therapies. Indeed, there are now several examples where genomic changes are used as molecular biomarkers to stratify patients most likely to benefit from a treatment (e.g. BRAF in melanoma). Despite these successes, the majority of cancer drugs have not been linked to specific molecular features that could be used to direct their clinical use to maximise patient benefit.

We are performing large-scale pharmacogenomic profiling in various in vitro models of human cancer, including cancer cell lines, cancer organoids, and ex vivo PDX cultures, as a biomarker discovery platform by systematically linking drug sensitivity data with extensive genomic information. I will present results from our most current analysis of drug screening including follow-up validation studies, as well as highlight new approaches we have developed to harness clinical sequencing data to guide our analyses.

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**Unravelling therapy resistance in mouse models of human breast cancer**

Jos Jonkers, The Netherlands Cancer Institute, Amsterdam, Netherlands

Mouse models of human cancer not only permit us to gain a detailed insight into the specific genetic changes that drive tumour development and metastasis but also provide powerful tools to study the mechanisms underlying drug response and acquired resistance. Once these processes are understood in sufficient detail it may be possible to design combination therapies that not only cause complete remissions but also eliminate remnant cells that elicit recurrent disease.
We have developed genetically engineered mouse models (GEMMs) of E-cadherin mutated lobular breast cancer. These mice develop mammary tumours that closely resemble the lobular morphology and the metastatic spectrum of the cognate tumours in humans. We have used Sleeping Beauty (SB)-based insertional mutagenesis (IM) screens in conditional E-cadherin mutant mice to identify cancer genes that collaborate with E-cadherin loss in mammary tumorigenesis. Approximately 50% of all tumours carry activating SB insertions in Fgfr2. These tumours are highly sensitive to FGFR inhibitors but eventually become resistant due to de novo SB insertions in genes that are causal to the resistance phenotype.

We have also established GEMMs and patient-derived xenograft (PDX) models for BRCA1-deficient triple-negative breast cancer. These mice develop mammary tumours that are characterised by genomic instability and hypersensitivity to DNA-damaging agents, including platinum drugs and PARP inhibitors. Nevertheless, none of these drugs are curative: tumours grow back after drug treatment and eventually become resistant. Resistance of BRCA1-deficient GEMM tumours to the PARP inhibitor olaparib can be induced by several mechanisms, including activation of drug efflux transporters, type of BRCA1 mutation and 53BP1 loss. Therapy resistance of BRCA1-methylated PDX tumours is driven by loss of BRCA1 promoter methylation or by a novel resistance mechanism involving de novo BRCA1 gene fusions created by intrachromosomal genomic rearrangements.

Human papilloma virus (HPV) – positive head and neck cancer

10.00 – 10.05
Hall 1B

Kevin Harrington,
The Institute of Cancer Research, London, UK

Introduction
Traditionally, in the Western world, squamous cell cancer of the head and neck (SCCHN) has been viewed as a disease caused by exposure to tobacco products and alcohol. Most patients present later in life with loco-regionally advanced disease in the context of a host of other tobacco/alcohol-related co-morbid conditions. In this classical form of SCCHN, treatment by surgery, radiotherapy and chemotherapy is associated with relatively poor outcomes. Patients frequently develop loco-regional disease recurrence and/or metastatic relapse and this is associated with dismal outcomes.

In contrast, in the last two decades we have witnessed the emergence of a new form of SCCHN that is unrelated to the classical aetiological agents. In this case, disease is caused by infection by high-risk human papilloma virus. The resulting disease (so-called HPV +ve cancer) occurs almost exclusively in the oropharynx in patients who are younger, less likely to have a significant smoking history and who are relatively free of co-morbid conditions. Treatment outcomes in this group of patients are significantly better than in the classical (HPV -ve) population. As a result, new therapeutic approaches are being explored in which HPV +ve and HPV -ve disease will be treated differently.

In this session, the biology of HPV positive disease will be explored and the implications for future treatment strategies will be discussed. In addition, an immunotherapeutic intervention against another virally-induced head and neck cancer (nasopharyngeal cancer) will be presented.
Human papillomavirus: the biology of carcinogenesis

Human papillomavirus (HPV) is the primary cause of nearly all cervical cancers. Since the sexual revolution of the 1960s, the prevalence of HPV has increased dramatically, such that approximately one in three women in their twenties are currently infected. Fortunately, measures to prevent HPV-associated disease have also developed rapidly, initially based on cytological screening in women and more recently on prophylactic vaccination in young girls.

In the last decade, awareness of the wider disease burden attributable to HPV, especially in men, has increased. It is now apparent that the increased incidence of oropharyngeal cancers (predominantly tonsil and base of tongue) is also attributable to HPV. In the USA, current data suggests that by 2020 the annual incidence of HPV-positive oropharyngeal cancers will exceed the annual incidence of cervical cancers. UK data show similar trends.

HPV-positive oropharyngeal cancers affect a different demographic group (generally younger, fitter men), and show markedly different clinical behaviour, to tumours associated with long-term tobacco and alcohol use. There is hence an urgent need to understand the biology of HPV in the oropharynx and determine whether tumours with a viral aetiology require different treatment to tumours associated with chemical carcinogenesis.

In the cervix, HPV exists primarily within an intraepithelial compartment and is regarded as being highly effective at hiding from the immune system. In tonsillar infections however, HPV causes proliferation in an environment with much greater exposure to the immune system. This talk will introduce the epidemiology and basic biology of HPV-associated carcinogenesis with a focus on the role of the immune system in controlling infection and proliferation.

Proffered paper: Clinical trials of MVA-EBNA1/LMP2, a therapeutic cancer vaccine designed to treat Epstein-Barr virus (EBV)-positive nasopharyngeal carcinoma (NPC)

Background

Most nasopharyngeal carcinoma (NPC) carry Epstein-Barr Virus (EBV) and consistently express two viral proteins, EB nuclear antigen 1 (EBNA1) and latent membrane protein 2 (LMP2). These proteins represent ideal targets for immunotherapy. MVA-EBNA1/LMP2 is an attenuated poxvirus-based therapeutic cancer vaccine designed to boost T cell immunity to these EBV-encoded tumour antigens in NPC patients.

Method

MVA-EBNA1/LMP2 was tested in phase 1 dose escalation trials in Hong Kong and the United Kingdom (UK). NPC patients, in remission or with low-volume disease received three 3-weekly intradermal injections of MVA-EBNA1/LMP2. Peripheral blood T cell responses to EBV and control antigens were measured by interferon-gamma ELIspot and their quality dissected by flow cytometry.

Results

Thirty four patients received MVA-EBNA1/LMP2. All had injections site reactions and some experienced systemic influenza-like symptoms but no dose limiting toxicities occurred. Following vaccination, increased T cell responses to EBNA1 and/or LMP2 were detected in 71% of patients with greater immunogenicity at higher vaccine doses. Changes in plasma
EBV genome levels, a marker of tumour burden, were observed for some patients with residual disease at time of vaccination. Flow cytometry data showed vaccination increased activation and polyfunctional properties of EBNA1 and LMP2-specific T cells. Immune responses were observed across populations with varying dominant EBV strains and human histocompatibility antigen alleles.

**Conclusion**

MVA-EBNA1/LMP2 is tolerable and immunogenic in NPC patients treated with chemo/radiotherapy and is suitable for use in both Chinese and Western populations. Further trials are ongoing using the most immunogenic dose. A phase 2 trial in Hong Kong is examining clinical benefit and immunogenicity in patients with active disease. A current phase 1b trial in seven UK centres, recruiting NPC patients after initial treatment or one course of salvage chemotherapy, is investigating the effect of vaccination on immune effectors and on memory elicited by subsequent vaccine challenge.

**Acknowledgements**

Vaccine manufacture and the trials are supported by Cancer Research UK, the UK Experimental Cancer Medicine Centres network, the Research Grant Council of Hong Kong (CUHK 460708), the Hong Kong Cancer Fund and the Kadoorie Charitable Foundation.

### What differences should there be in the way we treat HPV +ve and HPV -ve squamous cell cancer of the head and neck?

HPV +ve squamous cell cancer of the head and neck (SCCHN) mainly affects the oropharynx and occurs predominantly in younger patients who are frequently life-long non-smokers. These patients are, on average, fitter than their HPV -ve counterparts and have fewer co-morbid conditions. Across all types of treatment modality (surgery, radiotherapy, chemoradiotherapy), patients with HPV +ve tumours have been shown to have better treatment outcomes than HPV -ve patients. In addition, their younger age and greater likelihood of being cured of their disease means that HPV +ve patients may have to live for many decades with the treatment-related sequelae of curative regimens. Such considerations have resulted in a significant move towards personalised treatment for patients with HPV +ve (and, by extension, HPV -ve) disease. Currently, controversy exists regarding the role of induction chemotherapy, chemoradiotherapy, targeted therapy and surgery in this group of patients. In addition, the potential impact of new developments in targeted monoclonal antibody-based immunotherapy is being considered in the context of HPV +ve and HPV -ve disease.

In this presentation, current treatment strategies for HPV +ve and HPV -ve SCCHN will be discussed. In addition, ongoing trials will be reviewed and future directions for personalised therapies will be discussed.

### The immune response in HPV-positive oropharyngeal cancer

Although human papillomavirus (HPV)-positive oropharyngeal cancers (OPSCC) often present with metastasis, studies report significantly better long-term survival for most patients compared with HPV-negative disease. The reason for this survival advantage remains unclear, but it has led to suggestions that treatment, currently based on TNM staging (Tumour, Nodes, Metastases), be de-intensified to reduce therapy-related morbidity. However, within the HPV-positive OPSCC population, there remains a significant minority that responds poorly to treatment and has a poor prognosis, and there is no widely accepted strategy for identifying these patients.
In recent studies we found that TNM staging has little prognostic value in HPV-positive disease, and that improved survival is independent of treatment modality. Our analyses suggested that the improved survival seen in most HPV-positive oropharyngeal cancer patients results from a anti-tumour immune response, indicated by the presence of tumour-infiltrating lymphocytes (TIL). We found that most HPV-positive OPSCC are associated with an intratumoral immune response, and that levels of TIL stratify patients into high-risk and low-risk groups (3-yr survival; HPV-positive/TILhigh=96%, HPV-positive/TILlow=59%), with survival of HPV-positive/TILlow patients similar to those with HPV-negative disease [HR 1.01, p=0.98]. Molecular analysis of intratumoral T cells established the presence of HPV-specific T cells, an activated CD8-positive population and potentially targetable immune checkpoint regulators. We developed a prognostic model for HPV-positive tumours combining TIL-levels, heavy-smoking, and T-stage which effectively identified ‘high-risk’ HPV-positive patients (AUROC=0.87), validated on an independent patient cohort (detection rate 67%; false-positive rate 5.6%; AUROC=0.82).

Our data suggest that most HPV-positive patients have a pre-existing (albeit ineffective) anti-tumour immune response. Immunotherapy may be a logical choice for treatment de-intensification in this patient group. Thus, the administration of antibodies targeting T cell co-stimulatory/co-inhibitory molecules, including CTLA4, PD-1, PD-L1 and CD40, perhaps combined with a therapeutic anti-HPV-16 vaccine, may provide a useful therapeutic strategy for patients with HPV-positive OPSCC.
addition a better understanding the role of intratumoral heterogeneity and clonal evolution in disease progression is needed to improve the outcomes of patients with lung cancer.

**Proffered paper: Investigating small cell lung cancer molecular status and heterogeneity utilising circulating tumour cells**

**Background**
Small cell lung cancer (SCLC) is an aggressive, highly metastatic disease with dismal prognosis. Response rates to first line chemotherapy are high in most patients but progression free survival is short due to development of chemotherapy resistance via mechanisms not well understood. Serial biopsy in SCLC is challenging whereas the molecular analysis of circulating tumour cells (CTCs) offers a minimally invasive opportunity to study drug resistance mechanisms, evaluate CTC heterogeneity and reveal new drug targets.

**Method**
To monitor tumour genetics over time, we are applying single cell whole genome amplification, Sanger sequencing and next generation sequencing (NGS) to CTCs isolated by DepArray© from SCLC patients prior to chemotherapy and again at relapsed disease. Sanger Sequencing and low coverage whole genome sequencing (WGS) of CTCs were used to investigate key mutational changes and generate genome wide patterns of copy number alterations (CNA).

**Results**
Different TP53 mutations were identified by Sanger Sequencing in single CTCs from two patients that were absent in matched WBCs confirming the utility and specificity of the approach. Heterogeneity in TP53 mutations within a single patient’s CTCs was also noted. The CNA patterns of CTCs from two patients were not only markedly different from those of WBCs but also from each other. Intriguingly, analysis of pre-treatment and relapse CTCs from the same patient identified distinct CNA profiles at relapse which may be linked to resistance.

**Conclusion**
Our study highlights the accuracy and utility of the approach described for genetic profiling of single CTCs in SCLC. Further studies are underway which will include additional longitudinal patient samples and extend the analysis to include high depth WGS and whole exome sequencing in order to identify genetic changes associated with the development of chemotherapy resistance in SCLC. This approach will identify novel targets that may be exploited for better therapeutic control.

**Acknowledgements**
We are indebted to the patients who agreed to donate their blood samples for this study. We thank K Morris, M Dawson, M Lancashire, S Bramley, J Halstead and J Castle, who enumerated CTCs using CellSearch.
Parallel session abstracts (continued)

10.45 – 11.10
Room 3A
David Planchard,
Gustave Roussy,
Paris, France

Liquid biopsies: genotyping circulating tumour cells
Genotyping tumour tissue in search of somatic genetic alterations for actionable targets in non-small cell lung cancer (NSCLC) patients has become routine practice in clinical oncology to deliver optimal treatment to selected patients. Sampling tumour tissue is subject to selection bias resulting from tumour heterogeneity, and can be difficult to obtain. A key challenge is the development of predictive biomarkers which could be less invasive than a biopsy and more informative of tumour heterogeneity. Circulating tumour cells (CTCs) have emerged as potential biomarkers in several cancers, with a correlation between CTC number and patient prognosis. The detection and enumeration of CTCs is still a developing field. We evaluated whether specific molecular abnormalities could be performed by using circulating tumour cells.

11.10 – 11.35
Room 3A
Speaker TBC

Title TBC
Abstract not received.

11.35 – 11.40
Discussion

New methods for tumour functional imaging

10.00 – 10.05
Hall 1C
Kevin Brindle,
University of Cambridge, UK

Introduction
Imaging aspects tumour biology in the cancer patient can be used for tumour detection, grading, monitoring of treatment response and, using intra-operative imaging, can be used to guide surgical resection. This session, which should be of interest to both basic scientists and clinicians, will describe functional imaging methods that are used in the clinic. These include PET, MRI and intra-operative fluorescence imaging.

10.05 – 10.30
Hall 1C
Eric O Aboagye,
Imperial College London, UK

Developing novel radiotracers for positron emission tomography: probing different cancer phenotypes and therapy response in living subjects
Tumour cells exhibit several properties including deranged cell surface receptor expression and intracellular signalling that, together with their microenvironment, allow them to grow and divide. Radiotracers can be designed to detect and quantify several of these tumour cell-specific and aberrant microenvironment properties. The lecture will initially provide an overview of crucial tumour properties that can be described by current radio-probe technologies for imaging by positron emission tomography (PET) including DNA synthesis, apoptosis, extracellular/transmembrane receptor signalling, and intracellular signalling. The strategies for imaging cell surface receptors and intracellular effectors are distinct, thus, chemistry design exploits different molecular scaffolds including small molecules, peptides, affibodies and antibodies. Specific examples of such imaging strategies will be given to highlight: a) reporting of cell surface receptors with a view to stratifying patients for therapy; and b) imaging of intracellular caspase 3 cleavage for detection of therapy response. A ZHER2:2891 affinity labelled with fluorine-18 radioisotope can be used to detect HER2 expression in cells and xenografts independent of lineage. We show that
Background
There is great interest in the effects on cancer metabolism of the diabetes drug, metformin and its potential as a cancer treatment. Despite intense investigation it is still not clear as to its metabolic effects on primary human cancer in vivo.

Method
41 patients with primary breast cancer were recruited to a ‘window of opportunity study’ prior to neoadjuvant chemotherapy. Before and after 2 weeks of an escalating dose of metformin, dynamic 18F-FDG PET-CT scans were carried out, breast core biopsies of the primary tumour taken for RNASeq, metabolomics and immunohistochemistry analysis and host serum metabolic markers assessed.

Results
RNA sequencing of the first 21 paired samples revealed upregulation of many genes encoding components of complex 1, and the TCA cycle, glutaminolysis, and glycolysis pathways. Several genes encoding for glucose and glutamine transport were amongst those most consistently upregulated, including GLUT1, SLC38A1 and SLC7A5 (all p<0.0001). Dynamic PET-CT analysis of the first 17 paired scans demonstrated a trend toward a decrease in the variable K2 post-metformin (an estimate of 18F-FDG efflux from tumour intracellular pool back to blood), but with much variability between paired scans (0.70±0.11 vs 0.51±0.05 (p=0.14)). There was a decrease in serum C-peptide (0.56±0.04nmol/L vs 0.48±0.02nmol/L, pre- and post-metformin, p=0.003) consistent with reduced host insulin secretion.

Conclusion
This is the first study in the clinical setting to show that metformin has an effect on mRNA expression compatible with direct mitochondrial effects on the cancer cell leading to upregulation of the glutaminolysis and glycolysis pathways. The decrease in efflux of radiolabelled glucose may indicate retention of glucose and increased phosphorylation in response to metformin. We expect this study will help define biomarker development and future treatment strategies for metformin, in particular potential combination therapy. Analysis is ongoing and further data including metabolomics and correlative analysis will be presented at this conference.

Acknowledgements
This study was funded by the Cancer Research UK-EPSRC Oxford Cancer Imaging Centre.
TUMOUR DETECTION, TREATMENT PLANNING AND RESPONSE ASSESSMENT USING FUNCTIONAL MAGNETIC RESONANCE

MRI is widely used for cancer detection, diagnosis and staging, with a growing role in targeted screening. Most of these applications use morphological imaging, but functional imaging techniques play an increasingly important role, adding to information provided by the range of contrasts available from conventional imaging. In these applications, dynamic contrast enhanced imaging (DCE-MRI) can provide increased specificity, aid detection of disease and add information on the vascular support of tumours, reflecting the biological control of angiogenesis. Diffusion weighted MRI (DWI-MRI) is rapidly growing in use, informing on cellularity and the local barriers to water diffusion, with whole body measurements enabling surveys for metastatic spread. In addition to DWI images, the apparent diffusion coefficient (ADC) can be calculated, providing a quantitative assessment, contributing information that can characterise disease and may inform on perfusion.

These techniques are also widely used to assess response, providing information reflecting the biological changes that occur. Response to treatment can be complex, and the measurements will reflect the biology and tumour make up at the time of measurement, so may be affected by normalisation and repopulation. A range of further techniques are available, with newer techniques enabling a wide range of spatially registered metabolic and physiological information to be acquired. Techniques include relaxation time measurements affected by hypoxia, vascularity, protein binding together with a range of contrast agents; arterial spin labelling to evaluate perfusion; magnetic resonance spectroscopy (MRS) reporting on energetic and lipid metabolism and aiding diagnosis; hyperpolarised 13C measurements using pyruvate and a number of labelled metabolites; amino acid and glucose exchange saturation transfer; bound water content; MR elastography. Further developments in contrast agents and hyperpolarised probes are at the preclinical stage. Hybrid devices for MR/PET, MR/HIFU and MR/RT are entering clinical use or trial.
**Toxicities of anti-cancer therapies**

**Introduction**
Modern anti-cancer therapy – including targeted biological treatments – still carries a significant burden of toxicities which can impact on patients’ quality of life and at worst, leads to treatment reduction and may shorten life. The first toxicities to be managed with a scientific approach were infections and chemotherapy induced emesis. In the past decade there has been a leap forward in the understanding of these and other adverse effects of drugs and radiation therapy. The session will present a state of the art overview of supportive care research into mechanisms and management, which will benefit all who deliver anti-cancer treatments.

**Mucositis and personalised cancer medicine: supportive care makes excellent cancer care possible**
Cancer treatments become ever more complex over time, and the holy grail is tailored, personalised cancer medicine. However, most research in this field concentrates on interactions between tumour and treatment, somewhat downplaying those between treatment and host. We divide patients into Toxic and Non-Toxic Responders and Non-Responders, without fully exploring the implications.

The field of Supportive Care in Cancer (SCC) concentrates on the effects of cancer, and its treatment, on the patient. As cancer treatments evolve, so does supportive care. We have become experts at treatment and prevention of some of the common side effects of chemotherapy and radiotherapy, such as emesis and febrile neutropenia; but the new, targeted anti-cancer therapies bring new toxicities, some of which are rare but potentially devastating. SCC has to keep pace.

Mucositis can act as a demonstration toxicity – its mechanism after chemotherapy and radiotherapy is being more fully understood, leading to prevention and treatment strategies. Targeted agents cause a different mucosal damage (ranging from aphthous-like ulceration from m-TOR inhibitors to immune colitis and bowel perforation from immune checkpoint inhibitors), and newer combinations can be deadly.

Patients rarely suffer from a single toxicity, and links between toxicities show the potential for shared treatment if the mechanism can be targeted. Accurate risk prediction has remained elusive, but recent work in potential genomic risk prediction is very exciting.

Mucositis mechanism, connections and treatments; SCC and its integration into cancer care; and the future of SCC in the targeted and genomics era, will all be discussed.

**Competing interests**
I work with companies that make drugs which cause mucositis, and with companies that make drugs which attempt to ameliorate mucositis.
Parallel session abstracts (continued)

10.30 – 10.45
Room 3B

Catharine West,
University of Manchester, UK

Proffered paper: Radiogenomics Consortium meta-analysis of four genome wide association studies of late toxicity after radiotherapy for prostate cancer

Background
Studies are attempting to identify common genetic variants (single nucleotide polymorphisms, SNPs) that increase a cancer patient's risk of radiotherapy toxicity. To date few positive associations were replicated due to insufficient statistical power. Therefore, a meta-analysis was performed on existing genome wide association studies (GWAS).

Method
The meta-analysis included four GWAS in 1,614 men who received radiotherapy for prostate cancer: RAPPER (N=646), RADIOGEN (N=517), Gene-PARE (N=298), and Cross Cancer Institute (N=153). Imputation was used to obtain a uniform set of SNPs (2.2 million) across the studies. Toxicity was assessed 2-years following radiotherapy and changes in scores from baseline calculated. Four endpoints were studied (daytime urinary frequency, decreased urine stream, nocturnal frequency, proctitis/rectal bleeding) as well as overall toxicity. In each GWAS, multivariable analysis was performed by first fitting linear regression models for toxicity with non-genetic variables, to estimate the toxicity not explained by available patient- and treatment-related factors (residuals). The residuals were then tested for association with each SNP using linear regression. The results of the SNP-residuals association tests were then meta-analysed.

Results
Q-Q plots for each endpoint deviated from the null distribution at the upper tail, providing evidence that common SNPs are associated with risk of radiotherapy toxicity. A locus on chr11q22 was associated (meta-p-value=3.6x10^-8) with daytime urinary frequency and a locus on chr3p24 just failed to reach GWAS significance (meta-p-value=7.5x10^-8) for association with overall toxicity. Several loci neared significance (meta-p-values≈10^-7) for each of the endpoints studied.

Conclusion
This international study represents the largest effort to date to identify genetic predictors of radiotherapy toxicity. By increasing sample size and including multiple cohorts, this study identified a genetic locus that reached significance across cohorts. Further expansion of GWAS and meta-analysis should identify sufficient SNPs to for a clinically useful test.

10.45 – 11.10
Room 3B

Jervoise Andreyev,
The Royal Marsden NHS Foundation Trust, London, UK

A new era in understanding and managing chronic gastrointestinal (GI) consequences of cancer treatment

Toxicity is an inevitable consequence of cancer treatment. Most routinely used clinical scoring systems fail to identify important toxicities and as a result the frequency, severity and impact on patients’ lives of chronic GI consequences of cancer therapies has historically not been fully recognised by clinicians. Nor has it received the attention that it deserves in terms of research. Yet the iatrogenically driven morbidity of cancer treatments is an important human model of GI disease and has already yielded new insights which can be applied to benign and malignant diseases.

In the last 15 years, a largely unheralded but spectacular revolution in understanding why toxicity develops, how it should be measured, managed and described has gathered
What makes a target attractive for cancer drug discovery

10.00 – 10.05
Hall 1A
Donald Ogilvie,
Cancer Research
UK Manchester
Institute, UK

Introduction
The selection of a molecular target for drug discovery involves careful consideration of the relevance of the target hypothesis to the unmet clinical need and the feasibility of the technical approach. In terms of the latter, only a minor fraction of the expressed genome is accessible to drug modulation with current technologies. Experts will discuss the factors to be considered in the selection and validation of novel molecular cancer targets and in the selection of small molecule and antibody approaches to drug discovery.

10.05 – 10.30
Hall 1A
Graeme CM Smith,
Oncology iMED,
AstraZeneca,
Macclesfield, UK

Identifying and prosecuting the right targets in oncology
Over the last decade or so efforts in oncology drug discovery have shifted from a target based approach to one that is much more patient aligned. Whilst the former approach produced robust pipelines of potential targets, these often lacked strong disease linkage. Patient aligned drug discovery embeds the molecular definition of the cancer that the project aims to treat at the heart of the discovery cascade. The outputs of this transformation are that targets are selected with a clear line of sight to a defined and identifiable population in the clinic. This should ultimately allow earlier clinical decisions to be made and in a more cost-effective manner.

GI toxicity is a major limiting factor to the advance of oncological treatments. Many new solutions have emerged but require the harnessing of a multidisciplinary approach in a way that oncology has rarely used up to this point.

11.10 – 11.35
Room 3B
Jean Klastersky,
Jules Bordet Institute,
Brussels, Belgium

Title TBC
Abstract not received.

11.35 – 11.40
Discussion
In defining the required attributes of a cancer target, evidence must exist that a target contributes to the development or progression of the cancerous phenotype. Disease linkage can be identified by mutation, amplification or aberrant activation. Patient selection feasibility also needs to be considered along with how novel targets are linked to clinically defined populations and whether there is a clinically amenable biomarker. As has been classically performed in oncology drug discovery, feasibility of screens for novel oncology targets needs to be assessed along with the druggability of the identified target. Challenges still remain in the target identification and validation space with a greater understanding of novel targets needed in the context of a disease which exhibits intra and inter-patient heterogeneity and pathway redundancies. As well as discussing the concepts outlined above, specific examples of targets with a clear line of sight to clinical segments that we have been working on will be presented, along with more practical considerations.

**10.30 – 10.45**

**Hall 1A**

**Proffered paper: Pan-RAF inhibitor active in melanomas that are resistant to BRAF or BRAF/MEK inhibitor combinations**

**Maria Romina Girotti,**
Cancer Research UK
Manchester Institute, UK

**Background**
The protein kinase BRAF is mutated ~40% of human melanomas. BRAF is a component of the RAS/RAF/MEK/ERK pathway and BRAF or MEK inhibitors increase progression-free and overall survival in melanoma patients with BRAF mutations. However, most patients relapse with acquired resistance and ~20% of patients present intrinsic resistance and do not respond to these drugs.

**Method**
We pursued a drug discovery programme for the development of a novel compound that targets mutant BRAF and wild-type CRAF. The efficacy of this compound was tested both in vitro and in vivo.

**Results**
Our compound inhibited the growth of melanoma cells that were resistant to BRAF-selective inhibitors. ERK pathway reactivation is responsible for resistance to BRAF targeted therapies in ~60% of the patients and in ~25% of patients resistance is driven by acquisition of mutations in NRAS. We show that our compound inhibited the growth of melanoma cells that were resistant to BRAF-selective inhibitors due to pathway reactivation mediated by different mechanisms. We show that this drug was active against patient derived xenografts (PDXs) from patients with acquired or intrinsic resistance to BRAF-selective inhibitors and in whose tumours resistance was associated with ERK pathway reactivation. Further, our compound is active in a PDX from a patient whose tumour developed acquired resistance to a combination of a BRAF-selective plus a MEK inhibitor and associated with acquisition of an NRAS mutation.

**Conclusion**
Our panRAF inhibitor can inhibit melanomas with different mechanisms of acquired or intrinsic resistance to BRAF-selective and BRAF-selective/MEK inhibitor combinations, potentially providing first-line treatment for naïve patients and second-line treatments for a range of relapsed patients.
**Drug discovery targets for anti-cancer antibodies**

In this lecture we will focus on target selection for different types of anti-cancer monoclonal antibody, including those that target cancer cells directly such as rituximab and trastuzumab, and those that target the immune system to promote tumour immunity. This latter group of reagents has become particularly attractive with the recent clinical success of ipilimumab and the anti-PD-1/PD-L1 blockers, such as nivolumab and pembrolizumab, in a number of difficult to treat cancers. It might at first appear that the requirements for these two classes of drug would be very different, with the former acting by recruiting cytotoxic effectors to kill the unwanted cells and the latter by blocking inhibitory signals on cytotoxic T cells and thereby reversing T cell exhaustion. However as we learn more about their respective mechanisms of action we find that in both cases the optimum targets are often key signalling molecules where the antibody is required to either block or in some cases promote transmembrane signalling. The most recent data also suggest that some of the response to checkpoint blockers might be due to cytotoxic activity required to delete regulatory T cells. We will explore these data and how they change our thinking about target molecule selection and antibody engineering to promote efficacy.

**Small molecules in the selection and validation of cancer drug targets**

The discovery of small molecule anticancer drugs greatly benefits from the parallel development of chemical tools to investigate target biology and define the path to the clinic. The integration of largescale chemical, genomic and structural information enhances target selection and prioritisation, while the early identification of chemical tools validates pharmacological modulation as a therapeutic strategy. Chemical feasibility or ‘druggability’ is critical in prioritising targets for drug discovery, especially those from less established therapeutic classes, and influences the choice of strategy to find chemical starting points. Not all chemical tools are suitable for target validation studies or as starting points for drug discovery, and a compound’s physicochemical properties and selectivity are necessary factors to be considered. Using small molecule tools to identify pharmacodynamic biomarkers is essential to support optimisation of drug candidates and to translate preclinical findings into patients. Importantly, new chemical tools often lead to new biological findings and can change the proposed path to the clinic for modulators of a given cancer target. Examples from our research on oncogenic signal transduction and DNA damage response pathways show how targets are selected and prioritised for research, and how fit-for-purpose chemical tools have been used to validate targets for study, to identify potential clinical contexts and patient stratification, to define pharmacodynamic biomarkers predictive of target engagement and efficacy, and to establish combination scheduling strategies to inform the clinical development of candidate inhibitors.

**Competing interests**

The Institute of Cancer Research has commercial interests in the development of inhibitors of PKB and of CHK1.
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- **Academic Forum for Pathology Trainees – National Pathology Week**
  
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  Cancer patients and researchers need pathology. At our stand, learn more about what pathologists can do for you. We shall show you the vital importance of cellular pathology in cancer research. We represent the often invisible science of tissue diagnosis, assessing the biological properties of cells that affect how they function.

  **Contact:** Bridget Wilkins, NCRI Pathology Lead for NHS Engagement in Biobanking  
  **Email:** b.wilkins@nhs.net; bridget.wilkins@gstt.nhs.uk  
  **Phone:** +44 (0)20 7188 8542
  Cellular Pathology Department, 2nd Floor, N Wing, St Thomas' Hospital, London, SE1 7EH, UK

- **Agena Bioscience**
  
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  Agena Bioscience – formerly Sequenom Bioscience – has launched the modular HemoID™ panel for medium to high throughput molecular blood group typing on their MassARRAY® technology. It allows the user to focus on blood groups of interest by selecting content from a menu of modules and thereby save cost and time.

  **Contact:** Malcolm Plant, Senior Sales Manager Northern Europe  
  **Email:** malcolm.plant@agenabio.com  
  **Phone:** +44 (0)7764 449 084
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  **Contact:** Hitan Patel, Senior Medical Advisor  
  **Email:** hitanp@amgen.com
  240 Cambridge Science Park, Milton Road, Cambridge, CB4 0WD, UK
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Exhibition Stand: 67  
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ANGLE has developed a technology, known as Parsortix, for the capture and harvest of circulating tumour cells (CTCs) in blood. The system is antibody independent and provides CTCs ready for genetic or protein analysis so providing valuable ongoing information about the disease. The system is CE-marked and being used for clinical studies.

**Contact:** Michael O’Brien, Business Development Director  
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**Phone:** +44 (0)1483 685 830  
3 Frederick Sanger Road, Surrey Research Park, Guildford, GU2 7YD, UK

**Auto Q Biosciences Limited**

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**Contact:** Saj Rahman, Operations Director  
**Email:** saj@autoqbiosciences.com OR info@autoqbiosciences.com  
**Phone:** +44 (0)118 963 5881  
1210 Parkview, Arlington Business Park, Theale, Berkshire, RG7 4TY, UK

**Barts Cancer Institute**

Exhibition Stand: 26 & 27  
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Celebrating its 10th Anniversary year, the BCI’s ethos is interdisciplinary and integrated, focusing on haematology-oncology, pancreatic, lung, women’s and men’s cancer, with comprehensive tissue banks, now extended to include pancreatic and metastatic tissues. Key strengths include clinical trials, and basic science in genomics, tumour-stromal interactions, stem cells and ageing.

**Contact:** Katie Hale  
**Email:** khale@qmul.ac.uk  
**Phone:** +44 (0)20 7882 6007  
Old Anatomy Building, Charterhouse Square, London, EC1M 6BQ, UK
BGI Tech

BGI Tech, a subsidiary of BGI – the world’s largest genomics organisation, provides sequencing and bioinformatics service solutions for global customers in biomedical, agricultural and environmental areas. Equipped with the industry’s broadest array of cutting-edge technologies, BGI Tech delivers rapid, cost-effective, and high-quality results that enable researchers to achieve scientific breakthroughs.

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Bone Cancer Research Trust

The Bone Cancer Research Trust is an independent charity which aims to improve outcomes for those affected by primary bone cancer through research, information and support. The charity is the major funder of research into primary bone cancer in the UK, having committed over £1.7 million since being formed in 2006.

Contact: Julie Harrington, CEO
Email: info@bcrt.org.uk
Phone: +44 (0)113 258 5934
10 Feast Field, Horsforth, Leeds, LS18 4TJ, UK
Breast Cancer Campaign

We fund world-class breast cancer research with the greatest potential to save and improve lives, bringing together the brightest minds to share knowledge and produce better, quicker results. We do this because we passionately believe we owe it to every woman affected by breast cancer to explore every avenue to overcome and outlive this disease – in our lifetime.

Contact: Geraldine Byrne, Research Grants Manager
Email: gbyrne@breastcancercampaign.org
Phone: +44 (0)20 7749 4108
110 Clifton Street, London, EC2A 4HT, UK

Bristol-Myers Squibb

Bristol-Myers Squibb is committed to advancing the science of immuno-oncology, an area of research which involves agents that work directly with the body's immune system to fight cancer. Our goal is to change survival expectations for patients with advanced/metastatic disease and the way patients live with cancer.

Contact: Christina Cockley, Senior Medical Education Manager, Oncology
Email: christina.cockley@bms.com
Phone: +44 (0)7753 976 705
Uxbridge Business Park, Sanderson Road, Uxbridge, UB8 1DH, UK

British Association for Cancer Research (BACR)

The aim of the BACR is to promote the advance of research in relation to all aspects of cancer, both laboratory and clinical, and to encourage the exchange of information. Its functions are to organise scientific meetings and workshops; fund exchanges between laboratories to encourage knowledge transfer; provide opportunities for senior investigators to undergo further training; and to provide opportunities for junior investigators and research students to present their work at meetings and conferences.

Contact: Janet Alexander
Email: bacr@leeds.ac.uk
Phone: +44 (0)113 206 5611
C/o Leeds Institute of Cancer & Pathology, Clinical Sciences Building, St James's University Hospital, Leeds, LS9 7TF, UK
Cambridge Bioscience

Cambridge Bioscience is a leading distributor of life science products with a passion for bringing new and exciting technologies to researchers. Working with specialist suppliers around the world, we offer an innovating range of high quality products, services and instruments supporting many of the key areas of cancer research including epigenetics and cell signalling.

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Contact: Mike Kerins, Managing Director
Email: support@bioscience.co.uk
Phone: +44 (0)1223 316 855
2-3 Munro House, Trafalgar Way, Bar Hill, Cambridge, CB23 8SQ, UK

CaCTUS (Cancer Clinical Trials Unit Scotland)

Cancer Clinical Trials Unit Scotland (CaCTUS) is a partnership between the Cancer Research UK Clinical Trials Unit in Glasgow and the NHS ISD Cancer Clinical Trials Team in Edinburgh. CaCTUS is an accredited National Cancer Research Institute (NCRI) CTU and is a registered UK Clinical Research Collaboration (UKCRC) CTU.

CaCTUS offer support for all aspects of management of cancer clinical trials and is committed to working with Investigators to develop and manage new cancer clinical trials.

Contact: Judith Dixon-Hughes, Project Manager
Email: judith.dixon@glasgow.ac.uk
Phone: +44 (0)141 301 7540
West of Scotland Beatson Cancer Centre, Level 0, 1053 Great Western Road, Glasgow, G12 0YN, UK

Cancer Research Technology Ltd

Cancer Research Technology is owned by Cancer Research UK, the world’s largest charitable funder of cancer research. We’re dedicated to advancing discoveries to beat cancer by translating promising scientific research into attractive commercial propositions. We provide services to oncology institutions worldwide, as well as operating our own drug discovery laboratories.

Contact: Katie Worthing, Marketing Manager
Email: kworthing@cancertechnology.com
Phone: +44 (0)20 3469 6300
Angel Building, 407 St John Street, London, EC1V 4AD, UK

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Exhibitor information (continued)

- **Cancer Research UK**

  Exhibition Stand: S2
  www.cancerresearchuk.org

  Cancer Research UK is the largest single funder of cancer research in the UK. Launching our new strategy this year, Beating Cancer Sooner, we have set out an ambitious agenda for the years ahead. Visit our stand to find out more about our strategy, new funding schemes and ways you can get involved with us.

  **Contact:** Karen Walshe, Research Branding and Communications Lead
  **Email:** researcher.comments@cancer.org
  **Phone:** +44 (0)20 7242 0200
  Angel Building, 407 St John Street, London, EC1V 4AD, UK

- **Cancer Research UK Liverpool Cancer Trials Unit (LCTU)**

  Exhibition Stand: 21
  www.lctu.org.uk

  Cancer Research UK Liverpool Cancer Trials Unit (LCTU) designs, conducts, leads and supports high quality early and late phase clinical trials, systematic reviews and other well designed studies to improve patient care. LCTU is committed to working with Investigators and offering support on all aspects of trial design and management.

  **Contact:** Sarah Cottle
  **Email:** lctu@liverpool.ac.uk
  **Phone:** +44 (0)151 794 8285
  Block C, Waterhouse Building, 1-3 Brownlow Street, Liverpool, L69 3GL, UK

- **Caris Life Sciences**

  Exhibition Stand: 35
  www.carislifesciences.eu

  Caris Life Sciences, a leading biosciences company focused on fulfilling the promise of precision medicine. Caris Molecular Intelligence™, a comprehensive tumour profiling service, provides oncologists with clinically actionable biomarker/drug associations to individualise care, using advanced technologies that assess relevant biological components of a patient’s cancer. To learn more, please visit www.carislifesciences.eu.

  **Contact:** Arlene Campbell
  **Email:** arlene.campbell@carisls.com
  **Phone:** +800 12 12 3030
  St Jakobsstrasse 199, 40542 Basel, Switzerland
Celgene Europe Ltd

Celgene is a global biopharmaceutical company committed to improving the lives of patients worldwide. Celgene seeks to deliver truly innovative and life-changing medicines for patients. The company focuses on the discovery, development and commercialisation of products for the treatment of cancer and immunological and inflammatory conditions. For more information about Celgene visit www.celgene.co.uk.

Contact: Lynne Thompson, National Sales Manager, Oncology
Email: lthompson@celgene.com
Phone: +44 (0)20 8831 8300
1 Longwalk Road, Stockley Park, Uxbridge, UB11 1DB, UK

The College of Radiographers

The College of Radiographers is committed to developing the science and practice of radiography, radiotherapy, and clinical imaging, including ultrasound, nuclear medicine and magnetic resonance imaging. We promote study and research and make major contributions to health policy development in these fields.

Contact: Sarah James, Professional Officer
Email: info@sor.org
Phone: +44 (0)20 7740 7200
207 Providence Square, Mill Street, London, SE1 2EW, UK

Consumer Liaison Group

A key focus for patient and public involvement (PPI) across NIHR CRN Cancer and the NCRI is the Consumer Liaison Group (CLG), a national network of cancer patients and carers working with research teams to help develop and deliver patient focused research studies. The CLG works through various organisations to ensure information about research provided to patients and the public is easily understood and made widely available.

Contact: Karen Inns, NIHR CRN Cancer Patient & Public Involvement (PPI) Lead
Email: patient.crcncancer@nihr.ac.uk
Phone: +44 (0)113 343 2254
NIHR CRN Cancer, University of Leeds, MacMillan Wing, Fairbairn House, 71-75 Clarendon Road, Leeds, LS2 9PH, UK
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Contact: Stijn de Vries, Sales Director Europe
Email: info@dna-technology.dk
Phone: +45 8732 3000
Voldbjergvej 16B, DK-8240 Risskov, Denmark

Exhibition Stand: 41
www.dna-technology.dk

Doctors.net.uk

Doctors.net.uk is the largest most active network of GMC authenticated doctors in the UK. It is a trusted channel for information, communication and education and is used by more than 40,000 doctors every day.

Contact: Laura Knox, Senior Marketing Executive
Email: info@mess.doctors.org.uk
Phone: +44 (0)1235 828428
20 Western Avenue, Milton Park, Abingdon, Oxon, OX14 4SH, UK

Exhibition Stand: 81
www.doctors.net.uk

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Contact: Saba Anwer, Associate Market Development Director
Email: saba.anwer@quintiles.com
Phone: +1 919 760 3583
1037 White Peach Way, San Jose, CA 95133, USA

Exhibition Stand: 64
www.quintiles.com

Exhibitor information (continued)
**Eurogentec**

**Exhibition Stand: 34**

www.eurogentec.com

Eurogentec, part of Kaneka Corporation, is a leading supplier of specialty products and custom services. Through its three inter-related business units (Life Science Research, Diagnostic services and GMP BioManufacturing), the company provides high quality products to scientists involved in the life science, biotechnology, diagnostic and pharmaceutical markets. Eurogentec is ISO 9001, ISO 13485 certified, cGMP accredited by the Belgian Ministry of Health and approved by the US FDA for the manufacturing of a commercial biologic.

**Contact:** Marie Brike, Marketing Executive Operations  
**Email:** m.brike@eurogentec.com  
**Phone:** +32 (0)4 372 7400  
Rue Bois Saint-Jean, 5, 4102 Seraing, Belgium

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**EndoSoft**

Exhibition Stand: 75  
www.endovault.com

EndoVault® Oncology is a first of its kind HER designed specifically for oncologists. Unsurpassed in its comprehensive and broad scope of content, EndoVault® Oncology offers the basics of a scheduling, consultation and report writing software along with specialty specific content for oncologists practicing in all disciplines of oncology.

**Contact:** Bart van der Meer, Sr. Vice President Marketing & Sales  
**Email:** sales@endosoft.com  
**Phone:** +44 (0)116 255 4423  
The Crescent, 56 King Street, Leicester, LE1 6RL, UK

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**Elekta**

Exhibition Stand: 52  
www.elekta.com

MOSAIQ® Oncology Information Management System is designed to manage the complete spectrum of oncology treatments in a single patient record. For Chemotherapy, MOSAIQ provides a clear, flexible means of charting the patient's treatment across the medical assessment and chemotherapy administration process.

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**Contact:** Andre Silveira, OIS Sales Manager UK & Ireland  
**Email:** andre.silveira@elekta.com  
**Phone:** +44 (0)7867 353 294  
Linac House, Fleming Way, Crawley, West Sussex, RH10 9RR, UK

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FluidX

Our customers store chemical compounds and biological samples for long periods of time to enable them to develop a better understanding of disease processes and help develop new treatments for the future. At Fluidx we help this research by providing the storage and tracking products that enable scientists to carry out their research safe in the knowledge that their samples are preserved and identified for decades into the future. Who knows, maybe one day we’ll find that a key treatment is developed with the help of material stored in FluidX 2D-Coded Tubes!

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Contact: Emma Ryan, UK Sales Manager
Email: info@fluidx.eu
Phone: +44 (0)1625 861 614
Monks Heath Hall Workshops, Chelford Road, Nether Alderley, Cheshire, SK10 4SY, UK

European Association for Cancer Research (EACR)

Exhibition Stand: 77
www.eacr.org

The European Association for Cancer Research is Europe’s largest professional member society for cancer researchers with over 9500 members worldwide. We provide a wide range of services to members, facilitate communication and collaboration, and organise a series of cancer research conferences where education and interaction are the highest priorities.

Contact: Andrew Binns, Memberships Officer
Email: eacr@nottingham.ac.uk
Phone: +44 (0)115 951 5114
Sir Colin Campbell Building, University of Nottingham Innovation Park, Triumph Road, Nottingham, NG7 2TU, UK

Experimental Cancer Medicine Centres (ECMC) Network

Exhibition Stand: 62
www.ecmcnetwork.org.uk

The ECMC Network is a UK-wide initiative, jointly funded by Cancer Research UK and the four UK health departments, providing dedicated funding towards the infrastructure needed to both deliver world-leading early phase clinical trials and to enable a network of experts to drive the development of new cancer therapies for patients.

Contact: Guy Goodwin, Communications Project Manager
Email: ecmcadmin@cancer.org.uk
Phone: +44 (0)20 3469 5381
Angel Building, 407 St John Street, London EC1V 4AD, UK
Integrated DNA Technologies

Integrated DNA Technologies (IDT) is the world leader in custom nucleic acid manufacturing for the life sciences research and clinical diagnostics markets, servicing academic and clinical research, biotechnology, pharmaceutical development and agricultural research. IDT product applications include qPCR, gene construction, genome editing, next generation sequencing, SNP detection, and functional genomics.

Contact: David Hughes, EU Sales Manager
Email: custcare@idtdna.com
Phone: +32 (0)16 28 22 60
Interleuvenlaan 12A, B-3001, Leuven, Belgium

Genomic Health

Genomic Health is a provider of genomic-based diagnostic tests that address both the overtreatment and optimal treatment of early stage cancer. Genomic Health’s lead product, the Oncotype DX® breast cancer assay, has been shown to predict the likelihood of chemotherapy benefit as well as recurrence in invasive breast cancer.

Contact: Karen Watson, Marketing Communications Specialist
Email: kwatson@genomichealth.com
Phone: +44 (0)20 3440 5153
3 Devonshire Street, London, W1W 5DT, UK

Guys and St Thomas’ NHS Foundation Trust, Oncology and Haematology Clinical Trials (OHCT)

Oncology and Haematology Clinical Trials (OHCT) at Guys’ and St Thomas’ NHS Foundation Trust was developed as a trials support team to improve treatment choice, clinical care and outcomes for cancer patients through innovation, dedication and excellence in clinical research. The current portfolio includes 150 commercial and non-commercial trials.

Contact: Nicholas Gomm, Clinical Trials Manager
Email: nicholas.gomm@gstt.nhs.uk
Phone: +44 (0)20 7188 1430
Guys and St Thomas’ NHS Foundation Trust, Guys Hospital, Great Maze Pond, London, SE1 9RT, UK

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Contact: Gloria Lekai, Senior Marketing Support Co-ordinator
Email: biosales@licor.com
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4647 Superior Street, Lincoln, NE 68504, USA

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Email: Katie.Hanretty@thermofisher.com
Phone: +44 (0)141 814 6100
3 Fountain Drive, Inchinnan Business Park, Paisley, PA4 9RF, UK

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Contact: Ian John, Managing Director
Email: ian@lornelabs.com
Phone: +44 (0)118 921 2264
Unit 1, Cutbush Park Industrial Estate, Danehill, Lower Earley, Berkshire, RG6 4UT, UK
Macmillan Cancer Support

Exhibition Stand: 20
www.macmillan.org.uk

Macmillan is a leading charity that seeks to reach and improve the lives of everyone living with cancer and to inspire others to do the same. Evidence at Macmillan helps us to understand the numbers, needs and experiences of people affected by cancer and the solutions to these issues.

Contact: Nicolas Lee, Research Lead
Phone: +44 (0)20 7840 7840
Email: evidence@macmillan.org.uk
89 Albert Embankment, London, SE1 7UQ, UK

Manchester Cancer Research Centre

Exhibition Stand: 72
www.manchester.ac.uk/mcrc

The Manchester Cancer Research Centre (MCRC) is a partnership between The University of Manchester, The Christie NHS Foundation Trust and Cancer Research UK that brings together world-class research into cancer biology, drug discovery and clinical trials on one site. The MCRC has an integrated approach, which is essential in translating research findings in the laboratory into better treatments for cancer patients.

Contact: Esther Walker, Head of Operations
Email: mcrc@mcrc.man.ac.uk
Phone: +44 (0)161 446 3156
The University of Manchester, Wilmslow Road, Manchester, M20 4BX, UK

Marie Curie Cancer Care

Exhibition Stand: 25
www.mariecurie.org.uk/research

Marie Curie Cancer Care is a leading funder of palliative and end of life care research to benefit people with terminal illnesses at the end of life.

Visit our stand for information on the Marie Curie Cancer Care Research Programme, our research at our hospices and facilities, and our annual conference.

Contact: Rhiannon Smith, Research Information Officer
Email: rhiannon.smith@mariecurie.org.uk
Phone: +44 (0)207 091 4154
89 Albert Embankment, London, SE1 7TP, UK
Mela

Exhibition Stand: 31
www.mela.co.uk

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MedICUs Acute Oncology enables triage for treatment priority, analysis of patient information, assessments, interventions and outcomes – assisting AOTs with reducing hospital admissions and delivering quality patient care.

Contact: Adam Kershaw, Sales Executive
Email: sales@mela.co.uk
Phone: +44 (0)1753 480 460
PO Box2167, Gerrards Cross, SL9 8XF, UK

MRC-NIHR National Phenome Centre

Exhibition Stand: 04
www.imperial.ac.uk/phenomecentre

MRC-NIHR National Phenome Centre offers mass-spectrometry and Nuclear Magnetic Resonance capabilities for targeted and exploratory metabolic phenotyping including customisable informatics solutions and a functional interpretation of data. Open to academic or commercial researchers on fee-for-service basis or for collaborative projects, access to the facilities is via an independent committee.

Contact: Lynn Maslen
Email: phenomecentre@imperial.ac.uk
Phone: +44 (0)20 7594 3318
Imperial College London, Hammersmith Campus, Du Cane Road, London, W12 ONN, UK

Myeloma UK

Exhibition Stand: 68
www.myeloma.org.uk

Myeloma UK is the only organisation in the UK dealing exclusively with myeloma, a bone marrow cancer for which there is no cure, but many very effective treatments. Our broad and innovative range of services cover every aspect of myeloma from providing information and support, to improving standards of treatment and care through research and campaigning.

Contact: Renee Hamilton, Personal Assistant to the CEO
Email: renee.hamilton@myeloma.org.uk
Phone: +44 (0)131 557 3332
Broughton House, 31 Dunedin Street, Edinburgh, EH7 4JG, UK
Nanostring Technologies

Exhibition Stand: 66
www.nanostring.com

NanoString Technologies provides life science tools for translational research and molecular diagnostic products. The company’s nCounter® Analysis System, which has been employed in basic and translational research and cited in 100’s peer-reviewed publications, has also now been applied to diagnostic use with the nCounter Dx Analysis System.

Contact: Claire McDonnell, Marketing Manager
Email: cmcdonnell@nanostring.com
Phone: +44 (0)7538 301 168
11th Floor, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK

National Cancer Research Institute (NCRI)

Exhibition Stand: NCRI Stand
www.ncri.org.uk

NCRI is a UK-wide partnership between government, charity and industry, which promotes cooperation in cancer research among its 22 member organisations.

Through our initiatives and the NCRI Cancer Conference, we encourage knowledge sharing and cross-disciplinary collaboration for the benefit of patients, the public and the research community.

Contact: Nicola Harris, Communications Manager
Email: info@ncri.org.uk
Phone: +44 (0)20 3469 8460
Angel Building, 407 St John Street, London, EC1V 4AD, UK

NIHR CRN: Cancer

Exhibition Stand: 44
www.crn.nihr.ac.uk/cancer

The NIHR Clinical Research Network: cancer provides researchers with the practical support needed to make cancer clinical studies happen in the NHS, so that more research takes place and more patients can take part.

Our aim is to improve patient care by improving the speed, quality and integration of research.

Contact: Sue Redhead, Workforce Development & Communications Officer
Email: sue.redhead@nihr.ac.uk
Phone: +44 (0)113 343 0113
University of Leeds, MacMillan Wing, Fairbairn House, 71-75 Clarendon Road, Leeds, LS2 9PH, UK

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Exhibitor information (continued)

▶ Novus Biologicals

Exhibition Stand: 39  
www.novusbio.com

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Contact: Ben Mantle, European Business Development Executive  
Email: ben.mantle@novusbio.com  
Phone: +44 (0)1223 426 001  
12 Cambridge Science Park, Cambridge, CB4 0FQ, UK

▶ Oncology News

Exhibition Stand: 78  
www.oncologynews.biz

Oncology News is a unique FREE publication for cancer professionals, which provides reviews of oncology and related journals in a high quality glossy magazine format. Cancer care professionals value the magazine’s practical and accessible approach and, with a readership of over 6,750 specialists throughout UK, it is the most popular way to keep up-to-date on the latest news.

Contact: Patricia McDonnell, Publisher  
Email: patricia@oncologynews.biz  
Phone: +44 (0)28 8289 7023  
88 Camderry Road, Camderry, Dromore, Co Tyrone, BT78 3AT, UK

▶ Oxford Cancer Research Centre

Exhibition Stand: S1  
www.cancercentre.ox.ac.uk

Established in 2010, the Oxford Cancer Research Centre is a network and partnership between Oxford University, Oxford University Hospitals Trust and Cancer Research UK. It harnesses Oxford’s world-leading cancer research with the core aim of facilitating collaboration to ensure rapid translation from scientific discovery to treatments for patients and ultimately increase cancer cure rates.

Contact: Amanda Yu, Operational lead and Lucy Beesley, Administrator  
Email: cancercentre@oncology.ox.ac.uk  
Phone: +44 (0)1865 617 043  
Department of Oncology, University of Oxford, ORCRB, Roosevelt Drive, Oxford, OX3 7DQ, UK
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Contact: Richard Bennett, UK Business Manager
Email: richard.bennett@eu.panasonic.com
Phone: +44 (0)1509 265 265
9 The Office Village, North Road, Loughborough, Leicestershire, LE11 1QJ, UK

Pancreatic Cancer UK

Pancreatic Cancer UK is the only national charity fighting pancreatic cancer on all fronts: support, information, campaigning and research.

Our aim is to support the best and most innovative research into pancreatic cancer in the UK and across the world.

Registered Charity Number 1112708

Contact: Rachel Joynes, Head of Research
Email: research@pancreaticcancer.org.uk
Phone: +44 (0)20 3535 7090
2nd floor, Camelford House, 89 Albert Embankment, London, SE1 7TW, UK

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Contact: Mark Dronsfield, Director of European Sales
Email: mark.dronsfield@personalis.com
Phone: +44 (0)7500 663 646
1350 Willow Road, Suite 202, Menlo Park, CA 94025, USA
Exhibitor information (continued)

**Prostate Cancer UK**

Exhibition Stand: 02

www.prostatecanceruk.org

We believe men deserve better.

That’s why we invest millions of pounds in research each year. It’s why we provide our helpline, peer support and information leaflets. It’s why we’re providing prostate education to medical professionals. It’s why we don’t take no for an answer in our campaigns.

We are Prostate Cancer UK.

Prostate Cancer UK is a registered charity in England and Wales (1005541) and in Scotland (SC039332), Registered company 2653887.

Contact: Matthew Hobbs, Deputy Director of Research
Email: info@prostatecanceruk.org
Phone: +44 (0)20 3310 7000
Fourth floor, The Counting House, 53 Tooley Street, London, SE1 2QN, UK

**Public Health England**

Exhibition Stand: 76

http://phenet.phe.gov.uk/Pages/Home.aspx

Public Health England’s mission is to protect and improve the nation’s health and to address inequalities through working with national and local government, the NHS, industry, voluntary and community sector and academia. PHE is an operationally autonomous executive agency of the Department of Health.

Contact: Ekaterini Blaveri, Head of Research Coordination at PHE National Cancer Intelligence Network
Email: ekaterini.blaveri@phe.gov.uk
Phone: +44 (0)20 7654 8388
5th Floor, Wellington House, 133-135 Waterloo Road, London, SE1 8UG, UK

**QIAGEN**

Exhibition Stand: 71

www.QIAGEN.com

QIAGEN, the leading global provider of Sample & Assay Technologies, enables access to content from any biological sample. QIAGEN markets more than 500 products worldwide, both consumable kits and automation systems to customer in Molecular Diagnostics, Applied Testing, Pharma and Academia. Further information can be found at www.QIAGEN.com.

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Contact: Allen Huxley, UK & Ireland Research Sales Manager
Email: marketing@randox.com
Phone: +44 (0)28 9442 2413
55 Diamond Road, Crumlin, Co. Antrim, BT29 4QY, UK

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Contact: Anneliese Holland, Sales Manager HemoCue UK
Email: michelle.kelly@radiometer.co.uk
Phone: +44 (0)1293 517599
Manor Court, Manor Royal, Crawley, West Sussex, RH10 9FY, UK

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Contact: Susanne Hartmanns, Junior Product Manager EMEA
Email: shartmanns@sirtex-europe.com
Phone: +49 (0)228 184 0711
Joseph-Schumpeter-Allee 33, 53227 Bonn, Germany
Exhibitor information (continued)

**Source BioScience**

Exhibition Stand: 30
www.sourcebioscience.com

Source BioScience offers histopathology services, screening and reference laboratory diagnostic testing for cancer and other diseases, and additional predictive testing for treatment optimisation. We are CPA, GLP and GCP accredited with a state-of-the-art laboratory in Nottingham and draw on the expertise of over 60 of the leading RCPath qualified Pathologists.

Contact: Robin Bodicoat, Marketing Manager
Email: sales@sourcebioscience.com
Phone: +44 (0)115 973 9018
1 Orchard Place, Nottingham Business Park, Nottingham, NG8 6PX, UK

**Southampton Clinical Trials Unit, University of Southampton**

Exhibition Stand: 32
www.southampton.ac.uk/ctu/

Southampton Clinical Trials Unit, University of Southampton is a Cancer Research UK core funded unit that has expertise in the design, conduct and analysis of clinical trials. The unit specialises in working in partnership with clinical investigators running interventional and large multicentre studies.

Contact: Wendy Wood or Christina Thompson
Email: ctu@soton.ac.uk
Phone: +44 (0)2 8120 5154
Mailpoint 131, Southampton General Hospital, Tremona Road, Southampton, Hants, SO16 6YD, UK

**Stratech Scientific Limited**

Exhibition Stand: 18
www.stratech.co.uk

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Email: david@stratech.co.uk/gareth@stratech.co.uk
Phone: +44 (0)1638 782 600
Unit 7, Acorn Business Centre, Oaks Drive, Newmarket, Suffolk, CB8 7SY, UK
The Brain Tumour Charity

- The Brain Tumour Charity is at the forefront of the fight to defeat brain tumours and is the only national charity making a difference every day to the lives of people with a brain tumour and their families. We fund pioneering research to increase survival, raise awareness of the symptoms and effects of brain tumours and provide support for everyone affected to improve quality of life.

Contact: Alison Evans, Head of Research and Policy
Email: alison.evans@thebraintumourcharity.org
Phone: +44 (0)1252 794 044
Hartshead House, 61-65 Victoria Road, Farnborough, Hampshire, GU14 7PA, UK

The Christie School of Oncology

- The Christie School of Oncology delivers top quality cancer focused education and training events. The School brings together professional pre & post registration education with vocational and apprenticeship training. We work in partnership with universities to provide academic courses in cancer care for medics, scientists, nurses and AHPs. Our comprehensive events programme includes all medical and surgical cancer specialties.

Contact: Rob Boyle, Events & Education Programmes Manager
Email: education.events@christie.nhs.uk
Phone: +44 (0) 161 918 7409
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Exhibitor information (continued)

The Francis Crick Institute

Exhibition Stand: 17
www.crick.ac.uk

Due to open in late 2015, The Francis Crick Institute will be an inter-disciplinary medical research institute located in central London. The institute is a consortium of Cancer Research UK, the Medical Research Council, the Wellcome Trust, UCL (University College London), King’s College London and Imperial College London.

Contact: Melanie Davies, Communications and Engagement Assistant
Email: info@crick.ac.uk
Phone: +44 (0)20 7611 2213
Gibbs Building, 215 Euston Road, London, NW1 2BE, UK

The Institute of Cancer Research

Exhibition Stand: M4
www.icr.ac.uk

The Institute of Cancer Research, London, is one of the world’s most influential cancer research organisations. We are world leaders in isolating cancer-related genes and discovering new targeted drugs for personalised cancer treatment.

The Institute of Cancer Research (ICR) is a college of the University of London and ranked as the top academic research institute in the UK. We have charitable status and rely on support from partner organisations, charities, major donors and the public.

Contact: Lauren King, Communications Assistant
Email: lauren.king@icr.ac.uk
Phone: +44 (0)20 7153 5136
123 Old Brompton Road, London, SW7 3RP, UK

The Pathology Group

Exhibition Stand: 65
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Contact: Peter Wicks, Executive Recruitment Consultant
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The Royal College of Radiologists

Exhibition Stand: 48
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The Royal College of Radiologists (RCR) leads, supports and educates in medical imaging and cancer treatment. The RCR sets and maintains the standards for entry to and practice in the specialties of clinical oncology and clinical radiology and shapes their future development for the benefit of patient care.

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UCL Cancer Institute

UCL, together with our partner healthcare system London Cancer which incorporates clinical care for over 3 million patients, is an international hub of excellence in cancer research, training and clinical care. We are a Cancer Research UK Centre incorporating over 70 research groups, supported by the UCL Biomedical Research Council. Together with Manchester, UCL is the first designated Lung Cancer Centre of Excellence.

Contact: Alex Sullivan, Cancer Research UK – UCL Centre Manager
Email: a.sullivan@ucl.ac.uk
Phone: +44 (0)20 7679 6840
Paul O’Gorman Building, 72 Huntley Street, London, WC1E 6BT, UK

Warwick Clinical Trials Unit

Warwick Clinical Trials Unit (Warwick CTU) is an academic unit undertaking clinical trials addressing issues of local, national and international importance.

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Contact: Janet Dunn, Professor of Clinical Trials
Email: j.a.dunn@warwick.ac.uk
Phone: +44 (0)24 76 151 178
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Contact: Debbie Wheelans, Grants & Information Manager
Email: debbiew@worldwidecancerresearch.org
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NCRI Cancer Conference team
The NCRI Cancer Conference team have been instrumental in organising this event. The team will be onsite for the whole Conference. Please feel free to speak to them for any feedback or ideas. Ask at the General Enquiries desk to find them onsite; alternatively, send an email and they will get back to you: ncriconference@ncri.org.uk.

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Kirsty Lyons, Senior Programme Officer
Sharon Vanloo, Operations Manager
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Thank you to Sue Harrison, Sam Harrison and the team at H2 Events for the design and production of the exhibition stands.

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Thank you to RF Design, Peter Mahoney, Jack Towner and Insight Mobile for the design of the Conference materials, website and app.

Other NCRI staff
Thank you to all NCRI staff members for their input and support. Please enquire at the NCRI stand in Hall 2 if you wish to contact anyone on this list.

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Jodi Baxter, Operations Manager
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National Cancer Intelligence Network

HOLD THE DATE!
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“United Against Cancer”
Cancer Outcomes Conference 2015

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## Acronyms

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<th>A</th>
<th>ABPI</th>
<th>Association of the British Pharmaceutical Industry (an umbrella organisation to which many of the pharmaceutical companies in the UK belong)</th>
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<tr>
<td>ACoRD</td>
<td>Attributing the Costs of health and social care Research and Development (a framework for the NHS and its partners which clarifies the distinction between research costs, NHS support costs and treatment costs)</td>
<td></td>
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<tr>
<td>AHSN</td>
<td>Academic Health Science Network (local partnership working in England, new in 2012, which brings together academia, industry and the NHS to identify and deliver innovations into healthcare)</td>
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<tr>
<td>AICR</td>
<td>Association for International Cancer Research (a research funder and member of the NCRI Partnership)</td>
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<tr>
<td>AMRC</td>
<td>Association of Medical Research Charities (a membership organisation of the leading medical and health research charities in the UK)</td>
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<tr>
<td>AMS</td>
<td>The Academy of Medical Sciences (an independent body that promotes advances in medical science and campaigns to ensure these are translated into healthcare benefits for society)</td>
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<tr>
<td>APPGC</td>
<td>All Party Parliamentary Group on Cancer (brings together MPs and Peers to help improve cancer services)</td>
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<tr>
<td>ARSAC</td>
<td>Administration of Radioactive Substances Advisory Committee (provides governance over radioactive medicinal products in the UK)</td>
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<tr>
<td>B</td>
<td>BBSRC</td>
<td>Biotechnology and Biological Sciences Research Council (UK public funder of non-medical bioscience for scientific research institutes and university research departments in the UK, and member of NCRI Partnership)</td>
</tr>
<tr>
<td>C</td>
<td>CaRD</td>
<td>Cancer Research Database (an NCRI database of the cancer research funded by all its partners, with data collected each year and available online)</td>
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<tr>
<td>CCB</td>
<td>Confederation of Cancer Biobanks (an NCRI initiative that brings together different biobanks that hold tissue samples in the UK to work more closely)</td>
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<tr>
<td>CCLG</td>
<td>Children’s Cancer and Leukaemia Group (a charity for children and young people with cancer and leukaemia)</td>
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<tr>
<td>CCG</td>
<td>Clinical Commissioning Group (set up by the Health and Social Care Act 2012 to organise the delivery of NHS services in England)</td>
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<tr>
<td>CCRN</td>
<td>Comprehensive Clinical Research Network (part of the NIHR Clinical Research Network which provides support for clinical trials and well designed studies in all areas of disease and clinical need)</td>
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<tr>
<td>CLG</td>
<td>Consumer Liaison Group (a group made up of ‘consumers’ with current or recent experiences of cancer services as patients, carers, relatives, or members of the public, which aims to improve the quality and value of cancer research and help to raise public awareness)</td>
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<tr>
<td>CLRN</td>
<td>Comprehensive Local Research Network (25 local areas across England that collectively form the CCRN)</td>
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<tr>
<td>CPRD</td>
<td>Clinical Practice Research Datalink (a service designed to maximise the way anonymised NHS clinical data can be linked)</td>
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<tr>
<td>CR-UK</td>
<td>Cancer Research UK (a cancer charity and member of the NCRI Partnership)</td>
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<tr>
<td>Acronym</td>
<td>Definition</td>
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<tr>
<td>CSG</td>
<td>Clinical Studies Group (an NCRI group that brings together appointed researchers to develop a strategic portfolio of studies)</td>
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<tr>
<td>CSO</td>
<td>Chief Scientist Office (part of the Scottish Government which supports research in Scotland and advises the Scottish Government on how research contributes to improvements in health and healthcare. Also a member of the NCRI Partnership)</td>
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<tr>
<td>CSP</td>
<td>Coordinated System for gaining NHS Permission (an NIHR system to standardise and simplify the process of gaining NHS Permission for commercial and non-commercial clinical research studies in England)</td>
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<tr>
<td>CTIMP</td>
<td>Clinical Trial of an Investigational Medical Product (a study that looks at the safety or efficacy of a medicine/foodstuff/placebo in humans, as defined by the Medicines for Human Use (Clinical Trials) Regulations 2004)</td>
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<tr>
<td>CTAAC</td>
<td>Clinical Trials Awards and Advisory Committee (a CR-UK funding stream, mostly for phase II and III trials)</td>
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<tr>
<td>CTRad</td>
<td>Clinical and Translational Radiotherapy Research Working Group (an NCRI initiative that supports radiotherapy research)</td>
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<tr>
<td>CTU</td>
<td>Clinical trials unit (specialised biomedical research unit which designs, centrally coordinates and analyses clinical trials and other studies)</td>
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<tr>
<td>DH</td>
<td>Department of Health (a ministerial department supported by 23 agencies and public bodies which leads, shapes and funds health and care in England. Also a member of the NCRI Partnership)</td>
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<tr>
<td>ECMC</td>
<td>Experimental Cancer Medicine Centre (a centre that has been awarded funding from DH and CR-UK to help it develop early phase clinical trials in cancer)</td>
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<tr>
<td>EME</td>
<td>Efficacy and Mechanisms Evaluation (a funding stream that supports ‘science driven’ studies with an expectation of substantial health gain, EME evaluates new treatments)</td>
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<tr>
<td>eolcRIG</td>
<td>End of Life Care Research Interest Group (an NCRI initiative which brings together health research funders, care providers and related charities who promote high quality research in end of life care)</td>
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<tr>
<td>EORTC</td>
<td>European Organisation for the Research and Treatment of Cancer (an organisation that delivers trials, workshops and other Europe-wide initiatives in cancer)</td>
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<tr>
<td>EPSRC</td>
<td>Engineering and Physical Sciences Research Council (a research funder)</td>
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<tr>
<td>ESRC</td>
<td>Economic and Social Research Council (a research funder and member of the NCRI Partnership)</td>
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<tr>
<td>FP7</td>
<td>Seventh Framework Programme for research and technology development (a channel for researches in the European Community to access funding for trans-national collaborative research, or personal awards)</td>
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<tr>
<td>FTE</td>
<td>Full-time equivalent (a commonly used unit of measuring the amount of time that members of staff are employed or have time allocated to particular projects)</td>
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<tr>
<td>GCLP</td>
<td>Good Clinical Laboratory Practice (a system of management controls for research laboratories and organisations to ensure the uniformity, consistency, reliability, reproducibility, quality, and integrity of non-clinical tests)</td>
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<td>Acronyms (continued)</td>
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<tr>
<td><strong>GCP</strong></td>
<td>Good Clinical Practice (a set of guidelines that must be followed when conducting clinical trials to ensure that the rights and well-being of trial participants are protected and that data generated in the trial is valid)</td>
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<tr>
<td><strong>GPRD</strong></td>
<td>General Practice Research Database (UK database containing anonymised medical records from primary care)</td>
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<tr>
<td><strong>GRIST</strong></td>
<td>Growing Recruitment to Interventional Surgical Trials (the name of a surgical working group, funded by the NIHR)</td>
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<tr>
<td><strong>H</strong></td>
<td>Hospital episode statistics (an NHS database that records details of hospital admissions, outpatient appointments and A&amp;E appointments at NHS hospitals in England)</td>
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<tr>
<td><strong>HRA</strong></td>
<td>Health Research Authority (an NHS Special Health Authority to protect and promote the interests of patients and the public in health research)</td>
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<tr>
<td><strong>HSC</strong></td>
<td>Health and Social Care (the Northern Irish government department responsible for health research, and a member of the NCRI Partnership)</td>
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<tr>
<td><strong>HTA (1)</strong></td>
<td>Health Technology Assessment (an NIHR funding stream for research to evaluate healthcare treatments or tests)</td>
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<td><strong>HTA (2)</strong></td>
<td>Human Tissue Authority (ensures that human tissue is used safely and ethically, and with proper consent)</td>
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<td><strong>ICRP</strong></td>
<td>International Cancer Research Partnership (an alliance of cancer organisations, including NCRI, that works to enhance global collaboration and strategic coordination of research)</td>
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<tr>
<td><strong>IMI</strong></td>
<td>Innovative Medicines Initiative (European public-private initiative aiming to speed up the development of better and safer medicines for patients)</td>
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<tr>
<td><strong>IMP</strong></td>
<td>Investigational Medicinal Product (a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial)</td>
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<td><strong>INVOLVE</strong></td>
<td>(part of the NIHR, a national advisory group that supports greater public involvement in NHS, public health and social care research)</td>
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<td><strong>IRAS</strong></td>
<td>Integrated Research Application System (a UK-wide system that streamlines the process for applying for permissions and approvals to conduct health and social care research)</td>
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<td><strong>IRCI</strong></td>
<td>International Rare Cancers Initiative (a strategic collaboration between Cancer Research UK, the UK National Institute for Health Research Cancer Research Network, the US National Cancer Institute, and the European Organisation for Research and Treatment of Cancer to support the development of international clinical trials for rarer cancers)</td>
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<tr>
<td><strong>L</strong></td>
<td>Ludwig Institute for Cancer Research (a research funder and member of the NCRI Partnership)</td>
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<td><strong>LLR</strong></td>
<td>Leukaemia &amp; Lymphoma Research (a cancer charity and member of the NCRI Partnership)</td>
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<tr>
<td><strong>M</strong></td>
<td>Medicines and Healthcare products Regulatory Agency (an organisation that regulates medicines and medical devices in the UK to ensure they work and are safe)</td>
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<tr>
<td><strong>MRC</strong></td>
<td>Medical Research Council (a research funder and member of the NCRI Partnership)</td>
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<tr>
<td>Abbr.</td>
<td>Full Name</td>
<td>Description</td>
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<tr>
<td>NAEDI</td>
<td>National Awareness and Early Diagnosis Initiative (England-based initiative that includes activities and research to promote the earlier diagnosis of cancer)</td>
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<td>NCEI</td>
<td>National Cancer Equality Initiative (a Department of Health initiative to prompt more research on inequalities and to provide policy advice)</td>
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<tr>
<td>NCI</td>
<td>National Cancer Institute (coordinates the US National Cancer Program and conducts and supports a range of activities related to the causes, prevention, diagnosis, and treatment of cancer)</td>
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<tr>
<td>NCIC</td>
<td>National Cancer Institute of Canada (now the Canadian Cancer Society Research Institute which supports researchers through the administration of cancer research funding)</td>
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<tr>
<td>NCIN</td>
<td>National Cancer Intelligence Network (UK-wide for initiative improving and using the information collected about cancer patients for analysis, publication and research)</td>
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<tr>
<td>NCRI</td>
<td>National Cancer Research Institute (a partnership of UK research funders that supports coordination in cancer research)</td>
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<tr>
<td>NCRN</td>
<td>National Institute for Health Research Cancer Research Network (a managed research network that supports cancer trial delivery, through the provision of research nurses, data managers and other network staff)</td>
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<td>NCSI</td>
<td>National Cancer Survivorship Initiative (works to improve the ongoing services and support available for those living with and beyond cancer)</td>
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<tr>
<td>NICTN</td>
<td>Northern Ireland Cancer Trials Network (umbrella organisation responsible for the coordination of cancer clinical trial activity throughout Northern Ireland)</td>
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<tr>
<td>NIHR</td>
<td>National Institute for Health Research (part of the Department of Health; commissions and funds NHS, social care and public health research in England)</td>
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<tr>
<td>NIHR CRN</td>
<td>National Institute for Health Research Clinical Research Network (the umbrella under which other English research networks, including NCRN, fall)</td>
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<td>NISCHR</td>
<td>National Institute for Social Care and Health Research (Welsh Government department that develops strategy and policy for research in the NHS and social care, and a member of the NCRI Partnership)</td>
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<tr>
<td>NOCRI</td>
<td>NIHR Office for Clinical Research Infrastructure (aims to simplify the clinical research environment in the UK, and help research funders to navigate NHS infrastructure)</td>
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<td>NPRI</td>
<td>National Prevention Research Initiative (a national collaborative initiative that provides funding to support research into chronic disease prevention)</td>
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<tr>
<td>OSCHR</td>
<td>Office for Strategic Coordination of Health Research (takes an overview of the budgetary division and research strategy of both the MRC and NIHR, to ensure both of these government funding streams work in synergy)</td>
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<tr>
<td>PC-UK</td>
<td>Prostate Cancer UK (a cancer charity and member of the NCRI Partnership)</td>
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<td>PET</td>
<td>Positron emission tomography (a type of medical imaging that can be used in cancer)</td>
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<tr>
<td>PHE</td>
<td>Public Health England (executive agency of the Department of Health, with responsibility for public health)</td>
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<td>PPI</td>
<td>Patient and public involvement (a commonly used term for referring to the involvement of lay representatives in a variety of healthcare activities)</td>
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<tr>
<td>Acronyms</td>
<td>Description</td>
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<tr>
<td>QA</td>
<td>Quality Assurance (processes, activities or programs to assure or improve the quality of research in a defined setting)</td>
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<tr>
<td>RCR</td>
<td>Royal College of Radiologists (Royal College for the specialities of clinical oncology and radiology)</td>
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<tr>
<td>RCUK</td>
<td>Research Councils UK (strategic partnership of the UK's Research Councils)</td>
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<tr>
<td>RIPB</td>
<td>Research for Patient Benefit (an NIHR funding stream for regionally-derived applied research projects in health services and social care)</td>
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<tr>
<td>RTTQA</td>
<td>Radiotherapy trials quality assurance (a group working to unify, simplify and streamline the QA process for radiotherapy in research)</td>
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<tr>
<td>SCRN</td>
<td>Scottish Cancer Research Network (an umbrella organisation to increase, support and sustain clinical trial activity in cancer care, in partnership with the UKCRC)</td>
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<tr>
<td>SSCRG</td>
<td>Site-specific clinical reference group (established by NCIN to ensure that the data now available is used to improve clinical care and to advise on what data needs to be collected and what analyses conducted)</td>
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<tr>
<td>STFC</td>
<td>Science and Technology Facilities Council (one of the UK's publicly funded Research Councils responsible for supporting, coordinating and promoting research, innovation and skills development)</td>
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<tr>
<td>STRATU</td>
<td>M Strategic Tissue Repository Alliance Through Unified Methods (a collaborative biobanking project between the pharmaceutical industry and academia)</td>
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<tr>
<td>SuPaC</td>
<td>Supportive and Palliative Care Collaborative (an NCRI initiative to encourage more collaboration and interdisciplinary working in supportive and palliative care)</td>
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<tr>
<td>TSB</td>
<td>Technology Strategy Board (a UK public body operating at arm's length from the Government which offers support and funding to help develop new products and services)</td>
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<tr>
<td>TYA</td>
<td>Teenage and Young Adult (a commonly used acronym when talking about trials involving this age group)</td>
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<tr>
<td>UKCRC</td>
<td>United Kingdom Clinical Research Collaboration (a partnership of major stakeholders that influence clinical research in the UK, working collaboratively to address common goals)</td>
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<td>WCTN</td>
<td>Wales Cancer Trials Network (an umbrella organisation for cancer clinical researchers in Wales which aims to improve the infrastructure for cancer clinical research)</td>
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<tr>
<td>YCR</td>
<td>Yorkshire Cancer Research (a cancer charity and member of the NCRI Partnership)</td>
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