A celebrated career in DNA repair: Tomas Lindahl

16

Building capacity in research into cancers of unmet need is a key priority, a few of our researchers tell us what brought them to work on these cancers and what opportunities the research holds.

Coming home to the UK: Richard Gilbertson

12

A leading expert in childhood brain tumours, we caught up with Richard to find out about his return to the UK to lead the Department of Oncology and CRUK Major Centre in Cambridge.

Solving knotty problems

24

The opportunities and challenges in 'team science' and how we’re supporting new ways to drive collaboration and networking across geographic and discipline boundaries.

Getting a grip on intractability

16

Extending the frontiers of cancer research: Grand Challenge

28

The psychologist who changed cancer research: Jane Wardle

36

Cover data visualisation

40

Why aren’t we sharing?

42

An inspiring mentor and signalling pioneer: Chris Marshall

44

Where next for cancer immunotherapy?

46

A look at a cross-section of our research in immuno-oncology and some of the hottest topics preoccupying the global immunotherapy community.

The cancer cost conundrum

30

Prices of cancer drugs have increased in recent years, but are the price tags justified and can we afford them?

Asking the right questions in clinical research

34

Championing science at the heart of CRUK: Nic Jones

14

The last word

62

Acknowledgements

64

Achieving more through working in partnership

50

Translating great science towards patient benefit

52

Entering new worlds: the dual role of clinical academics

54

Thinking differently: innovation in research funding

56

Recognising excellence: CRUK prizewinners

58

Honouring a lifetime’s work: Mel Greaves

60

The last word

62
This year has seen us truly embedding the principles of partnership and collaboration outlined in our Research Strategy across everything we do.

We have supported team science in a number of ways, including our eight Centres’ Network Accelerator Awards, which will act as hubs of excellence and drive productive collaborations across our UK network. We have also sought to open up new opportunities through the launch of our first international funding opportunities in the form of Grand Challenge and Catalyst Awards. And our multidisciplinary awards, a joint funding venture with the Engineering and Physical Sciences Research Council (EPSRC), are proving extremely popular, reaching across boundaries into communities who might never have considered CRUK as a potential funder of their work. I encourage you all to help us bang the drum – convince your colleagues that the intellectual challenges in cancer research are vast enough to accommodate many more talented scientists from many more fields: if they have good ideas, we’d like to hear them!

As ever, we are grateful for your contribution to our own team venture. We couldn’t function without the many scientists who peer review grants for us, advise us on scientific strategy, sit on our funding committees, and help us with public engagement and fundraising. I’d like to thank you all for your time, energy, patience and insight. And your opinions are incredibly important to us too – we want to hear from you not only about what we’re doing right, and what might work better, but also what obstacles you face.

Cancer research is a truly multinational effort and at CRUK we fund an incredibly vibrant and multinational research community and the vast majority of our researchers collaborate extensively across the globe. I believe strongly that science advances when the best minds are brought together from around the world to share ideas and expertise, and the UK scientific culture and CRUK’s research portfolio is all the richer for embracing this approach.

This year’s vote for the UK to leave the European Union has led to some understandable concerns from many of us involved in research and its funding. The referendum result raises important questions for us all, many of which will be impossible to answer until after Government activates Article 50 and the two-year-long negotiations of the UK’s exit commence. CRUK will be working in the lead up to, and throughout, the exit negotiations to influence the future relationship between the UK and the EU, seeking to minimise any risk to current and future research and looking for opportunities to improve the environment in which we work. In addition to researcher mobility and EU funding, we will also focus on the systems governing therapeutic marketing authorisations and clinical trial approvals. We will do this in consultation with the European research community, so that together we ensure our research effort continues to benefit cancer patients in the UK, Europe and beyond.

At CRUK we often have occasion to celebrate the achievements of our scientists. And in 2015, the award of the Nobel Prize for Chemistry to Tomas Lindahl has made it a very special year indeed. We’re proud to have provided the long-term funding which allowed Tomas to pursue his Nobel-winning work, and to develop the LRI Clare Hall Laboratories (now part of the Francis Crick Institute) into an internationally renowned powerhouse for research into DNA repair and replication.

This year, we appointed a new Chief Scientist, Karen Vousden, and I’d like to welcome her into her new job on behalf of the whole community. We’re all looking forward to seeing Karen more frequently, but of course this means that we’re bidding farewell to Nic Jones. Although we will be continuing to work with Nic in his role leading the Manchester Cancer Research Centre, I would like to take this opportunity to thank him for everything he has done to get us to where we are today. We are incredibly grateful for his wisdom, his belief in CRUK, his inspiration in driving forward change, and his unwavering support for you, our researchers; you could not have had a better advocate.

This publication celebrates some of the many achievements over the last year, highlights some examples of your incredible work and outlines a few areas of current interest to us and the wider community. We thank all of you who contributed to this publication – we could not have done it without you. We hope you enjoy reading it.
Last year (2015/16) we supported research worth £376 million across all cancer types, making us the largest independent funder of cancer research in Europe and the world’s leading charity dedicated to cancer research. We are committed to funding high-calibre, innovative research that we believe has the potential to provide the greatest benefit to the public and cancer patients.

Our diverse portfolio spans a breadth of research areas, from fundamental discovery research to understand the biology and causes of cancer, through translational research to bring the latest discoveries to the benefit of patients, to drug discovery to identify potential new treatments, clinical research to deliver the best treatments for patients, and population-level research covering epidemiology, prevention and early diagnosis of cancer.

We provide support through a range of funding schemes and initiatives, balancing response-mode funding for new research with directed investments in specific initiatives and infrastructure.

OUR PEOPLE
We are proud to support 4,000 researchers, doctors and nurses in many different institutions across the UK. Our progress is dependent on these outstanding individuals and teams conducting high-quality research.

We are dedicated to supporting people from the start of their career through to providing programme awards for world-class group leaders. During the year 2015/16 we supported 682 PhD students, around 850 post-docs, 81 Fellows, 210 project holders, 163 programme holders and 60 group leaders.

We have a strong tradition of excellence, having funded seven Nobel Prize winning researchers recognised for their outstanding contribution to cancer research.

OUR DISCOVERY SCIENCE PORTFOLIO
Our discovery science portfolio continues to be an area of major importance. We remain committed to funding curiosity-driven research supporting a broad range of activities through our institutes, and response-mode awards.

OUR TRANSLATIONAL PORTFOLIO
We want the research we fund to lead to patient benefit, and in recent years our spend on translational research has increased. We also support preclinical development and early-phase trials through our Centre for Drug Development (CDD) and the Experimental Cancer Medicine Centre (ECMC) network.

OUR CLINICAL PORTFOLIO
We currently support over 250 clinical trials, with more than 28,000 people joining our trials each year. More than 1 in 5 adult cancer patients in the UK take part in a clinical trial – a higher proportion than anywhere else in the world. Our clinical trials are not restricted to drug trials; we also support a number of studies aiming to improve surgery and radiotherapy – important areas not commonly invested in by pharmaceutical companies.

FACTS AND FIGURES

Last year (2015/16) we supported research worth £376 million across all cancer types, making us the largest independent funder of cancer research in Europe and the world’s leading charity dedicated to cancer research. We are committed to funding high-calibre, innovative research that we believe has the potential to provide the greatest benefit to the public and cancer patients.

Our diverse portfolio spans a breadth of research areas, from fundamental discovery research to understand the biology and causes of cancer through translational research to bring the latest discoveries to the benefit of patients, to drug discovery to identify potential new treatments, clinical research to deliver the best treatments for patients, and population-level research covering epidemiology, prevention and early diagnosis of cancer.

We provide support through a range of funding schemes and initiatives, balancing response-mode funding for new research with directed investments in specific initiatives and infrastructure.

OUR PEOPLE
We are proud to support 4,000 researchers, doctors and nurses in many different institutions across the UK. Our progress is dependent on these outstanding individuals and teams conducting high-quality research.

We are dedicated to supporting people from the start of their career through to providing programme awards for world-class group leaders. During the year 2015/16 we supported 682 PhD students, around 850 post-docs, 81 Fellows, 210 project holders, 163 programme holders and 60 group leaders.

We have a strong tradition of excellence, having funded seven Nobel Prize winning researchers recognised for their outstanding contribution to cancer research.

OUR DISCOVERY SCIENCE PORTFOLIO
Our discovery science portfolio continues to be an area of major importance. We remain committed to funding curiosity-driven research supporting a broad range of activities through our institutes, and response-mode awards.

OUR TRANSLATIONAL PORTFOLIO
We want the research we fund to lead to patient benefit, and in recent years our spend on translational research has increased. We also support preclinical development and early-phase trials through our Centre for Drug Development (CDD) and the Experimental Cancer Medicine Centre (ECMC) network.

OUR CLINICAL PORTFOLIO
We currently support over 250 clinical trials, with more than 28,000 people joining our trials each year. More than 1 in 5 adult cancer patients in the UK take part in a clinical trial – a higher proportion than anywhere else in the world. Our clinical trials are not restricted to drug trials; we also support a number of studies aiming to improve surgery and radiotherapy – important areas not commonly invested in by pharmaceutical companies.
FUNDING ACROSS THE RESEARCH PIPELINE

Our investment covers the full pipeline of research, from basic through to clinical.

50% BASIC
30% TRANSLATIONAL
20% CLINICAL

FUNDING BY LOCATION

We support research in over 90 institutions in 40 towns and cities across the UK.

OUR FACTS AND FIGURES 2015/16

FUNDING ON CLINICAL TRIALS

Since 2010, we have spent over £85 million funding over 300 clinical trials.

FUNDING BY DISEASE TYPE

Our funding covers research into a wide range of cancer types.

- LUNG: £39.6M
- LIVER: £3.8M
- SKIN: £4.0M (excluding melanoma)
- COLON & RECTAL: £35.1M
- BREAST: £32.8M
- LEUKAEMIA: £18.5M
- PANCREATIC: £18.3M
- PROSTATE: £16.9M
- MELANOMA: £13.3M
- OVARIAN: £12.0M
- BRAIN: £10.0M
- NON-HODGKIN’S LYMPHOMA: £8.2M
- OESOPHAGEAL: £6.9M
- MYELOMA: £5.2M
- BLADDER: £4.7M
- LUNG: £39.6M

FUNDED TRIALS
- PRECLINICAL: >10
- PHASE I: >60
- PHASE II: >100
- PHASE III: >120

ENDORSED TRIALS
- 2
- 4
- 32
- 16

† Includes research into over 100 other cancers.

Our funding covers research into a wide range of cancer types.

- LUNG: £39.6M
- LIVER: £3.8M
- SKIN: £4.0M (excluding melanoma)
- COLON & RECTAL: £35.1M
- BREAST: £32.8M
- LEUKAEMIA: £18.5M
- PANCREATIC: £18.3M
- PROSTATE: £16.9M
- MELANOMA: £13.3M
- OVARIAN: £12.0M
- BRAIN: £10.0M
- NON-HODGKIN’S LYMPHOMA: £8.2M
- OESOPHAGEAL: £6.9M
- MYELOMA: £5.2M
- BLADDER: £4.7M
- LUNG: £39.6M

FUNDED TRIALS
- PRECLINICAL: >10
- PHASE I: >60
- PHASE II: >100
- PHASE III: >120

ENDORSED TRIALS
- 2
- 4
- 32
- 16

† Includes research into over 100 other cancers.

Our funding covers research into a wide range of cancer types.

- LUNG: £39.6M
- LIVER: £3.8M
- SKIN: £4.0M (excluding melanoma)
- COLON & RECTAL: £35.1M
- BREAST: £32.8M
- LEUKAEMIA: £18.5M
- PANCREATIC: £18.3M
- PROSTATE: £16.9M
- MELANOMA: £13.3M
- OVARIAN: £12.0M
- BRAIN: £10.0M
- NON-HODGKIN’S LYMPHOMA: £8.2M
- OESOPHAGEAL: £6.9M
- MYELOMA: £5.2M
- BLADDER: £4.7M
- LUNG: £39.6M

FUNDED TRIALS
- PRECLINICAL: >10
- PHASE I: >60
- PHASE II: >100
- PHASE III: >120

ENDORSED TRIALS
- 2
- 4
- 32
- 16

† Includes research into over 100 other cancers.

Our funding covers research into a wide range of cancer types.

- LUNG: £39.6M
- LIVER: £3.8M
- SKIN: £4.0M (excluding melanoma)
- COLON & RECTAL: £35.1M
- BREAST: £32.8M
- LEUKAEMIA: £18.5M
- PANCREATIC: £18.3M
- PROSTATE: £16.9M
- MELANOMA: £13.3M
- OVARIAN: £12.0M
- BRAIN: £10.0M
- NON-HODGKIN’S LYMPHOMA: £8.2M
- OESOPHAGEAL: £6.9M
- MYELOMA: £5.2M
- BLADDER: £4.7M
- LUNG: £39.6M

FUNDED TRIALS
- PRECLINICAL: >10
- PHASE I: >60
- PHASE II: >100
- PHASE III: >120

ENDORSED TRIALS
- 2
- 4
- 32
- 16

† Includes research into over 100 other cancers.

Our funding covers research into a wide range of cancer types.

- LUNG: £39.6M
- LIVER: £3.8M
- SKIN: £4.0M (excluding melanoma)
- COLON & RECTAL: £35.1M
- BREAST: £32.8M
- LEUKAEMIA: £18.5M
- PANCREATIC: £18.3M
- PROSTATE: £16.9M
- MELANOMA: £13.3M
- OVARIAN: £12.0M
- BRAIN: £10.0M
- NON-HODGKIN’S LYMPHOMA: £8.2M
- OESOPHAGEAL: £6.9M
- MYELOMA: £5.2M
- BLADDER: £4.7M
- LUNG: £39.6M

FUNDED TRIALS
- PRECLINICAL: >10
- PHASE I: >60
- PHASE II: >100
- PHASE III: >120

ENDORSED TRIALS
- 2
- 4
- 32
- 16

† Includes research into over 100 other cancers.

Our funding covers research into a wide range of cancer types.

- LUNG: £39.6M
- LIVER: £3.8M
- SKIN: £4.0M (excluding melanoma)
- COLON & RECTAL: £35.1M
- BREAST: £32.8M
- LEUKAEMIA: £18.5M
- PANCREATIC: £18.3M
- PROSTATE: £16.9M
- MELANOMA: £13.3M
- OVARIAN: £12.0M
- BRAIN: £10.0M
- NON-HODGKIN’S LYMPHOMA: £8.2M
- OESOPHAGEAL: £6.9M
- MYELOMA: £5.2M
- BLADDER: £4.7M
- LUNG: £39.6M

FUNDED TRIALS
- PRECLINICAL: >10
- PHASE I: >60
- PHASE II: >100
- PHASE III: >120

ENDORSED TRIALS
- 2
- 4
- 32
- 16

† Includes research into over 100 other cancers.

Our funding covers research into a wide range of cancer types.
Every year we invest around £350 million into cancer research, made possible entirely through the generosity of our supporters and the public. They give generously in the expectation that we will deliver benefits to patients and the public, and we take that responsibility seriously.

It is incumbent on us to fund research of the highest calibre, and much of this funding is awarded through our committees, each with a specific remit, enabling us to support a breadth of basic, translational, clinical, population and behavioural research.

We are proud of our funding structures and processes which allow us to evaluate applications across the spectrum of research our researchers want to undertake. Our commitments are split across different funding mechanisms, supporting the best research in the most effective ways, from our core-funded institutes, to funding grants and awards through our committees, and the UK-wide infrastructure network that exists for our whole community to benefit from.

Our funding committees are comprised of UK and international experts, ensuring that our decisions are well informed and that we continue to fund pioneering research across a wide range of disciplines. The rigorous process for reviewing funding proposals involves many people across the community, from those who give their time to sit on our funding committees and panels, to peer reviewers who provide expert evaluation of individual applications. It is only through the hard work, enthusiasm and commitment of these many individuals that we can continue to support research that will have the biggest impact and bring significant progress to the field.

**Research commitments in 2015/16 by funding mechanism**

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Number of Outputs</th>
<th>Funding (£M)</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core-funded Institutes</td>
<td>7,000+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infrastructure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Institutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Number of outputs from CRUK research collected in Researchfish in 2016**

<table>
<thead>
<tr>
<th>Type of Funding</th>
<th>Award</th>
<th>Number</th>
<th>Funding (£)</th>
<th>Success rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCC</td>
<td>Fellowships</td>
<td>5</td>
<td>£4.8M</td>
<td>29%</td>
</tr>
<tr>
<td>CRC</td>
<td>Clinical Trials</td>
<td>11</td>
<td>£6.7M</td>
<td>55%</td>
</tr>
<tr>
<td>CRIC</td>
<td>Sample Collections</td>
<td>6</td>
<td>£0.9M</td>
<td>55%</td>
</tr>
<tr>
<td>DRCC</td>
<td>Programmes</td>
<td>2</td>
<td>£5.7M</td>
<td>40%</td>
</tr>
<tr>
<td>DDRU</td>
<td>Projects 1</td>
<td>14</td>
<td>£3.1M</td>
<td>58%</td>
</tr>
<tr>
<td>EDAG</td>
<td>Projects 2</td>
<td>3</td>
<td>£0.3M</td>
<td>33%</td>
</tr>
<tr>
<td>EDRU</td>
<td>Drug Development Projects</td>
<td>4</td>
<td>N/A</td>
<td>40%</td>
</tr>
<tr>
<td>PRC</td>
<td>Preclinical Grants</td>
<td>11</td>
<td>£0.5M</td>
<td>61%</td>
</tr>
<tr>
<td>PAC</td>
<td>Trial Grants</td>
<td>8</td>
<td>£0.9M</td>
<td>73%</td>
</tr>
<tr>
<td>NIC</td>
<td>Awards and Fellowships</td>
<td>11</td>
<td>£15.8M</td>
<td>10%</td>
</tr>
<tr>
<td>PAF</td>
<td>Projects</td>
<td>8</td>
<td>£1.3M</td>
<td>10%</td>
</tr>
<tr>
<td>PRC</td>
<td>Programmes</td>
<td>2</td>
<td>£4.9M</td>
<td>100%</td>
</tr>
<tr>
<td>PRC</td>
<td>Projects 2</td>
<td>10</td>
<td>£0.6M</td>
<td>25%</td>
</tr>
<tr>
<td>PRC</td>
<td>Fellowships</td>
<td>3</td>
<td>£0.7M</td>
<td>33%</td>
</tr>
<tr>
<td>SC</td>
<td>Programmes</td>
<td>17</td>
<td>£35.1M</td>
<td>49%</td>
</tr>
<tr>
<td>SC</td>
<td>Programme Foundation Awards</td>
<td>7</td>
<td>£8.2M</td>
<td>57%</td>
</tr>
<tr>
<td>SC</td>
<td>Projects</td>
<td>20</td>
<td>£7.2M</td>
<td>13%</td>
</tr>
<tr>
<td>SEB</td>
<td>Centres’ Network Acceleration Awards</td>
<td>8</td>
<td>£50.6M</td>
<td>44%</td>
</tr>
<tr>
<td>TAG</td>
<td>Programmes</td>
<td>3</td>
<td>£1.6M</td>
<td>100%</td>
</tr>
<tr>
<td>TAG</td>
<td>Projects</td>
<td>16</td>
<td>£0.9M</td>
<td>76%</td>
</tr>
</tbody>
</table>

1. Funding previously awarded through Clinical Trials Award and Advisory Committee (CTAC)
2. Funding previously awarded through Science Committee (SC)

**Funding previously awarded through Clinical Trials Award and Advisory Committee (CTAC)**
We recognise the crucial role that infrastructure plays in creating a dynamic and responsive research environment, where our researchers can deliver world-class results. Our long-term investment has helped to create a thriving network of research at 90 institutions and in more than 40 towns and cities across the UK. Collaborating across our UK network and beyond will also be critical to achieving maximum impact from our research.

Our five core-funded research Institutes provide an exceptional environment for discovery science, offering long-term support, core scientific services and equipment. In 2015/16 we invested £102.3 million in our Institutes.

Our 15 Centres form a unique national multidisciplinary network, accelerating the translation into research into the clinic. In 2015 we established three specialist Major Centres with the support to become internationally-recognised hubs of excellence in their fields. In 2014 we opened our first specialist Centre of Excellence, the Lung Cancer Centre of Excellence to advance cutting-edge lung cancer research. In 2014 we opened our first specialist Centre of Excellence, the Lung Cancer Centre of Excellence to advance cutting-edge lung cancer research. In 2015/16 we invested £51 million across our Centres network, including infrastructure, training and Centres’ Network Accelerator Awards.

Our Cancer Imaging Centres, a partnership with the Engineering and Physical Sciences Research Council (EPSRC), integrate preclinical and clinical research to facilitate the improved detection, diagnosis and treatment of cancer. In 2015/16 we invested £7.3 million in our imaging centres.

Our work in drug discovery is supported by four Drug Discovery Facilities, located alongside Institutes or Centres where they benefit from our wealth of basic research. In 2015 we set up a biotherapeutics laboratory, the CRUK-MEDI Alliance Laboratory. In 2015/16 we invested £15.2 million in these drug discovery and biotherapeutics facilities.

Cancer Research Technology (CRT), our development and commercialisation arm, operates two Discovery Labs, bridging industry and academia and facilitating the exploration of novel areas of science with the potential to yield commercially attractive projects. In 2015/16 we invested £7.4 million in these Discovery Labs.

Our Centre for Drug Development (CDD) operates its own state of the art Manufacturing Facilities: the Biotherapeutics Development Unit (BDU) manufacturing biological drugs such as monoclonal antibodies, recombinant proteins and DNA, and the Formulation Unit producing clinical formulations for small molecule drugs. In 2015/16 we invested £3 million in these Manufacturing Facilities.

Our Experimental Cancer Medicine Centre (ECMC) network brings together researchers and clinicians at 18 locations around the UK to deliver an integrated approach to early phase trials and experimental medicine. In 2015/16 we invested £3.7 million in ECMCs, a figure which is collectively matched by the four UK health departments.

Our Stratified Medicine Programme (SMP) Technology Hubs undertake genetic testing on tumour samples using innovative Next Generation Sequencing technology. In 2015/16 we invested £1.2 million in our SMP Technology Hubs.

We support eight Clinical Trials Units (CTUs), providing the academic cancer research community with expertise to design and run clinical trials at all phases. In 2015/16 we invested £8.6 million in our CTUs.
The more you climb, the more you should care about those around you and their personal success.

In 2015, Professor Richard Gilbertson returned to the UK to lead the Department of Oncology and CRUK Major Centre at the University of Cambridge after 15 years at St Jude’s Children’s Research Hospital in Memphis.

One of the world’s leading experts in childhood brain tumours, Richard has led international efforts that have dramatically advanced our knowledge of the biology of many of these tumours. Driven by a lack of biological understanding, his research has demonstrated that paediatric brain tumours are not single diseases, but distinct entities of the molecular and clinical level because they arise from different cells within the nervous system, and have different driver mutations. His findings are now translating into new treatments.

We caught up with Richard to find out more about his work and new life in Cambridge, why he has returned to the UK and the part CRUK played in enticing him back.

My interest in medulloblastoma was first ignited in 1987 when I did my first project as a medical student in Newcastle, nearly 35 years ago now. Back then we knew little about the biology of brain tumours. Driven by this lack of understanding, I realised I could have the greatest impact on patients with cancer by staying in research, and working closely with colleagues studying adult cancer could reveal clues relevant to paediatric cancer.

Since I joined, we have identified 505 people working on cancer across the many schools and institutions in Cambridge. We have organised them into a new 12-programme structure that focuses around the eight most common and deadly cancers. We also have programmes in cell and molecular biology and cancer imaging as well as an onco-innovation programme that brings together scientists and clinicians with a diverse mix of people from medicine, engineering, physics and chemistry. Engaging these disciplines in cancer diagnostics and treatment is very exciting, and working closely with colleagues studying adult cancer could reveal clues relevant to paediatric cancer.

COMING HOME TO THE UK: RICHARD GILBERTSON

It’s great to be back in the UK – it really is a fantastic place to live and do research. The scientific diversity, deep intellect and innovative spirit of the people here is first class. The UK scientific community is comparable to, or exceeds, what I have experienced in the US. Cambridge is a truly multidisciplinary research environment that includes world-leading chemists, engineers and physicists. Engaging these disciplines in cancer diagnosis and treatment is very exciting, and working closely with colleagues studying adult cancer could reveal clues relevant to paediatric cancer.

When I was working in the US I heard a lot of concerns about UK science, such as lack of opportunity, poor infrastructure, and underfunding. This has not been my experience – I think the opportunities for cancer research in the UK are fantastic. Yes, the UK is smaller than the States with fewer universities, but it is home to a world-class research community where you can have a big impact.

The partnership between Cambridge University and CRUK played a major role in attracting me back. CRUK’s senior leaders took the time to get to know me personally. Their investment in my own research meant that I could leave a very well-resourced environment at St Jude. Since returning I’ve been welcomed into the CRUK community, and I’m privileged to sit on the Clinical Research Committee and be involved in many new CRUK initiatives.

The UK’s cancer research community is poised more than ever before to play an international leadership role in cancer. And I can testify that it welcomes anyone interested in joining the vision to bring forward the day when all cancers are beaten.
After five years as Cancer Research UK’s Chief Scientist, Nic Jones stepped down in February 2016. His time in the job has seen the launch of major new initiatives in funding, which, coupled with the launch of the organisation’s Research Strategy in 2014, have laid a solid foundation for the future of cancer science in the UK.

This progress is no small part down to Nic’s skill as a scientific emissary into the world of a research funder. That his achievements aren’t perhaps as well known as they could be is part of his success: he’s been the perfect conduit.

A good Chief Scientist has to have the respect of both CRUK-funded researchers and the wider community, and overturning the perception that basic and clinical research exist in parallel universes. Both these things are crucially important, breaking down barriers to progress and both would have been a lot harder without Nic in the job.

Increasing engagement and interaction between CRUK and its scientists was something Nic tackled right away as his appointment in 2011 coincided with the launch of consultations for the new Research Strategy. In a way that had never been done before, Nic went out to talk to everyone he could think of, canvassing opinion from both CRUK-funded researchers and the wider community in the UK and overseas, to create the scientific consensus. Nic was happy in his element: “There’s nothing better than spending time talking about where we’re at, where the science is going, what’s also exciting is where the challenges are.”

Perthshire University consultant Princess was one of Nic’s personal qualities, what most people mention, apart from his unreasonable devotion to Manchester United, is the breath of fresh air he brought into the building including his ability to induce giggles in meetings with a strategically raised single eyebrow! But the last word must go to Nic himself: “Being Chief Scientist was an incredible privilege as well as immensely enjoyable. There was an openness that allowed me to get on and do stuff, and it was very, very rewarding. I was always a temporary migrant rather than a permanent settler in the CRUK office, but it was a lot of fun getting to know the team at CRUK better.”
Two years post-launch, we’ve seen an increase in funding for research into lung, pancreatic, and oesophageal cancers and brain tumours – together totalling £74.7 million in 2015/16.

Not only are we spending more, but we’re also attracting more people into the area. However, we’d like to get even more scientists thinking about cancers of unmet need, applying for grants, and helping to build effective research communities in this area. There are challenges of all flavours, from the most basic discovery research, to those directly related to patient benefit. So why might this field be of interest to you and your colleagues? We’ve been talking to a few of our researchers to find out what brought them to work on these cancers of unmet need and what opportunities the research holds.

For CRUK, cancers of unmet need are those with poor five-year survival rates, and limited improvements in treatment in the past decade. We urgently need to transform the outlook for patients with tumours in this category, which includes lung, pancreatic, oesophageal cancers and brain tumours. However, despite highlighting lung, oesophageal and pancreatic cancers as areas of priority in our previous strategy, we did not see research effort increase by as much as is needed. This is why we’re now being far more proactive.

Research in each of the four tumour types holds different challenges, and communities are often smaller and less well developed than those studying more mainstream cancers. Therefore, we’ve been working with researchers to develop and support relevant activities in each area and cancer type by providing funding, supporting conferences and bringing people together. We know that tackling a task of this scale is going to require investment and innovation – and we’re committed to making it happen. We’re confident that there are huge opportunities to carve out an outstanding research career in this area, whilst simultaneously having the chance to significantly improve patient outcome.

Cancers of unmet need share common features which make them particularly difficult to treat. Firstly, they are difficult to diagnose early, as in their early stages they can be asymptomatic or share symptoms with more innocuous problems. However, if they are diagnosed, they respond well to treatment at this early stage.

The problem of early diagnosis is one that has preoccupied Cambridge-based clinician scientist Professor Rebecca Fitzgerald for much of her career. Rebecca works on oesophageal cancer, where the odds of surviving the two main subtypes, adenocarcinoma and squamous cell carcinoma, improve remarkably if they are caught early.

As Rebecca says, “Most adenocarcinoma patients will have come through a pre-malignant stage, called Barrett’s oesophagus, and if we really want to turn survival around, finding those people is very important”.

Cases of Barrett’s oesophagus aren’t picked up as often as they should be, and even if the condition is diagnosed and the patient enters a surveillance programme, progression of the disease may be missed. To solve this problem, Rebecca and her colleagues developed the...
CANCERS TAKE THEIR DEEP TISSUE OF ORIGIN

Where does Barrett's oesophagus come from? And can we learn any lessons on cancer risk by studying the evolution of the disease based on concurrent analysis of the genetic and architectural features of Barrett's? This is the research focus of Dr Stuart McDonald, of London's Bart's Cancer Institute, and he's recently proposed a theory about the origin of the lesion that may overturn current thinking.

In 2016, Stuart was awarded a CRUK Programme Foundation Award, a funding scheme we introduced to provide support for mid career researchers to establish or develop their own group. Stuart, originally an immunologist, came into Barts' research through his interest in the inflammatory response. But in the course of his work, detailed phenotypic characterisation of biopsy samples led him to an unexpected conclusion. "The traditional view is that Barrett's glands develop from the normal lining of the oesophagus, but actually, they look really similar to pre-cancerous changes seen in the stomach lining," Stuart says. "What we think is that when patients get heartburn, it's corrosive, so it strips the normal oesophageal epithelium, leaving behind an empty ulcerated landscape. And then that's preferentially colonised by stomach epithelium, which is better adapted to acid conditions and over time exhibits features of intestinal metaplasia – much like that observed in H. pylori infection in the stomach."

This idea, though still controversial, is gaining ground, as Stuart says, "there isn’t a smoking gun link yet – we’re still working on that."

A further observation made by Stuart’s lab and others is that Barrett’s glands can be seen in a variety of identifiable gland types in Barrett’s lesions. These range from those that are similar to acid-secreting glands in the stomach to those that look like intestinal crypts – indeed intestinalisation, the sequencing of a normally non-intestinal cell type. This gland type, called Barrett’s intestinal metaplasia (BIM), is diagnostic for Barrett’s oesophagus. Most prevalent in Barrett’s oesophagus, BIM is rare in normal tissue.

"BIM is unique because it can spread throughout the oesophagus, whereas normal intestinal metaplasia is usually seen in the lower oesophagus and stomach. However, we don’t know the role of BIM in Barrett’s disease and we aren’t sure what the normal role of this cell type is. We think it may be involved in the pathogenesis of Barrett’s disease, but we need to better understand what the cell types are doing in different locations.

Our recent study, published in Nature, shows that BIM cells are highly proliferative, have a hyper-methylation signature and are enriched in the lower oesophagus. The proliferation is driven by MYC, which is overexpressed in BIM cells, contributing to the increased risk of developing oesophageal adenocarcinoma, a type of cancer that is currently the third largest cause of cancer-related death in the UK. The study also identified a number of other genes that are upregulated in BIM cells, including PDL1, which is involved in the immune response and may be a novel target for treatment.

Additionally, we found that BIM cells are more resistant to radiation therapy than other cell types, which could have implications for treatment strategies. Overall, our findings highlight the importance of further research into the role of BIM in the development of Barrett’s disease and oesophageal adenocarcinoma, as well as the potential for new therapeutic targets.
WHAT WERE YOUR EARLY SCIENTIFIC INSPIRATIONS?

Steve Pollard is a CRUK Senior Research Fellow and Group Leader at the MRC Centre for Regenerative Medicine. His approach is to target the ‘stemness’ of the cells driving a glioma, and change them into something less lethal: “We want to target lineage drug targeting. Neural stem cells have only very limited function in the adult brain, so a drug able to destroy all the neural stem cells may not cause catastrophic damage.

In a disease where human tissue is an essential resource, standardisation of cell lines and making them available to the community is incredibly important. To that end, Steve has successfully coordinated a bid for a CRUK Centres’ Network Accelerator Award, shared between the University of Edinburgh, the Francis Crick Institute, UCL and The Institute of Cancer Research. The Glioma Cellular Genetics Resource will provide high quality well-characterised cellular models of glioma with matched normal stem cells, together with all the validated genome editing tools that the community needs. Steve’s hope is that in addition to its more practical functions, it will act as a community hub, where anyone working on glioma can get the information and datasets they needed to get a project underway: “The zebrafish, mouse and fly communities have these kind of databases and repositories and we should be thinking about them for human cancers as well – making it more like a model system.”

The extra financial support CRUK has given to cancers of unmet need is paying dividends – more and more researchers are clearly turning their attention to this underexplored area. However, the journey towards a cure may be a long one. CRUK will be supporting these fledgling communities every step of the way as they take on the challenges that lie ahead. Identifying and solving tough clinical challenges; linking basic to translational research; provocative thinking; and strategic provision of communal resources; these factors, coupled to excellent science, will go a long way towards cracking the difficult problem posed by cancers of unmet need. We have every confidence in our researchers’ abilities to make the scientific advances so desperately needed by thousands of patients, and in return, we pledge that we’ll be there to help you.”

Dr Steve Pollard, of Edinburgh’s MRC Centre for Regenerative Medicine, brings another perspective to the glioma problem: “Now is a good time to think about cancer biology with a developmental biologist’s hat on” he says, “it’s not new, but it’s come back again as the field moves on from analysing the molecular biology of cancer into a tissue specific context. Stem cell methodologies like culture conditions, sorting, and how to grow and transfect cells are all tools we can apply now to human brain cancers. And CRISPR has completely and utterly transformed the field, as we can do rapid gene targeting now in primary human neural stem cells.”

Steve’s lab works on neural stem cell specific transcription factors, and his focus, like Simona’s, is to strip out all the heterogeneity and focus on universal features common to all gliomas. His approach is to target the ‘stemness’ of the cells driving a glioma, and change them into something less lethal: “We want to target lineage identity and self-renewal rather than just cell proliferation” he says, “the big advantage is that the proteins involved might be tissue specific so there may not be many side effects.” A lot is known about the transcription factors important for self-renewal and maintenance of neural stem cells, but degrading these is notoriously difficult. Instead, Steve’s lab is working on their mechanism of action to see whether there are co-factors or partners that may be vulnerable to drug targeting. Neural stem cells have only very limited function in the adult brain, so a drug able to destroy all the neural stem cells may not cause catastrophic damage.

In a disease where human tissue is an essential resource, standardisation of cell lines and making them available to the community is incredibly important. To that end, Steve has successfully coordinated a bid for a CRUK Centres’ Network Accelerator Award, shared between the University of Edinburgh, the Francis Crick Institute, UCL and The Institute of Cancer Research. The Glioma Cellular Genetics Resource will provide high quality well-characterised cellular models of glioma with matched normal stem cells, together with all the validated genome editing tools that the community needs. Steve’s hope is that in addition to its more practical functions, it will act as a community hub, where anyone working on glioma can get the information and datasets they needed to get a project underway: “The zebrafish, mouse and fly communities have these kind of databases and repositories and we should be thinking about them for human cancers as well – making it more like a model system.”

The extra financial support CRUK has given to cancers of unmet need is paying dividends – more and more researchers are clearly turning their attention to this underexplored area. However, the journey towards a cure may be a long one. CRUK will be supporting these fledgling communities every step of the way as they take on the challenges that lie ahead. Identifying and solving tough clinical challenges; linking basic to translational research; provocative thinking; and strategic provision of communal resources; these factors, coupled to excellent science, will go a long way towards cracking the difficult problem posed by cancers of unmet need. We have every confidence in our researchers’ abilities to make the scientific advances so desperately needed by thousands of patients, and in return, we pledge that we’ll be there to help you.”
IT’S NICE AT THE END OF YOUR CAREER TO HAVE RECOGNITION THAT WHAT YOU HAVE DONE IS ACTUALLY IMPORTANT

In 2006 we were proud to receive news of the seventh Nobel Prize awarded to a CRUK-funded scientist, Tomas Lindahl, Emeritus Professor at the Francis Crick Institute in London. Together with Aziz Sancar and Paul Modrich, won the Nobel Prize for Chemistry for their work identifying key DNA damage and repair processes.

Here we look at how Professor Lindahl’s discoveries have profoundly changed our understanding of cell response to cytotoxic therapies, and the substantial implications this has for cancer prevention and treatment today.

Tomas Lindahl, recognised as one of the founders of the DNA repair field, began his career in genetics at a time when the field of nucleic acid biochemistry was just opening up. Undertaking post-doctoral research on transfer RNA in the 1960s, and encountering the usual difficulties of working with RNA, he was the first to show that the molecule’s instability in the laboratory could not be blamed exclusively on contamination with ribonucleases. Having established that RNA is naturally unstable, this raised a question for Professor Lindahl: Is this true of DNA?

This simple question challenged long-established scientific dogma: that genes, as a conduit of inherited characteristics, are very stable over time and across generations, so the molecules carrying them must themselves be tough and well protected. Indeed, before the discovery of the structure of DNA and the first mechanistic insights into molecular biology, there was little reason to doubt it. But Tomas was amongst the first to recognise the existence of DNA repair mechanisms early in his career at the Karolinska Institute in the 1970s. He realised that, in addition to presenting insights into molecular biology, there was still so much more to learn, and that’s still so much more to learn,” says Laurence.

Understanding DNA repair has already made a huge impact. And it is clear this is just the beginning, with several new treatments now in clinical trials. “The cell’s inability to DNA damage is absolutely fundamental to the origins of cancer, and understanding how it works is bringing us to new medicines that attack the common features of the disease,” says Laurence.

The discovery that inherited mutations in DNA repair genes notably the BRCA genes are behind many familial cancers opened up new opportunities, such as ‘synthetic lethality’ strategies, to treat these cancers. And understanding that tumour cells can use DNA repair mechanisms as a defence against chemotherapy and radiotherapy has led to the pursuit of co-targeting strategies that are helping to challenge resistance.

LOOKING TO THE FUTURE...

Following the discovery and approval of olaparib, the first PARP inhibitor to be licensed for clinical use, other PARP inhibitors are now being tested in clinical trials. The majority of these are monotherapy trials in BRCA-mutated tumours, but they are also being tested in non-BRCA-mutated tumours with mutations in other DNA damage response-related genes. And beyond PARP, new treatments targeting other DNA damage response processes could be on the horizon. At 2015’s American Association for Cancer Research (AACR) Annual Meeting, there was much cause for optimism with promising results from several new experimental drugs targeting DNA damage response proteins.

Tomas served as Director at Clare Hall for 20 years, before handing over to another of the institute’s team of international DNA-damage experts, John Diffley. In 2015, teams at the laboratory officially became a part of the Francis Crick Institute, which this year move into the state of the art building in central London. It is the end of an era for this compact laboratory with its concentration of high impact science, and the beginning of an exciting new one in the diverse, multidisciplinary environment of the Crick.

We are delighted that Tomas Lindahl’s research has been recognised with this well-deserved Nobel Prize, and proud that CRUK has played a crucial part in developing a field with so much potential for cancer patients in the years to come.

A CELEBRATED CAREER IN DNA REPAIR: TOMAS LINDAHL

In 2015 we were proud to receive news of the seventh Nobel Prize awarded to a CRUK-funded scientist, Tomas Lindahl, Emeritus Professor at the Francis Crick Institute in London, together with Aziz Sancar and Paul Modrich, won the Nobel Prize for Chemistry for their work identifying key DNA damage and repair processes.

Here we look at how Professor Lindahl’s discoveries have profoundly changed our understanding of cell response to cytotoxic therapies, and the substantial implications this has for cancer prevention and treatment today.

Tomas Lindahl, recognised as one of the founders of the DNA repair field, began his career in genetics at a time when the field of nucleic acid biochemistry was just opening up. Undertaking post-doctoral research on transfer RNA in the 1960s, and encountering the usual difficulties of working with RNA, he was the first to show that the molecule’s instability in the laboratory could not be blamed exclusively on contamination with ribonucleases. Having established that RNA is naturally unstable, this raised a question for Professor Lindahl: Is this true of DNA?

This simple question challenged long-established scientific dogma: that genes, as a conduit of inherited characteristics, are very stable over time and across generations, so the molecules carrying them must themselves be tough and well protected. Indeed, before the discovery of the structure of DNA and the first mechanistic insights into molecular biology, there was little reason to doubt it. But Tomas was amongst the first to recognise the existence of DNA repair mechanisms early in his career at the Karolinska Institute in the 1970s. He realised that, in addition to presenting insights into molecular biology, there was still so much more to learn, and that’s still so much more to learn,” says Laurence.

Understanding DNA repair has already made a huge impact. And it is clear this is just the beginning, with several new treatments now in clinical trials. “The cell’s inability to DNA damage is absolutely fundamental to the origins of cancer, and understanding how it works is bringing us to new medicines that attack the common features of the disease,” says Laurence.

The discovery that inherited mutations in DNA repair genes notably the BRCA genes are behind many familial cancers opened up new opportunities, such as ‘synthetic lethality’ strategies, to treat these cancers. And understanding that tumour cells can use DNA repair mechanisms as a defence against chemotherapy and radiotherapy has led to the pursuit of co-targeting strategies that are helping to challenge resistance.

LOOKING TO THE FUTURE...

Following the discovery and approval of olaparib, the first PARP inhibitor to be licensed for clinical use, other PARP inhibitors are now being tested in clinical trials. The majority of these are monotherapy trials in BRCA-mutated tumours, but they are also being tested in non-BRCA-mutated tumours with mutations in other DNA damage response-related genes. And beyond PARP, new treatments targeting other DNA damage response processes could be on the horizon. At 2015’s American Association for Cancer Research (AACR) Annual Meeting, there was much cause for optimism with promising results from several new experimental drugs targeting DNA damage response proteins.

Tomas served as Director at Clare Hall for 20 years, before handing over to another of the institute’s team of international DNA-damage experts, John Diffley. In 2015, teams at the laboratory officially became a part of the Francis Crick Institute, which this year move into the state of the art building in central London. It is the end of an era for this compact laboratory with its concentration of high impact science, and the beginning of an exciting new one in the diverse, multidisciplinary environment of the Crick.

We are delighted that Tomas Lindahl’s research has been recognised with this well-deserved Nobel Prize, and proud that CRUK has played a crucial part in developing a field with so much potential for cancer patients in the years to come.
A KNOTTY PUZZLE MAY HOLD A SCIENTIST UP FOR A CENTURY, WHEN IT MAY BE THAT A COLLEAGUE HAS THE SOLUTION ALREADY AND IS NOT EVEN AWARE OF THE PUZZLE THAT IT MIGHT SOLVE.

Isaac Asimov, The Robots of Dawn

At CRUK, we’re committed to helping our scientists make the connections that will stimulate their thinking, and part of this commitment is to support new methods of driving collaboration and networking. We also have a strategic imperative to support team science effectively: put simply, some problems in cancer research are just too big or complicated to be run any other way.

Effective team science isn’t easy — it requires a commitment to collaboration, which in turn means understanding how to interact with a sometimes highly disparate group of researchers, who may be spread across the world and across many disciplines. And it’s becoming clear that the existing career structures and methods of recognition are not well-adapted for team science — funding bodies, including CRUK, have acknowledged that they need to make some fundamental changes to how they review and reward scientific endeavour so that collaboration is more attractive to the best researchers.

David Scott, Director of Discovery Research and Centres at CRUK, is very clear that the two concepts of team and individual science are not mutually exclusive: “It’s really important that people know CRUK will always be interested in funding individuals with fantastic ideas,” he says, “but there’s a place for team science too, and you can be really successful doing both.” And there’s a mounting body of data confirming that successful collaboration is the key to individual advancement — papers featuring multi-lab collaborations are cited more frequently than single lab publications, and making the right ties to other researchers can significantly boost your career.

CRUK’s Accelerator Awards, first awarded in 2015, aim to drive increased collaboration across the network, sharing expertise and platforms so researchers can access the resources they need for particular projects. Catrin Pritchard, whose CRUK Leicester Centre received £1.7 million to better integrate structural biology into drug development, says that the centres involved in the award are already seeing the benefits: “Within the Centres Network, there were drug discovery groups without the capacity for structural studies who previously had to make ad hoc arrangements, she says. “But now we’re combining the expertise of all the different locations, so when you have an interesting target, you already have access to the right people.”

ONE CHALLENGE IS TO GET PEOPLE THINKING COLLABORATIVELY EARLY IN THEIR CAREERS, AND ONE WAY WE’RE ENCOURAGING THIS IS THROUGH SANDPIT WORKSHOPS (SEE BOX ON RIGHT). TARGETED AT EARLY CAREER RESEARCHERS, MODERATED BY MORE SENIOR SCIENTISTS AND FEATURING REAL-TIME PEER REVIEW AND INSTANT DECISIONS, THEY’VE PROVED EXTREMELY EFFECTIVE.

IN THIS ARTICLE

David Scott
Director of Discovery Research and Centres, CRUK

Sara Courtneidge
Associate Director for Translational Sciences, Oregon Health & Science University.

Gerard Evan
Professor of Biochemistry, University of Cambridge

Catrin Pritchard
Director, CRUK Leicester Centre

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE

IN THIS ARTICLE
qualified to assess the scientific merits of the crossover research faces: the lack of referees highlighted another common problem that says. “We need cancer ambassadors, who’ll go on further activities, retaining the EPSRC as a valuable partner: “We should be talking with the community fall into that category,” he says. “What obviously, many in the physics and engineering community, as Fiona Reddington, Head of Population, Prevention and Behavioural Research at CRUK, explains: “Groups in the UK told us that if we wanted to be internationally competitive, we needed to provide researchers with “guile money” that would allow them to work as a cohesive whole. They said that getting the top groups in the world to choose their cohorts and expertise could be transformative, but there was no funding stream that fitted the remit.”

Each of the Catalyst Awards must be shared by at least three institutions, and will be funded up to £5 million over five years. There’s been a lot of interest – the 2016 call received applications from all over the world, which were shortlisted to nine expressions of interest. Applicants had the opportunity to present their ideas to one another at a joint meeting, allowing some to merge and learn from others to improve their ideas through further development. The community has welcomed the new award as they feel they’re being listened to,” Fiona says, “and the international component means there’s potential to shift our engagement in the world of population research and enable some really exciting collaborations.”

Two more international funding ventures new for CRUK are the Stand Up To Cancer (SU2C) Cancer Research UK-Ludwigian Foundation pancreatic Cancer Dream Team, and our own Grand Challenge.

Continued from previous page
EXTENDING THE FRONTIERS OF CANCER RESEARCH: GRAND CHALLENGE

Last year we launched our most ambitious funding scheme ever: Grand Challenge. It was a call to arms for the global research community to answer some of the biggest questions in cancer research that hold the potential to transform our approaches to preventing, diagnosing and treating cancer. Here members of the advisory panel, Professors Ed Harlow, Suzanne Cory and Brian Druker, provide insight into the qualities and approaches that helped make a successful application.

WHERE TO START?

The diverse nature of the Grand Challenge questions meant that applications covered a wide range of scientific approaches to answering the seven challenges. However, a couple of qualities were common across successful applications: attacking the problem through a broad scale of approach, or utilising novel techniques.

Teams that addressed the challenges by proposing to scale up existing approaches highlighted the value that could be derived from drawing together greater resource in terms of samples, data and people. These applicants clearly showed how the Grand Challenge funding would deliver a result greater than the sum of its parts.

Ed Harlow describes the ambition that the panel were looking for: “The teams had to be willing to move beyond the next logical step. They needed to be thinking about major leaps forward that would really open up the field and allow substantial progress.”

The panel were impressed when teams proposed novel ways to tackle challenges. “Some of the teams focused on new technologies they understood that to answer the question we need to develop entirely novel technologies, and had at least a glimmer of an idea about how to go about developing them,” says Ed.

OVERCOMING OBSTACLES

Forming an international, interdisciplinary consortium of eminent researchers from across the globe isn’t simple. Successful teams all recognised these boundaries – geographical and other – that they would have to overcome and addressed them within their application.

Suzanne Cory explains that having a shared vision is fundamental. “The teams needed to present a really convincing case that they will act as a fully integrated programme rather than as a series of parallel, related, but independent, projects.” Forming a consortium isn’t achievable following a formula – the process should be tailored to meet the unique needs of what the team is trying to achieve, accounting for locations, individuals and milestones that need to be met.”

“Some teams proposed an advisory panel to help steer the programme;” Ed explains – “an approach useful in supplementing knowledge and expertise within the teams. Some groups realised that further down the line they would benefit from involving individuals who would push them to think about things in new ways.”

This demonstrated to the panel that these teams anticipated that further questions may arise and were prepared to seek the right guidance when this occurred.

FURTHER MARKERS OF SUCCESS

Our Grand Challenge set the ambition that teams should form new collaborations to drive progress in innovative ways. Ed says the panel was pleased to see many of the teams recognised this vital element. “We were impressed with the number of groups who had reached outside their local environment or their own discipline to involve individuals who might come at the question from a completely different angle.”

Brian Druker explains: “The successful teams clearly embraced the collaborative nature of these Challenges and recognised that the purpose was to solve a problem. Accordingly, they reached out to the best people around the world, whether in academia or industry, and presented clearly articulated plans for how they would build upon each other’s strengths.”

Another recurring feature of the short-listed teams was that they kept the ultimate goal of the Challenges – improving survival for patients – at the forefront of their applications. Brian believes that the inclusion of patient advocates in the applications helped keep the teams focused and motivated. “As scientists, we often get bogged down in details and occasionally blame administrative hurdles for our lack of progress. Patient advocates remind us why our work is so important and compel us to break through these barriers.”

When we launched our Grand Challenge, we had the bold ambition of galvanising a revolution in how we prevent, diagnose and treat cancer. A year on, we are impressed to see how the research community has responded to our call and are thrilled to have short-listed nine exemplary teams. Whether they go on to secure the Grand Challenge Award or continue to hone their programmes in the future, we look forward to seeing how the collective expertise drawn together by the Grand Challenge will take us boldly in new directions, reaching new frontiers in cancer research.

Find out more at cruk.org/grandchallenge
The prices of cancer drugs have sky-rocketed in recent years, increasing pressure on an already troubled NHS and sparking heated debate. But are these hefty price tags justified and can we afford them?

Cancer research has never been more exciting than it is today. From super-boosting the immune system to developing personalised approaches, research is changing the face of cancer treatment.

This comes at a cost. The new immunotherapies, for instance, have price tags of more than £100,000 per patient per year. And these innovative drugs aren’t the only ones costing a small fortune; a global trend of soaring cancer drug prices has been going on for some time.

A 2015 study by the US National Bureau of Economic Research says the prices of cancer drugs have increased 10% every year between 1995 and 2013.

There is real concern that cancer treatment is becoming unsustainable. And, in recent years, it has been in the media spotlight. Sparking debate on spiralling costs is the Cancer Drugs Fund (CDF). The CDF, founded in 2004 to enable access to new targeted medicines, has come under intense criticism for turning a small fortune; a global trend of soaring cancer drug prices.

Meanwhile, the Cancer Drugs Fund (CDF) – set up in 2013 to plug gaps in NHS funding for cancer drugs – has been allocated a budget by 55% between 2015 and 2016, ballooning into a fund that, over its lifetime, cost £1.27 billion. The realisation that the CDF overspent so drastically has come under intense criticism for turning a small fortune; a global trend of soaring cancer drug prices.

The truth is, healthcare systems around the globe, including the NHS, are struggling to afford cancer drugs. There are no signs this trend for hefty price tags will abate any time soon or that these prices can be easily reined in. There is concern around where these prices are heading and the implications on cancer treatment, in light of financially constrained healthcare systems.

PRICING IS OUT OF HAND

“Pharma is out of hand,” says Professor Richard Sullivan, director at King’s College London’s Institute of Cancer Policy. “The cost basis of what’s happening to medicines is very elastic – the prices just keep going up. It’s not about value but what the market can bear.” According to the American Institute of Cancer Research, cancer costs the world more money than any other disease – about $895 billion a year. Alongside drugs, that includes the costs of diagnosis, radiotherapy, imaging, pathology, surgery, and end-of-life care. Interestingly, says Richard Sullivan, medicines account for almost 45% of total improvements in outcomes, with most control and cure through surgery and radiottherapy, yet medicines dominate public policy and media attention. “It’s incredible how medicines have got into the public psyche when it’s not the major modality of cancer care,” he says.

The problem with these expensive drugs is the knock-on effect in the NHS, both on its budget and on the availability and affordability of other treatments. The CDF overspent so drastically has come under intense criticism for turning a small fortune; a global trend of soaring cancer drug prices.

The prices of cancer drugs have sky-rocketed in recent years, increasing pressure on an already troubled NHS and sparking heated debate. But are these hefty price tags justified and can we afford them?
That’s a problem for industry, says Paul Catchpole, value and access director at the ABPI, when the threshold has largely stayed unchanged for 16 years and doesn’t reflect inflation or increases in healthcare expenditure over that time. However, he adds: “It would be wrong to say industry doesn’t recognise that drug prices are high and represent a challenge in the context of healthcare systems that face significant affordability and sustainability issues. Innovation in pricing and reimbursement models is needed, along with a greater focus on moving towards paying for health outcomes. It’s not just the high prices that are the problem but also the ability to pay for them. In the UK, this has become an increasingly contentious topic as NHS budgets are squeezed. Pharma companies and the NHS already negotiate prices – allegedly for discounts in the region of 25-30% – but these NHS budgets are squeezed.

Pharma companies have previously had access to, the CDF looks at new cancer drugs appropriately.

Although the original Fund allowed 85,000 patients access to cancer drugs, they wouldn’t have previously had access to, the CDF experience shows there aren’t a huge amount of cost containment, says Zoe. This is needed to ensure the healthcare system can continue to afford effective drugs and get value for money. She believes NICE is best placed to be that cost-containment mechanism but says it needs to be ‘somewhat more flexible’, though there’s no consensus on what that might mean. The industry would like a more transparent mechanism to make price negotiations public. The CDF experience shows there aren’t huge amounts of cost containment, she says. This is needed to ensure the healthcare system can continue to afford effective drugs and get value for money.

Peter Clark believes the new CDF and distribution of public money.

Although the original Fund allowed 85,000 patients access to cancer drugs, they wouldn’t have previously had access to, the CDF experience shows there aren’t a huge amount of cost containment, says Zoe. This is needed to ensure the healthcare system can continue to afford effective drugs and get value for money. She believes NICE is best placed to be that cost-containment mechanism but says it needs to be ‘somewhat more flexible’, though there’s no consensus on what that might mean. The industry would like a more transparent mechanism to make price negotiations public. The CDF experience shows there aren’t huge amounts of cost containment, she says. This is needed to ensure the healthcare system can continue to afford effective drugs and get value for money.

Paul believes it would be possible to build on other mechanisms that are often already employed in NHS negotiations, such as patient access schemes and new commercial access arrangements. Peter agrees, suggesting NHS negotiating teams should have more flexibility in the structure of confidential commercial access agreements. He believes pharma will be more accommodating with its prices if this is guaranteed. “If we can do that, we can protect the company’s list price and no one will know when the deal is done. We need to get pharma to help us to help the patient.” However, not everyone agrees with such an opaque approach. “I cannot accept that we can get a better deal for the public by hiding it from them in the deep dark shadows,” says Leonard. One area gaining widespread traction is the call for a move to a value-based pricing system, where price is directly linked to the value a drug provides. Such a system was due to be introduced in the UK but complexity in the negotiations has seen this, and its iteration, value-based agreements, shelved. However, following the CDF experience and in light of the NHS’s financial situation, there is renewed vigour in discussions around the need for a value-based pricing model. Richard Sullivan says it is crucial to move the discussion away from access and affordability of cancer treatment to one around the real value and affordability of cancer medicines.

Richard notes that a focus on value can be complicated, but that improved cancer outcomes require the cancer system to work together, from prevention and early diagnosis through to excellence in surgery. “The new model will work well if it gets the other bits of the system working together.”

There is no easy solution to the problem and getting agreement across the board will be difficult. It can be argued that small steps are being made with the reformed CDF, where more emphasis on collecting data on the effectiveness of the cancer drugs will go some way towards more accurately defining value and what we are prepared to pay for it. However, it seems, as global healthcare systems buckle under financial pressures, there will be more insistence on outcomes and data collection in the future, particularly in a real-world capacity, rather than just under the confines of controlled clinical trials. This data collection is something Richard Sullivan believes is not necessarily difficult.

But if the system is left unchecked, Leonard fears drug prices will continue to rise, and he notes that we are already at a point where drugs are starting to cost hundreds of thousands of dollars per person per year. Society, he says, has been reluctant to discuss prices and affordability because it’s not an easy conversation. “But we have to talk about it – common sense says the current situation cannot continue.”
ASKING THE RIGHT QUESTIONS IN CLINICAL RESEARCH

Over the last year we have been looking at how we are set up to support the changing landscape of clinical research, with the ambition to maintain a broad portfolio and grow our overall investment in this area. We have made changes to our clinical research funding structures, and introduced a new Statement of Intent to provide greater clarity on the types of clinical research applications we want to receive and fund in the future.

Clinical cancer research is becoming much more complicated both in terms of the questions being asked and the complexity of trial design. Clinical researchers need to be collaborating more widely to address the difficult underlying questions that are emerging, and a ‘one-size-fits-all’ trial design approach is no longer relevant for the vast majority of research questions.

At CRUK, this shift in the clinical cancer research landscape has been evident from the increasingly complex research programmes being proposed by the community. Researchers are designing ambitious programmes of work which include a clinical trial element alongside genomics and translational research. In response to this evolution, we have transformed the way we support clinical research, to drive progress and ensure maximum patient benefit from all trials we fund.

In 2015, we set up a new Clinical Research Committee (CRC) to oversee funding decisions across our whole clinical research portfolio, including late phase clinical trials, feasibility studies, sample collections and biomarker projects.

The committee is supported by two expert review panels: the Experimental Medicine Expert Review Panel (EMERP) and the Clinical Expert Review Panel (CERP). Alongside this new structure, we have introduced a new scheme, the Experimental Medicine Programmes Award, Tim describes how this fills a gap in the CRUK portfolio. “The scheme provides a new avenue for in depth scientific evaluation of translational questions in a clinical setting. These types of studies are vital for us to understand what’s happening when we treat people and as cancer develops.”

Alongside this new award, we have updated the scope and guide costs of our other clinical research funding schemes to enable more translational work to be embedded into trials.

DELIVERING THE GREATEST BENEFIT FROM EVERY TRIAL

“The changes are designed to make sure we maintain the best of what was being funded previously,” says Tim, “whilst ensuring there are the right opportunities for research that will change technical practice and improve outcomes for patients. As researchers, we know that to drive game-changing research we need to learn much more from all patients on our clinical trials.”

A key aim of the Statement of Intent is to drive innovation in trial design so that research fund can push boundaries across all modalities and disease sites.

Tim goes on to explain what the committee hopes to see from future applications: “Clinical researchers need to be engaging with the best basic researchers in their field to better understand the big questions of today, such as diversity within patient responses to treatment. By collaborating with scientists who have complementary expertise, they can create an integrated application with clinical leadership and strong science. This approach will enable researchers to identify ways of tailoring the right treatment, for the right patient, for their greater benefit.”

NEW AND UPDATED FUNDING SCHEMES

“The changes mean that CRUK, and the CRC in particular, has greater strategic oversight of all potential trials funded by CRUK, helping us to support scientifically rich and complex studies,” explains Tim.

The new two-tiered review process uses the Expert Review Panel (ERP) to assist the scientific rigour of the clinical research proposed. The committee then applies a more strategic filter which helps bring to life the clinical ambitions of our Research Strategy. To support more biologically rich clinical research, we have

plasmaMATCH

plasmaMATCH is a multiple paraloid cohort, multicentre Phase II trial jointly led by Dr Nicholas Turner and Professor Judith Bliss at the Institute of Cancer Research (ICR).

This study exemplifies the genomically complex trials that we hope to see more of within our portfolio.

The trial combines a screening component, based on assessment of circulating tumour DNA (ctDNA) from a simple blood test, and a therapeutic component, evaluating the activity of different novel agents directly targeted towards the mutation identified through ctDNA screening. It aims to generate proof of principle efficacy data for these targeted therapies in metastatic breast cancer (MBC). Current treatment for MBC is non-curative, often involving cytotoxic chemotherapy, and advanced stages of the disease are associated with considerable morbidity.

The novel trial design attempts to match patients with a rare mutation identified by ctDNA screening, regardless of tumour histology, to a drug expected to work through the mutated pathway. plasmaMATCH aims to establish an alternative, non-invasive method of characterising tumour molecular profiles with ctDNA. This would simplify screening, reduce costs, and reduce risk to patients by avoiding an invasive procedure to biopsy the patient’s tumour. The study will underpin and inform the feasibility of ctDNA as a screening tool, if it is successful, there is the potential for future integration into routine NHS practice.

FOLLOWING THE THREADS OF CLINICAL TRIALS

To reach our clinical research ambitions, it’s important for us to find ways to help the public and patients understand the role of clinical trials in developing new treatments and improving existing treatments, and motivating them to participate.

In 2016 we collaborated with Rising Ape Collective, a Bristol-based group of science communicators, to develop a live event to celebrate the extraordinary contributions of all those involved in cancer clinical trials. We wanted the audience to hear real stories from researchers, nurses and patients, and to engage with the choices being made every day by the thousands of people involved in cancer research.

The resulting event, Your Choice, is a unique performance that combines personal clinical trial stories with fast-paced role play games, setting scenes competing against each other to carry out research, putting the audience in the hot seats of cancer researchers. By combining stories with board games, the audience are taken on a journey to understand what clinical trials are and why they are important.

A member of the audience at the Cardiff performance reflected: “The game was an innovative and fun way to understand how research works, and alongside the actors’ poignant and powerful performances, it really made me think.”

To date, Your Choice has been performed in Bristol and Cardiff and will be staged at the Edinburgh Festival 2016 and in other cities across the UK in the future.

To find out more about the remit of the new committee and our Statement of Intent, visit crank.org/clinical-research-committee
Professor Jane Wardle was a pioneering psychologist who died in 2015, leaving an incredible legacy of research. Here we look at one of her many achievements, her work on bowel cancer screening.

**JANE’S RESEARCH**

The breadth of Jane’s research and collaborations was staggering. In addition to bowel cancer screening, two other major areas of her work included obesity and weight management and early diagnosis.

**OBESITY AND WEIGHT MANAGEMENT**

- Pioneered work on how genes influence eating behaviour, including landmark studies to show how the FTO gene affects appetite.
- Established Gemini, the largest study of twins ever set up to study genetic and environmental influences on weight from birth.
- One of the first behavioural scientists to explore how habit formation can influence healthy lifestyle habits.
- Developed Top Ten Tips leaflet, influential in developing the first expert meeting to discuss plans for a bowel scope trial.
- Started to look at how behavioural science could be used to explore how habit formation can influence eating behaviour, including how the FTO gene affects appetite.
- Influential in developing the first expert meeting to discuss plans for a bowel scope trial.

**EARLY DIAGNOSIS**

- Influential in developing the first validated measure of public recall and recognition of signs and symptoms of cancer, the Cancer Awareness Measure.
- Pivotal to the thinking about early diagnosis and establishing the National Awareness and Early Diagnosis Initiative (NAEEDI).
- Pivotal to the thinking about early diagnosis and establishing the National Awareness and Early Diagnosis Initiative (NAEEDI).
- Pivotal to the thinking about early diagnosis and establishing the National Awareness and Early Diagnosis Initiative (NAEEDI).

In 2010 a landmark paper was published that transformed the outlook for bowel cancer prevention and survival. The culmination of over 15 years of research, it was a true breakthrough.

The story of how that research came to be reveals how one remarkable researcher, Professor Jane Wardle, brought an insight and approach to cancer research that has changed the field forever.

**A BOLD HYPOTHESIS**

Sometimes in science it can take one simple but bold hypothesis to forge a new path. Back in the early 1990s, Professor Wendy Atkin, an epidemiologist at Imperial College, had such a hypothesis. At the time, the UK had no screening programme for bowel cancer, despite the disease killing more people each year than breast and cervical cancer. As a cancer that is typically silent until an advanced stage, early diagnosis is key to improving survival.

Wendy proposed that a one-off sigmoidoscopy, using a flexible endoscope to look inside the large bowel, could not only detect bowel cancer earlier, but also offer significant protection against the cancer for the rest of a person’s life.

Wendy had noted that most colorectal cancers develop from benign polyps, in a slow transition that can take decades. So a screening programme that removed these just once, at the right age, could prevent bowel cancer developing. She estimated that such a programme could prevent 5,500 bowel cancer cases and 3,500 deaths in the UK each year. As Wendy recalls, “I was suggesting that having a one-off intervention could halve your risk of getting bowel cancer for the next 10 years. It was a daemonic thing to say.” She urged that a large randomised controlled trial, to demonstrate the benefits of one-off sigmoidoscopy, be started without delay.

**AN UNLIKELY COLLABORATION**

Around the same time, Wendy became aware of the work of a clinical psychologist who had recently joined a small team called the Health Behaviour Unit, funded by the Imperial Cancer Research Fund (a predecessor charity to CRUK). Professor Jane Wardle had produced some influential work on obesity, and had started to look at how behavioural science could support cancer prevention. At the time, this was a marginal area, and the unit was only a handful of researchers. Yet Wendy was impressed with Jane’s research and invited her to be part of the first expert meeting to discuss plans for a bowel scope trial.

As Dr Christian von Wagner of today’s Health Behaviour Research Centre at UCL puts it, “Wendy realised she had the science for a test that could be extremely effective clinically. But one that was going to be a hard sell to patients, so behavioural input was going to be critical.” This was the start of a close collaboration that would last decades, and was key to the success of the trial. The solid scientific approach of Jane’s behavioural work was to underpin every aspect of the bowel scope studies, and set a new paradigm of embedding behavioural science in cancer research.

**WHAT DO POLYPS GROW?**

Diagram adapted from the original Flexi-Scope Test leaflet to explain how the test works and how it helps prevent cancer.

10—60 year old person

Two small polyps have formed. There are no symptoms.

6 months later

One of the polyps has grown but there are still no symptoms.

1 year later

The polyp has grown into the centre of the bowel and is very large, but there are still no symptoms.

3 years later

The polyp has become cancerous and may bleed. It can now spread to other parts of the body.

10 years later

During the Flexi-Scope Test, the nurse can see the polyps by inserting a tiny camera into the bowel.

The nurse can then remove the polyps with the tiny Flexi–Scope. This doesn’t hurt.

Once all the polyps have been removed, they cannot turn into cancer.

The bowel is now clear.
to see if the ambitious hypothesis would be force behind the work. It was then a waiting game. An amazing feat and a testament to Jane’s driving clinical service. The team achieved over 40,000 country, with a host of doctors, nurses and management, the Department of Health, funders, the public, but also with the clinical set up, the in all of it. Not only was she brilliant at dealing with just felt you could do anything. She was involved never felt overwhelmed. “Working with Jane you test of their colon, but thanks to Jane, Wendy such a large number of people to have an invasive overcome them, and above all how to achieve people’s motivations for attending screening BEHAVIOUR AS KEY

Jane produced hard evidence to understand people’s motivations for attending screening or not, to understand people’s fears and how to overcome them, and above all how to achieve high uptake. It was a huge operation, galvanising such a large number of people to have an invasive test of their colon, but thanks to Jane, Wendy never felt overwhelmed. “Working with Jane, you just felt you could do anything. She was involved in all of it. Not only was she brilliant at dealing with the public, but also with the clinical set up, the management, the Department of Health, funders, the whole lot.”

The trial took place in 14 hospitals around the country, with a host of doctors, nurses and administrators all involved in delivering the new clinical service. The team achieved over 40,000 sigmoidoscopy examinations in just two years. An amazing feat and a testament to Jane’s driving force behind the work. It was then a waiting game to see if the ambitious hypothesis would be played out in the results, which would be assessed over a decade later.

During this time, Jane’s team conducted many studies on the cohort group, including influential work into socioeconomic inequality in screening programmes. She went on to direct a team of world-renowned experts to establish how public health trials could overcome this.

BEYOND BOWEL CANCER

As the bowel scope studies progressed, Jane’s research was also expanding in many other areas. Under her direction, behavioural research was becoming key to projects as diverse as skin cancer, diet and obesity, cervical cancer screening, and public awareness of cancer. Despite this, the research group was still in a precarious position. Professor Martin Jarvis was part of the Health Behaviour Unit at UCL from its inception, and a colleague of Jane’s for over 40 years. He remembers the unit’s funding review in 2000, when budgets were tightening. “Word was that the review panel might be coming to discontinue the unit’s funding. There was a feeling that compared to cell and molecular science, they might think behavioural science unimportant. I remember a real sense that we were singing for our survival!”

The review panel included two eminent molecular biologists who would go on to win Nobel Prizes. Jane, now as Director of the unit, had to present to them. “She absolutely wowed them,” recalls Martin. “She blew them away with the scientific rigour of the research. I see that review as a real turning point. From then on, it felt that the importance of behavioural work was understood and supported.” Jane had not only saved the behavioural research group, but catapulted the work firmly into the mainstream. Major advances, such as the introduction of the human papilloma virus (HPV) vaccine in 2008, were made possible by Jane’s work. Health behaviour was becoming of central importance to cancer research. DRAMATIC RESULTS

In 2010, the results of the 40,000 people who had undergone flexible sigmoidoscopy were compared with the control group. The results were dramatic. After 11 years of follow-up, incidence of bowel cancer was reduced by a third, and the risk of dying from bowel cancer reduced by over 40%, in those who underwent screening. In fact for someone who did not have bowel cancer diagnosed at screening, future risk of developing bowel cancer was reduced by over 50%, just by having the test.

By the end of this year, screening centres across England should offer bowel scope screening. But to realise the huge potential of the programme, the NHS urgently needs to unlock endoscopy capacity, to allow a dramatic increase in the numbers of people screened. More specialist nurses need to be trained to deliver the programme fully, so that the benefit of decades of research can be realised, and the true impact on bowel cancer mortality achieved.

LASTING LEGACY

Jane’s work on bowel scope shows how behavioural science can be the key that translates research from the lab into policy and practice. Under Jane’s direction, the original Health Behaviour Unit had grown from a handful of researchers to a thriving team of over 70. She published an incredible 600 papers in her lifetime, and supervised over 40 PhD students. Her mentorship was remarkable. Kathryn Whitaker, who joined Jane’s team as a post-doctoral researcher remembers, “Jane was incredible, she seemed to operate in some sort of time vacuum, the group kept expanding yet she always had time for everyone. She created an environment where we all knew what everyone was working on, which is significant in the cross collaborations and success of the group.” As Martin Jarvis states, “Jane trained this huge army of researchers. A whole future generation, which is an extraordinary legacy in itself.”
The striking data visualisation used on the cover of our 2015/16 publication has CRUK research at its heart. It shows international collaborations resulting from CRUK research.

Building on Researchfish™ submissions, the graphic uses the addresses of co-authors of research papers, resulting from CRUK funded research and published in the last five years, to map collaborations across countries.

Dots represent the volume of joint papers published with authors located in each country. The more dots within a cluster, the more countries there are that authors in that country were collaborating with.

Note: Colours do not represent anything specific and are purely aesthetic.

Sizes of dots represent the volume of papers between those countries. The bigger the dot, the more joint author papers.

Lines represent jointly authored papers between countries, showing our connected community is vast and spans the globe.

Thickness of lines represent the volume of jointly authored papers. The thicker the line, the more joint author papers between those two connected countries.

Please note, location of countries is an aesthetic choice and not relative to their geographic location.

Data Visualisation by Brendan Dawes.

Download your copy at cruk.org/pioneering-research
In April 2016, Vice President Joe Biden addressed the American Association of Cancer Research (AARC) annual meeting in New Orleans to expand on the US Government’s ‘moonshot’ for cancer. In a broad-and-heartfelt speech about the billion dollar initiative, he chose to make the need for greater sharing of research data one of the key themes of his talk.

What once might have been dismissed by some as a bureaucratic distraction from getting on with the business of science, or even going against a threat to future work, is now recognised as an essential element to beating cancer sooner. And with a technological revolution creating new opportunities – and raising new challenges – for sharing and reusing data, it’s increasingly exciting you, our research community.

At CRUK we know that good management and sharing of the data produced with our funds is a crucial element to achieving our ambitious goals. We must synthesise data from across disciplines to generate innovative insights into the origins, prevention and treatment of cancer. Data sharing planning is now an established part of our policies and procedures in applying for funding, and our Funding Managers and Committee members are always on the lookout for opportunities to maximise the value of our research outputs.

But sharing data is also great for individual researchers. We caught up with three of our researchers to find out why this is important to them and they’ve placed data sharing at the heart of their research programmes.

WE ARE NOT SHARING!

In this article

Breaking barriers

One of the most conspicuous success stories for data sharing is the field of genomics, where innumerable mature systems and vast databases make sharing and reusing data easy, and where inimmunoe research projects rely in part or in whole on publicly available resources.

“Data is the lifeblood of science,” says Florian Markowetz, group leader at the CRUK Cambridge Institute. “We have the infrastructure, and we’ve all required to deposit our genomics data in the databases to be able to publish. It’s second nature. And that has really demonstrated its value. Pretty much every dataset that I might want to access, I’m able to.”

While genomics has been bizazzling trails, pioneering technology and standards and developing a mature culture of data sharing, other fields of cancer research have struggled to overcome some of the barriers. Florian is exasperated by what he sees as excuses for not sharing data, but he is also mindful of the real challenges that need to be addressed.

“There are challenges when it comes to protecting patient data. When I first started out, I assumed that you could just anonymise data and you wouldn’t be able to identify patients. But actually with genetic data that might not be the case. It’s possible that you might be able to reverse engineer the data to work out which patients it came from. So it requires more careful consideration.”

It’s a challenge that Professor Mark Lawler. Chair in Translational Cancer Genomics at Queen’s University Belfast, is also tackling.

In genomics the situation’s quite simple,” says Dr Florian Markowetz, group leader at the CRUK Cambridge Institute. “We have the infrastructure, and we’ve all required to deposit our genomics data in the databases to be able to publish. It’s second nature. And that has really demonstrated its value. Pretty much every dataset that I might want to access, I’m able to!"

While genomics has been bizazzling trails, pioneering technology and standards and developing a mature culture of data sharing, other fields of cancer research have struggled to overcome some of the barriers. Florian is exasperated by what he sees as excuses for not sharing data, but he is also mindful of the real challenges that need to be addressed.

“Access restrictions really hinder progress,” Nick says. “Accessing medical records, for example, is really difficult. If you do manage to get hold of the data, you end up with these discrete, disparate pieces of data that you can’t put together. What little can be done takes a lot of manual work, so it just can’t scale.”

“There needs to be a cultural shift in medicine. There are some real reasons why people have negative views, including privacy and whether data can be misused. But there’s a mismatch between what we think the risks are and the public’s perception of risk.”

“Also there are researchers who want to keep hold of their data and tightly control it, or they get strange ideas about credit and that they should be considered co-authors on any subsequent work that looks at their data. That’s a real shame because sharing data speeds up progress – as genomics shows.”

Addressing some of these problems is the eMedLab project, funded by the Medical Research Council. “There are lots of standard datasets that people want to look at. In the past you had to go out and get that data and install your own local copy, and if the data wasn’t published openly that might mean a lot of effort before you even start your project.”

To use eMedLab, researchers need a virtual machine on the high-performance computing cluster, from which they can run analyses on standard public datasets, plus data provided by industry and by organisations including the Farr Institute and Genomics England. “With eMedLab we’re turning the process on its head,” Nick says. “Rather than bring the data to your programme, you take your programme to the data.”

The increasing need for and value of interoperable data will require more than just ensuring that the data is published. In fact, Florian Markowetz believes data analysis needs to be transparent:

“Just having a bunch of data is not the whole story,” says Florian. “Really, the data alone are not all that interesting. You need to know how people analysed it, which annotations they used, which computer programmes. That’s what unlocks the value – the reproducibility, the reuse and interoperability.”

But Florian doesn’t simply appeal to altruism, preferring to emphasise what he calls the selfish reasons for sharing data and analysis. “If you’re not sharing the detail, people won’t understand what you’re trying to do, and won’t be able to reproduce your results. That’s not just bad for science, it’s bad for you. You’ll have a hard time from peer reviewers who want to know this stuff, you’ll have difficulty maintaining continuity of projects when lab members move on, and in the worst case scenario, your experiments will have been wasted and you’ll have to withdraw a paper or a project because you haven’t documented how your results were achieved.”

Future directions

Just as technological advances create new opportunities for data management, sharing and analysis, they also create opportunities for gathering even more complex and difficult data.

“Some of the new ways that technology allows us to collect data on populations in the wild are extremely exciting,” says Nick. “But we can’t be complacent about progress. Genomics shows that it takes a conscious effort to prevent secrecy and restrictions creeping back in.”

Breaking barriers

One of the most conspicuous success stories for data sharing is the field of genomics, where innumerable mature systems and vast databases make sharing and reusing data easy, and where inimmunoe research projects rely in part or in whole on publicly available resources.

“The challenge is how do you share clinical and genomic data in a way that’s effective and workable, but also ethically responsible?” says Mark. “While we’re able to collect massive amounts of data, the problem is that these datasets are stored in different silos which don’t currently talk to each other.”

Mark is co-lead of the Global Alliance for Genomics and Health (GA4GH) Clinical Cancer Task, which develops tools and standards for interoperable data sharing with the aim of synchronising sequencing and clinical research efforts, and enabling computer systems to exchange and make use of information.

“GA4GH is a coalition of the willing,” says Mark. “Scientists, clinicians, industry, patient advocacy groups, IT and life sciences companies – over 400 organisations from about 60 countries have come together to work on a catalogue of projects.”

And they can point to a number of successes too, such as the BRCA Exchange database and website, which pools many disparate groups’ data on BRCA gene variants and their associated disease risk and allows expert curators and analysts to link genetic and clinical data to improve our understanding of breast and ovarian cancer. Or the Matchmaker Exchange which has built a similar resource for rare diseases, allowing clinical and genetic data from across the world to be ‘matched’, leading to improved disease diagnosis and treatment.

We owe it to the patients who contribute their data to get this right – and if we do, the data will keep on giving back.

In this article

Powering up

At the Francis Crick Institute, Professor Nick Luscombe has less patience for data access restrictions, and is using supercomputer power to literally accelerate data processing.

“A key restriction really hinders progress,” Nick argues. “Accessing medical records, for example, is really difficult. If you do manage to get hold of the data, you end up with these discrete, disparate pieces of data that you can’t put together. What little can be done takes a lot of manual work, so it just can’t scale.”

“Also there are researchers who want to keep hold of their data and tightly control it, or they get strange ideas about credit and that they should be considered co-authors on any subsequent work that looks at their data. That’s a real shame because sharing data speeds up progress – as genomics shows.”

Addressing some of these problems is the eMedLab project, funded by the Medical Research Council. “There are lots of standard datasets that people want to look at. In the past you had to go out and get that data and install your own local copy, and if the data wasn’t published openly that might mean a lot of effort before you even start your project.”

To use eMedLab, researchers need a virtual machine on the high-performance computing cluster, from which they can run analyses on standard public datasets, plus data provided by industry and by organisations including the Farr Institute and Genomics England. “With eMedLab we’re turning the process on its head,” Nick says. “Rather than bring the data to your programme, you take your programme to the data.”

The increasing need for and value of interoperable data will require more than just ensuring that the data is published. In fact, Florian Markowetz believes data analysis needs to be transparent:

“Just having a bunch of data is not the whole story,” says Florian. “Really, the data alone are not all that interesting. You need to know how people analysed it, which annotations they used, which computer programmes. That’s what unlocks the value – the reproducibility, the reuse and interoperability.”

But Florian doesn’t simply appeal to altruism, preferring to emphasise what he calls the selfish reasons for sharing data and analysis. “If you’re not sharing the detail, people won’t understand what you’re trying to do, and won’t be able to reproduce your results. That’s not just bad for science, it’s bad for you. You’ll have a hard time from peer reviewers who want to know this stuff, you’ll have difficulty maintaining continuity of projects when lab members move on, and in the worst case scenario, your experiments will have been wasted and you’ll have to withdraw a paper or a project because you haven’t documented how your results were achieved.”

Future directions

Just as technological advances create new opportunities for data management, sharing and analysis, they also create opportunities for gathering even more complex and difficult data.

“Some of the new ways that technology allows us to collect data on populations in the wild are extremely exciting,” says Nick. “But we can’t be complacent about progress. Genomics shows that it takes a conscious effort to prevent secrecy and restrictions creeping back in.”
Professor Chris Marshall, who died in August 2015 at the age of 66, from the disease he spent his life studying, was one of cancer biology’s most eminent scientists.

CHRIS MARSHALL
AN INSPIRING MENTOR
AND SIGNALLING PIONEER
CHRIS MARSHALL

CHRIS WAS NOT ONLY A BRILLIANT SCIENTIST
BUT AN OUTSTANDING CITIZEN. HE BELIEVED
STRONGLY THAT CRUK, THE FUNDER OF THE
MAJORITY OF HIS WORK, HAD AN OBLIGATION TO ITS SUPPORTERS
TO DO THE BEST SCIENCE FOR THE GREATEST PATIENT
BENEFIT. HIS CONTRIBUTIONS TO THE STRATEGIC
AND SCIENTIFIC DECISION MAKING OF THE ORGANISATION
WERE INVALUABLE, AND HIS HOND OF RIGOUR AND
INFORMALITY WILL BE SORELY MISSED BY CRUK STAFF.

His international scientific reputation rests on his research into tumour cell signalling, where his many achievements include the discovery of the NRAS oncogene. He leaves a lasting legacy of pioneering discoveries, his research having paved the way for four new classes of cancer drug, two of which are currently in widespread clinical use, benefiting patients worldwide.

CHRIS WAS A GREAT MENTOR, FRIEND AND COLLEAGUE.
IMPRESSIVELY, HE MENTORED WHILE TREATING YOU AS AN
EQUAL; THERE WAS NEVER ANY ‘PREACHING’, JUST
INFORMAL SUGGESTIONS AND ADVICE, MINGLED IN THE
CONVERSATION. AS A FRIEND, I PARTICULARLY ENJOYED
HEARING ABOUT HIS BIKE EXPLOITS, EVEN THOUGH I
HAVE NEVER USED A BIKE EXCEPT OUT OF NECESSITY.
THEIR ENTHUSIASM WAS CAPTIVATING.

Chris received a succession of major honours and awards throughout his career. He was elected as a Fellow of the Royal Society and the European Academy of Cancer Sciences, he was a founding member of the Academy of Medical Sciences, and he was a member of the European Molecular Biology Organisation. He was awarded the 1999 Novartis Medal of the Biochemical Society, the 2008 Buchanan Medal of the Royal Society, and in 2013 the Biochemical Society Centenary Award. Chris had a long association with us at CRUK and in 2011 was awarded the CRUK Lifetime Achievement in Cancer Research Prize.

At The Institute of Cancer Research, where he spent the bulk of his career, Chris was a generous and surprisingly soft-hearted colleague, and an excellent mentor with an eye for highly talented youngsters; notable Marshall lab alumni include:

Professor Karen Vousden, CRUK Chief Scientist;
Dr Erik Saha, Group Leader at the Francis Crick Institute; and Professor Richard Marais, Director of the CRUK Manchester Institute.

To sum up Chris’s unique contribution to the scientific community, here we share some reflections from colleagues and friends.

I first met Chris on a rainy August day in 1981. I was just coming to the end of my PhD and had answered an advert in Nature for a postdoc in his lab. I have no idea why he hired me. I knew nothing about cell biology, nothing about cancer, nothing about anything really. He sat me in a chair where my legs didn’t touch the ground and talked to me with such excitement and enthusiasm about what he wanted to do that I was smitten. I started in the lab a month later and I was like walking from a sepia tint world into bright Technicolor.

Chris was so supportive of the many of us who were lucky enough to pass through his lab. His warmth and generosity of spirit enveloped us, and we kept us going. For myself, I wanted nothing more than to please him, to make him proud of me. We wrote our first paper and sent it to Nature – and he read all of Chris’s work before meeting him – but even so, when I actually started working for him it was a revelation. He had such an influence on me and I wanted to be the same kind of scientist. He taught me how to be thorough, meticulous and how to get excited about data. I will deeply miss talking science with him as there was nothing more challenging than a good scientific discussion with Chris.

We had read all of Chris’s work before meeting him, but even so, when I actually started working for him it was a revelation. He had such an influence on me and I wanted to be the same kind of scientist. He taught me how to be thorough, meticulous and how to get excited about data. I will deeply miss talking science with him as there was nothing more challenging than a good scientific discussion with Chris.

Chris was so supportive of the many of us who were lucky enough to pass through his lab. His warmth and generosity of spirit enveloped us, and we kept us going. For myself, I wanted nothing more than to please him, to make him proud of me. We wrote our first paper and sent it to Nature – and he read all of Chris’s work before meeting him – but even so, when I actually started working for him it was a revelation. He had such an influence on me and I wanted to be the same kind of scientist. He taught me how to be thorough, meticulous and how to get excited about data. I will deeply miss talking science with him as there was nothing more challenging than a good scientific discussion with Chris.

Chris was such an important person as a scientist – but even more so as the man who helped and supported so many of us. We will miss him immeasurably, but what a joy to share part of the journey with him.

Karen Vousden, CRUK Chief Scientist

CHRIS’S RESEARCH

After discovering a major oncogene, NRAS, early on in his career, Chris went on to show how Ras proteins transmit signals from the outside of the cell, and how this signalling pathway becomes deregulated in cancer. He and his colleagues started by demonstrating that to signal effectively, Ras proteins must become associated with the cell membrane. Then, in a series of seminal papers, they showed that membrane-bound Ras proteins stimulate normal growth by switching on a signalling cascade called the MAP kinase pathway, and that mutant Ras proteins cause cancer by constitutively activating this pathway.

Chris was one of the major driving forces in subsequent research to dissect the MAP kinase cascade, which turns out to be a vital universal signalling pathway. The details are highly complex, but in essence, Ras activates members of the Raf family, which then fire up a protein called MEK, which in turn switches on MAP kinase itself.

Chris’s work helped transform our understanding of how all cells, not just those in tumours, communicate – taking us from understanding of how all cells, not just those in tumours, communicate – taking us from

..
WHERE NEXT FOR CANCER IMMUNOTHERAPY?

Cancer immunotherapy is going from strength to strength, as first and second generation therapies that alert the immune system to hidden tumours by switching off checkpoint controls continue to have spectacular success in the clinic. Inevitably there have been setbacks, as many patients do not respond, or cannot tolerate the often toxic side effects of treatment. But a future where immunotherapy replaces chemotherapy as the first-line treatment for many cancer types seems likely.

While there is still intense interest in further refining existing therapies targeting checkpoint controls, attention in both the academic and pharmaceutical sectors has also turned to the next big challenge: the problem of why some patients and tumour types are non-responders. The solution, according to many, lies in combination therapy – using both old and new ways of manipulating the anti-tumour immune response in concert with relief of checkpoint controls. Protocols combining immunotherapy with radio and virotherapy are also being developed globally.

The advent of immunotherapy is truly a step-change in our ability to treat many cancers. As the excitement settles into a consideration of how best to move forward, it has never been more important to support and develop the immunotherapy community within the UK. Of course, as in any field, scientists will always be the key to progress, but funding organisations also have an important part to play. CRUK has the resources and ambition to turn your ideas into patient benefit as quickly and efficiently as possible, so come and talk to us – we can help you to help us step into a new era of cancer therapy.

THE CRUK-MEDI ALLIANCE LABORATORY: CROWDSOURCING NEW IDEAS IN ANTIBODY THERAPY

Monoclonal antibody-based drugs have provided the platform for the success of immunotherapeutic checkpoint inhibition. The exquisite specificity of antibody variable regions as a means of manipulating the immune system and its tumour targets, means that the role of antibody-based biotherapeutics has never been more important.

The CRUK-MEDI Alliance Laboratory is testament to CRUK’s determination to put immunotherapeutic checkpoint inhibition front and centre of our research. The lab, a joint project between CRUK and MedImmune, is an opportunity to crowdsource ideas for new targets, and rapidly put them into practice. According to Rob Williams, Chief Drug Development Scientist for our Centre for Drug Development (CDD): “The philosophy is that we don’t know what’s coming next; so we want to tap into the community to pick up exciting ideas, and turn them into novel biological therapeutics”.

The lab specialises in phage display technology, which allows researchers to quickly scan through millions of randomly-generated antibodies to find ones that recognise important molecules involved in cancer. Maria Groves believes MedImmune is the perfect partner for such a strategy. “MedImmune provide 20 years of phage display expertise and in-depth knowledge of the technology and drug discovery and disease processes”, she says. But collaboration will be the key: “Building a network of principal investigators generating novel ideas for oncology therapeutics will be central to the success of this exciting new venture”, Maria continues.

The lab has already reviewed over 20 applications, several of which are now major active projects. Whilst access to the lab was initially open only to CRUK-funded researchers, in autumn 2016, this will be opened up to all researchers. Rob’s message to the research community is clear: “We want people to think imaginatively about novel ways of using biotherapeutics to fight cancer, and to come to us with those ideas. CRUK has the infrastructure and funding schemes to develop new concepts into tomorrow’s medicines – we want to hear from you!”
Once jump-started by immunotherapy, successful tumour killing needs the anti-cancer immune response to become self-driven. Aiding this crucial transition, whilst preventing it from running out of control, is the rationale behind combination therapy. For clarity, it’s helpful to consider the anti-cancer immune response as a cycle, as proposed by Dan Chen and Ira Mellman in an influential Immunity review in 2013 (as above).

The Cancer–Immunity Cycle begins when cancer cell antigens are released (step 1), and presented to the immune system (step 2), resulting in priming and activation of T cells (step 3). Activated T cells must then migrate to and infiltrate the tumour (steps 4 and 5), where they bind to tumour cells (step 6), and collaborate with the innate immune system to kill them (step 7). Cell killing leads to the release of more cancer antigens, resulting in another revolution of the cycle. Each successive revolution amplifies the response. Steps 3 and 7 are the points in the cycle at which checkpoint controls can kick in, putting the brakes on the cycle and stopping it dead. The recent immunotherapeutic breakthroughs have resulted from the development of agents to prevent the tumours from escaping the response (steps 4 and 5), and creating anti-tumour T cells (step 6), and then load dendritic cells in vitro with cancer antigens, has severely limited progress. Our CDD has an innovative take on this.

**RECOGNITION OF CANCER CELLS BY T CELLS**

Cancer cells can transport the oncolytic virus Ad[I/PPT-E1A] to their surface, allowing them to enter a clinical trial in lung cancer in 2017.

**PRIMING AND ACTIVATION**

Step 3 is the point of the cycle at which the effector regulator T cell balance of the immune response is established. CTLA4-blocking antibodies such as ipilimumab move the balance over to favour effector T cells, allowing a more vigorous immune response, trial led by Janet Bown, also in Sheffield, and in collaboration with our Centre for Drug Development (CDD).

Combined radio- and immunotherapy is attracting attention, although the caveat is that efforts to rev up the immune system whose brakes are firmly on are not always effective. Alternatives, such as agonistic antibodies able to switch on positive regulators of effector T cells, are being trialled in combination therapies, but, whilst promising, it’s too early to say whether such strategies will be widely applicable due to sometimes severe toxicity.

**INFILTRATION OF T CELLS INTO TUMOURS**

Analysis of cancers where checkpoint inhibitors have been ineffective has shown that in some cases, notably pancreatic cancer, tumours can construct a fortress around themselves so that immune cells cannot penetrate. In 2014, Morton and Owen Sansom, working in collaboration with AstraZeneca have recently demonstrated that a patient’s own macrophages, by releasing the chemokine CXCL12, can transport the oncolytic virus Ad[I/PPT-E1A] to the tumour, attracting attention, due to the abscopal effect, where stem cells can be differentiated into dendritic cells, and then load dendritic cells in vitro with cancer antigens, has severely limited progress. Our CDD has an innovative take on this.

In partnership with Astina Biotechnologies, they’ve developed an on the shelf approach using artificial Chimeric Antigen Receptors, capable of binding to and killing cancer cells. Using CRISPR to knock out negative regulators of effector T cells, allowing a more vigorous immune response, whilst promising, it’s too early to say whether such therapies would have to be strictly topical, perhaps delivered by injection into the tumour.
Developing partnerships and working collaboratively are underlying principles of our Research Strategy. We are one of the many players in the global fight against cancer and we need to work effectively with a range of partners if we are to achieve our goal to deliver the greatest impact for patients.

Underpinning all our collaborations is the high quality of the research undertaken and the ability to achieve more through the partnership than we can on our own. We draw together unique capabilities from different players across the research community to create mutually beneficial partnerships that support our own research objectives and those of our partners.

Our partnerships cross all areas of our research, from our approach to funding, to supporting and delivering research as well as the ways in which we influence policy.

Ian Walker, Director of Strategic Partnerships at CRUK, tells us through the CRUK approach to developing partnerships and outlines a few examples which demonstrate our achievements at CRUK, talks us through the CRUK approach we influence policy.

“Successful partnerships start with a shared vision and scientific interest” says Ian. “It’s not just about connecting the dots and identifying the right people to work with, wherever they are located. We can work together to make use of strengths from across the global community. Our scientists work internationally all the time, they’re collaborating on a permanent basis and our international and partnerships agenda is developing in response to this. By working with the best people we are able to deliver outstanding results in a productive way.”

Each partnership is different, set up to deliver specific objectives which are mutually beneficial to the parties involved.

“There is no one definition of what a partnership looks like for CRUK. What is important is that they’re about facilitating the science - helping pool resources and expertise, bringing a shared vision and, ultimately, driving quality and impact that could not be achieved working in isolation.”

“Our portfolio of partnerships includes activities at every stage of the research pipeline, and across all cancer types. However, we’re always on the lookout for opportunities to develop new or strengthen existing partnerships.” Ian thinks CRUK is uniquely placed to help break down the boundaries between behaviour organisations and research disciplines. “We look forward to developing our partnerships further so we can accelerate progress in all areas of our efforts to tackle cancer.”

In 2021, we entered into a multiyear research agreement with the Knight Cancer Institute at Oregon Health and Science University (OHSU) because they share our strategic focus on developing the emerging field of early detection of cancer. This partnership aims to meet the urgent need for better methods to detect cancer in its earliest stages – an area that could make a big difference to cancer survival.

Our synergy in interests will enable both parties to further their agenda and deliver greater benefit to the research community. Ian describes what this partnering offers. “Early detection is a nascent field that needs so much more thinking. We are starting on a journey together – by building a partnership at this early stage we have a unique opportunity, working together to set the questions and define what the priorities should be.”

The partnership began with a workshop in 2015 to identify the key areas and set the direction of travel for research within this field. The key challenges identified included the need to define the agenda for an annual international conference bringing together experts from around the world, which will alternate locations between the US and the UK. Ian explains: “By bringing together experts and thought leaders in a wide variety of disciplines, from biomedicine to technology and engineering, we’re exploring the challenges from multiple angles. We don’t have the answers yet, but by working in partnership, we will leverage the full power of our communities to tackle this area.

In 2015, we entered into a multiyear research partnership with the Engineering and Physical Sciences Research Council (EPSRC) is an example of two organisations committed to investing in outstanding UK expertise, coming together to enable innovative collaborations between researchers in different disciplines.

“CRUK has had a close working relationship with the EPSRC for a number of years - this partnership came about from having an existing relationship in place and spotting an opportunity which aligned strategic priorities from both organisations” explains Ian. The result is a multiyear funding scheme which requires applicants to partner with researchers from another discipline, drawing together biologists with engineers or physical scientists to address important cancer questions.

Our partnership with the Engineering and Physical Sciences Research Council (EPSRC) facilitates the delivery of multidisciplinary working in the most efficient and realistic way possible” explains Ian. “Engineers and physical scientists bring a different problem solving perspective which complements the way that biologists work – this can help move the conversation forward in a way that wouldn’t have been possible otherwise.”

REALISING THE PROMISE OF PRECISION MEDICINE: MOLECULAR ANALYSIS FOR PERSONALISED THERAPY (MAP) CONFERENCE

While the technologies used for personalised medicine are robust, how best to interpret the resulting molecular analyses is still a matter of debate. And more work needs to be done to understand which molecular alterations should be targeted in cancer patients.

To address this challenge we have joined forces with UNCancer, an umbrella organisation for all the French Comprehensive Cancer Centres, and ESMO, Europe’s leading medical oncology society, to deliver a world-class scientific meeting that explores ways to better use existing research data to improve clinical oncologists’ personalised treatment programmes for patients.

The MAP conference represents a partnership driven by researchers. Experts working in precision medicine identified the need to set up a specific agenda to deliver greater benefit to the research community. Ian describes what this looked like for CRUK. “It’s about moving scientifically, we’re exploring the challenges from multiple angles. What is important is that they’re about facilitating the science - helping pool resources and expertise, bringing a shared vision and, ultimately, driving quality and impact that could not be achieved working in isolation.”
The obvious opportunity for commercialisation is the development of new cancer drugs, which is why Geoff Higgins, CRUK Clinician Scientist and honorary consultant oncologist in Oxford, approached CRT around five years ago. He and his team are working on POLQ – an unusual polymerase involved in DNA damage repair that is overexpressed in many types of cancers but not found in most healthy cells.

"By making inhibitors to POLQ, we may be able to make radiotherapy more effective in killing tumours while not exacerbating the side effects," he explains. Additionally, blocking POLQ seems to cause synthetic lethality in tumours that are unable to repair their DNA through homologous recombination, pointing to another clinically important protein. So far he and the CRT-DL team have made significant progress and are at the exciting stage of testing compounds that seem to have activity against POLQ. "As a clinician I want to develop drugs that will be clinically useful and get them, eventually, to patients – and that’s something we hope we are closer to being able to do."

But it’s not just drugs that are ripe for commercialisation. At the CRUK Cambridge Institute, Nitzan Rosenfeld is developing a PCR-based sequencing technique (TAM-Seq) that can detect DNA shed from cancer cells into the bloodstream. This approach, usually referred to as liquid biopsy, is a non-invasive way to provide oncologists with clinically-actionable information to stratify patients, monitor treatment progress and identify emerging resistance. There is also the long-term possibility of developing blood tests to diagnose cancer in its earliest stages.

Together with CRT, Nitzan launched the spin-out company Invivata, with the aim of developing the technology platform and taking it forward for commercial validation. From £4 million seed funding in 2014, the company has grown to encompass two research labs with dozens of employees. In January 2016 Invivata received a further boost, securing investments totalling £3.15 million.

It’s exhilarating and exhausting, but ultimately very satisfying," says Nitzan. "I’m grateful to CRUK and CRT for the support they’re giving them for everything in their power to help turn this valuable technology into a commercial clinical reality."

Commercial opportunities don’t always take the form of drugs and diagnostics. Jack Cuzick at the Wolfson Institute of Preventive Medicine in London asked CRT to step in when profit-making companies started asking if they could use the breast cancer risk-assessment software that he and his colleague Jonathan Tyrer had created.

"The IBIS software arose out of the need to better assess the risk of individuals who were being considered for the BIS-I prevention trials, testing whether tamoxifen could reduce the risk of breast cancer in high risk women," he says. "We had a number of specific entry criteria, but developed the model to take into account family history and lifestyle factors such as weight and age at menopause."

Jack was keen for the software to be freely available for non-commercial use, and he turned to CRT to help develop licensing and royalty collection from companies who wanted to include it as part of paid-for products. "It was never designed to be a commercial hit – we just wanted it to be used as widely as possible. But the fact that the software is available on commercial platforms has increased awareness, and it’s now the most widely used model across the world."

The first step from bright idea to commercial venture is as simple as getting in touch with the team at CRT. Fiona Middleton (see box above) explains how the process works. "We act as the bridge between academia and industry, going out and talking to the scientists funded by CRUK, helping them identify anything that might have significant potential," she says. "We then help develop and protect these ideas, and use our contacts to partner scientists up with industry or build collaborations, so we can get new treatments and tests to patients quicker. And, importantly, all the money we make is returned to CRUK to be reinvested into research, to support even more life-saving ideas."

Nitzan has advice for researchers who think they may have hit on a brilliant idea that is ripe for commercialisation. "Think about intellectual property early on in the process. Even though something is promising and could make a big difference to patients, if you want to get private investors then you won’t happen if you don’t have a sensible intellectual property position. It means thinking a little about the endpoint before rushing to publish, otherwise you can find yourself in a position where you have a very good idea but it’s not investable."

If you’ve got a bright idea, get in touch with CRT on enquiries@cancertechnology.com
Clinical academics are uniquely placed to bridge the gap between the lab and patients. At CRUK, we recognise the value in bringing those with clinical skills and perspectives into the research world, so we provide support for clinicians to launch and progress their research careers while continuing with their clinical roles.

Two of our recently funded CRUK Clinician Scientists, Drs Samra Turajlic and Simon Buczacki, reflect on the rewards and challenges of making the transition into this dual clinical and research role.

Samra, CRUK Clinician Scientist Fellow (CSF) at the Francis Crick Institute and Consultant Medical Oncologist at the Royal Marsden Hospital in London, has found that the dual role of a clinician scientist carries a number of advantages when it comes to her research. “When I design my research projects I think about how they could help patients in the long term. To me the two aspects of my role are synergistic: I want to make a difference to cancer patients overall, not just to the individuals that I treat, and my clinical work helps me keep sight of why I’m doing the research.”

She also likes the fact that, with research, there is an extra element of innovation. “It’s exciting and always varied, just like clinical work, but there is an added layer of unpredictability about research and making discoveries.”

ENTERING THE WORLD OF SCIENCE

Changing fields and navigating through the options available in academia, is not without its challenges. Samra explains, “I didn’t know how people became principal investigators or how you could combine this with a clinical career. I was inspired by Charlie Swanton and knew I wanted to work with him if I could – I was lucky enough to be introduced to him by my clinical supervisor during my PhD. Charlie offered guidance and highlighted CRUK funding available to me post-PhD.”

Samra points out that even when clinicians have successfully made the leap into the lab, they face a range of unique challenges in their careers, stemming from the difficulties of maintaining clinical practice whilst securing funding and finding time to carry out research.

THE CAREER PATHWAY AND CRITICAL GAPS

Historically, clinicians have followed varied routes to move into a clinical academic career, largely because of gaps in the funding available, including one at the critical transition following a PhD. “There were few funding opportunities for clinicians to do postdoctoral research, other than the intermediate fellowships such as the CSF offered by CRUK,” explains Simon Buczacki, CRUK CSF at our Cambridge Institute and Consultant Colorectal Surgeon at Addenbrooke’s Hospital.

Encouraging more clinicians into research is so important to many funding bodies that several of them, including CRUK, recently undertook a review of career pathways of clinical academics in the UK. The resulting cross-funder report, published by the Medical Research Council, explored the experiences and career paths of early-career clinical academics, to understand enablers and barriers to their progression, identifying support needed at critical stages along this journey.

Only a small minority found it easy to pursue a clinical academic career, with difficulties reported across the availability of funding and positions; balancing clinical and academic commitments; and a lack of integration between academic and clinical departments. However, the report identified key ways to improve the career path for clinical academics, including offering mentorship at critical career stages, providing greater flexibility in fellowship funding and improving support for clinical academics at universities and hospitals.

Supporting Clinical Researchers Throughout Their Career

Over the last year we have overhauled our funding opportunities for clinical academics to ensure we provide the right support at critical points in the career pathway.

To address the gap that existed post-PhD we introduced a new bursary to provide funding for clinical trainees, enabling them to remain active in research after completion of their PhD.

Professor Tony Green, Chair of CRUK’s Clinical Careers Committee, says of the changes: “CRUK has substantially revised the way it supports Clinician Scientists and now provides funding schemes appropriate to all stages of their career. Providing the right support at the right time will be crucial for nurturing the leaders of the future.”

Our ambition is to double the number of fellowships we fund to build a pipeline of world-leading clinical academics in cancer research. In order to achieve this, we have increased the funding available for CSFs and developed a more flexible framework to expand the duration to five years and allowing more time for awareness to carry out research. We have also introduced a new Advanced CSF, offering senior clinician scientists the opportunity to develop independence and leadership in their field of academic research.

Both CSFs and Advanced CSFs are paired with a senior clinician on the CRUK mentorship panel for the duration of the fellowship. Mentors are usually based at another university and can offer independent and confidential guidance as well as regularly checking in on progress.

Whilst funding is the core element, non-financial resources and support are equally crucial. Simon explains, “The annual CRUK fellowship meeting, where all clinical academics meet up, is very useful. We get an update on current funding streams and a bit of science. Having this all in one place is really helpful.”

LOOKING TO THE FUTURE

Supporting more clinical researchers is so important if we are to build capacity in this area of critical need. Peter Johnson, CRUK’s Chief Clinician, explains: “We depend on having people who understand the clinical problems and can help bring the power of our research to bear on them. Finding and helping to train the next generation of clinical researchers is vital for us to achieve our goal of reducing deaths from cancer.”

Through the recent changes to our funding schemes and providing continued support for our clinical researchers, we hope to build a world-leading community of clinical academics in cancer research.

There is still some way to go before we overcome all existing barriers, however, those changes bring us a step closer.

To find out more about our revised funding for clinical academics, visit cruk.org/clinical-careers
THINKING DIFFERENTLY: INNOVATION IN RESEARCH FUNDING

As the saying goes, if you do what you’ve always done, you’ll get what you’ve always got. And if we’re going to achieve our aim of 3 in 4 people surviving cancer by 2034, we need to think differently.

Every year we spend hundreds of millions of pounds supporting high-calibre cancer research in the UK, and increasingly across the world, which we believe has the potential to provide the greatest benefit to the public and cancer patients.

Throughout our portfolio we rely on the creativity and innovation of our research community, but as a funder we need to find novel ways to spark and fund creative ideas, and encourage fresh thinking for how to tackle cancer challenges. That’s why we’ve developed exciting new ways of supporting research and generating novel research ideas across our funding portfolio. This set-up is already proving successful, and we want to continue to drive innovation throughout our research funding.

FINDING FRESH IDEAS

One such innovation is our Population Research Innovation Workshops. First created as part of the CRUK/BUPA Foundation Cancer Prevention Initiative, we’ve been running a series of three-day ‘sandpit’ workshops aimed at identifying new ways to prevent cancer and diagnose the disease earlier.

These workshops bring together 25 participants from a range of different disciplines to explore cancer challenges in population research, build new collaborations and encourage participants to ‘think outside the box’ to develop a pitch for a research project that’s potentially funded on the spot.

“New ideas come from the intersection between disciplines,” says Professor Frank Kee, director of the first workshop, held in July 2014. “Social scientists call it the Medici Effect, when you let people peer over the fence and get a fresh view and drive innovation, but we realise that not all new ideas, which have the potential to make a big impact on cancer survival.

Offering funding of up to £200,000 over two years, the awards are unusual in a number of ways. For a start, the initial application is just two pages long, rather than a conventional lengthy form. Applications are encouraged from a broad range of disciplines, such as population researchers, computer scientists, mathematicians and software developers, in addition to more traditional biomedical research fields, and all applications are anonymised, removing any unwarranted bias. Finally, applicants have to pitch their idea in a ‘Dragon’s Den’-style presentation, to experts drawn from a range of scientific and technology backgrounds, to convince them that their idea is worth a shot. It’s a fast process, from initial application to receiving funding can be as little as four months, with proposals being considered three times a year.

So far we’ve run five of these sandpits, and funded 29 projects. The ideas generated are as diverse as a ‘Bank of Good Times’, an app that captures positive emotions to help motivate people to continue with physical activity. Then there’s ‘Hisnextress’ – a virtual reality app aimed at getting kids to understand their future risk of cancer and adopt healthy habits that will last a lifetime, and IBAC – an online tool to identify new ideas, which have the potential to make a big impact on cancer survival.

As well as encouraging fresh thinking, we’re also funding projects that might not be supported through more traditional routes. Through our Pioneer Awards we’re taking on high-risk, high-reward ideas from researchers in any field and at any stage of their career. Rather than focusing on this track record of the applicant, the committee is looking for outstanding and exciting new ideas, which have the potential to make a big impact on cancer survival.

One successful applicant is Gavin Garland, a postdoctoral scientist in the Department of Pathology at the University of Cambridge. His diagnosis with lymphoma as a teenager was a prime motivator in his decision to follow a career in cancer research, and also the reason behind his winning idea. “When I had cancer my consultant spoke to me about the hypothetical idea of a drive-in treatment that would fire radiation directly at the cancer. I started thinking: is anyone still looking for magic bullets? I was going to do an experiment, that’s what I would do.”

Gavin’s thoughts led him to the idea of co-culturing cancer cells together with healthy cells and bacteria, until the bacteria produce oxygen microbubbles could improve efficacy of treatments. Funding has been awarded to do experiments on a scale that are suitable for testing a new treatment.

For a start, the initial application is just two pages long, rather than a conventional lengthy form. Applications are encouraged from a broad range of disciplines, such as population researchers, computer scientists, mathematicians and software developers, in addition to more traditional biomedical research fields, and all applications are anonymised, removing any unwarranted bias. Finally, applicants have to pitch their idea in a ‘Dragon’s Den’-style presentation, to experts drawn from a range of scientific and technology backgrounds, to convince them that their idea is worth a shot. It’s a fast process, from initial application to receiving funding can be as little as four months, with proposals being considered three times a year.

There are 10 of these projects who have been shortlisted, with three winners announced in February. Among the applications that have been shortlisted, one that stands out is one from a group of researchers working on developing a mobile app which will allow people to track their physical activity in real-time and see how well they’re doing. The app will allow them to set goals and track their progress, and send them reminders to continue with physical activity. Then there’s ‘Hisnextress’ – a virtual reality app aimed at getting kids to understand their future risk of cancer and adopt healthy habits that will last a lifetime, and IBAC – an online tool to identify new ideas, which have the potential to make a big impact on cancer survival.

As well as encouraging fresh thinking, we’re also funding projects that might not be supported through more traditional routes. Through our Pioneer Awards we’re taking on high-risk, high-reward ideas from researchers in any field and at any stage of their career. Rather than focusing on this track record of the applicant, the committee is looking for outstanding and exciting new ideas, which have the potential to make a big impact on cancer survival.

Offering funding of up to £200,000 over two years, the awards are unusual in a number of ways. For a start, the initial application is just two pages long, rather than a conventional lengthy form. Applications are encouraged from a broad range of disciplines, such as population researchers, computer scientists, mathematicians and software developers, in addition to more traditional biomedical research fields, and all applications are anonymised, removing any unwarranted bias. Finally, applicants have to pitch their idea in a ‘Dragon’s Den’-style presentation, to experts drawn from a range of scientific and technology backgrounds, to convince them that their idea is worth a shot. It’s a fast process, from initial application to receiving funding can be as little as four months, with proposals being considered three times a year.

We’re embracing innovation and pioneering new approaches across our organisation, including how we share discoveries with our supporters. Thanks to you, last year more than 13,000 people visited a CRUK-funded lab in person, seeing first-hand how the science they help to fund is making a difference. These trips are as inspiring as they are informative; we know that experiencing our science first-hand is incredibly motivating for our supporters. We want more people to have the opportunity to engage directly with our research, helping to generate more funds we can plough into research.

With a goal of increasing the reach of our public engagement activities, our Research Engagement team got together with two digital agencies to create a virtual lab by using cutting-edge smartphone virtual reality headsets. Moving seamlessly from basic biology to clinical trials, it’s a 360-degree immersive viewing experience of life at our CRUK Manchester Institute. The tour gives viewers access to the world of science without ever having to set foot in a lab. Introduced by researcher Marina Pary, virtual visitors can navigate through the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.

This is the first time a virtual tour has been created in this way, and we’re excited to take this to the next level, by developing a mobile app which will allow users to get a behind-the-scenes tour of the lab from every angle and even peer at cells down a microscope. Everyone has a complete 360-degree view of their surroundings, as the camera moves in tandem with every subtle turn of their head.
At CRUK we award prizes to members of the research community to recognise their outstanding achievements. Our awards support and celebrate the incredible work, dedication and scientific innovation of those at the forefront of advancing our ability to prevent, detect and treat cancer, and their ability to engage and inspire the public with our research and cause, critical to raising our required funds.

FUTURE LEADERS

The future of cancer research in the UK relies on the creativity, talent and original thought of the next generation of researchers. Our Future Leaders Prize recognises the very best researchers early in their careers. In 2015 we received more nominations than ever before, and the competition was fierce, meaning that, for the first time, we awarded three prizes.

Dr Chris Bakal, from the Institute of Cancer Development (ICD), led by Professor Alan Rickinson, who are behind the MVA EBNA1/ LMP2 therapeutic vaccine for Epstein-Barr virus (EBV) associated cancers.

EBV is a major global health burden, known to be associated with over 200,000 cases of cancer worldwide each year. However, EBV-associated cancers express viral proteins, making them a promising target for immunotherapies. The EBV vaccine team designed a candidate therapeutic cancer-vaccine that has shown clinical activity in early phase trials.

RESEARCH ENGAGEMENT

Communicating complex research to a lay audience can be a big challenge but one that it vital we overcome so the public and our supporters understand the impact of their donations and are inspired to continue to raise funds for our life-saving research. The commitment and ingenuity of our research community in finding creative ways to bring the impact of our research to life is astonishing, and in 2015 we launched three new prizes to celebrate the most inspiring science communicators.

The Inspiring Leadership in Research Engagement Prize honours someone who demonstrates significant commitment to public engagement with science, and has embedded a culture of public engagement within their institution or research group. In 2015 this was awarded to Edd James from the CRUK Southampton Centre. Edd has captured the imagination of people from all walks of life, by taking complex concepts and making them accessible, whether exploring cells through homemade microscopes or taking cancer immunotherapy whilst shooting targets with lasers.

The Rising Star in Research Engagement Prize recognises someone who demonstrates commitment to stimulating enthusiasm and interest in cancer research among the general public. In 2015 this prize went to Andrew Holding at the CRUK Cambridge Institute for his creative approach to research engagement across a broad range of activities, including radio, podcasting, and school visits. Andrew has a talent for encouraging other scientists to use humour to communicate their research, and his enthusiasm has motivated many researchers within the Institute to get involved in research engagement.

The Communications and Brand Ambassador Prize recognises an inspiring communicator of CRUK research to the public through media work. In 2015 this was presented to Vicky Forster from the Northern Institute for Cancer Research at Newcastle University for sharing her personal journey with a broad audience. Vicky draws on her experience of cancer to bring her research into the public domain, bridging the gap between patients and laboratory science.

Producing science communication events and activities that captivate lay audiences whilst maintaining the integrity of the underlying research is a real skill, and we are proud to have so many accomplished and inspiring communicators within our community. We were delighted with the response to our inaugural research engagement prizes: the volume and quality of engagement demonstrated by all nominees was inspirational.

CRUK Research Prizes closed in March and winners will be announced in November. Nominations for 2017 awards open in November 2016. We will be awarding 2017 Research Engagement Prizes in summer 2017, with nominations opening early in 2017. Check out cruk.org/researchprizes to find out more.
A LEGACY IN LEUKAEMIA

In his mission to improve the diagnosis, therapy and prevention of leukaemia, Mel can undoubtedly claim to have made an extraordinary impact. Early in his career he applied his training in immunology, creating antibody probes with which to explore the characteristics of different types of leukaemia and differentiate between types of leukaemia in the clinic.

In more recent years, Mel and his team have made impressive leaps in our understanding of the preclinical development of leukaemia. His research programme has incorporated many creative methods, including the use of identical twin pairs and archived neonatal blood spots to uncover the in utero origins of childhood leukaemia and the temporal sequence of key genetic events.

Much of this research revolves around Mel’s ‘delayed infection’ model, or ‘hygiene hypothesis’, which provides an evolutionary explanation of causation for childhood acute lymphoblastic leukaemia (ALL).

“The idea incorporates the paradox that common infectious exposure in infancy is beneficial because it primes the immune system,” explains Mel. “A deficit of such exposures in modern hygienic societies leaves the immune system vulnerable to abnormal responses to later ‘delayed’ infections, which can trigger the emergence of overt leukaemia.”

UNFINISHED BUSINESS

Mel joined The Institute of Cancer Research in 1984, and led the Leukaemia Research Fund Centre for Cell and Molecular Biology for many years. More recently, he founded the institute’s Centre for Evolution and Cancer, assembling an impressive new team to research how tumours evolve, with a particular focus on drug resistance.

In addition to his outstanding research achievements, he has had a significant impact as a teacher and mentor, including publishing two popular science books about cancer research.

Our Prizes Panel had no doubt that he was a worthy winner of the Lifetime Achievement Prize.

“I was very pleased to get this prize. My dear friend and colleague Chris Marshall, who received this prize a few years ago, called it the ‘Old Geezer’s Award’. This old geezer intends to carry on as long as I’m excited by science and there’s still unfinished business.”
**THE LAST WORD**

Following another busy year for Cancer Research UK, Peter Johnson, our Chief Clinician, reflects on highlights from the last year, future focus and challenges ahead.

**YOU'RE ABOUT TO START WORKING WITH YOUR THIRD CHIEF SCIENTIST – WHAT ARE YOUR THOUGHTS?**

I’m really going to miss Nic Jones of course, but I’m also looking forward to having Karen Vousden as a colleague. Like her two predecessors, she’s got world-class expertise in discovery science but also a keen eye for how that supports the goals and aims of CRUK. I know Karen will bring a fresh perspective and I’m looking forward to CRUK, and we’re also looking forward to seeing that from our new Chairman of Trustees, Professor Sir Leszek Borysiewicz, who takes up this role from November 2016.

**WHAT DO YOU THINK THE MOST EXCITING AREA OF CANCER SCIENCE IS RIGHT NOW?**

It’s still cancer immunotherapy. There have been really interesting insights into the relationship between treatment response and the genomic makeup of tumours which will be massively important for understanding the mechanisms, and how we design clinical research in this area. I’m very pleased that CRUK is building such world-class expertise in discovery science – as a colleague. Like her two predecessors, she’s got world-class expertise in discovery science. We’ve received applications for lots of early phase clinical trials and translational research, so there are plenty of new ideas coming through.

**ARE THERE ANY AREAS YOU’RE PARTICULARLY FOCUSED ON AT THE MOMENT?**

The trials and tribulations of clinical academic careers have preoccupied me since I started this job, pretty much from the first day. I’m still very preoccupied with making academic careers more flexible. For many years we’ve developed a postdoctoral bursary scheme to help academic clinical lecturers to remain active in research until they can apply for personal fellowships. I’m cautiously optimistic that our numbers of clinical academics will continue rising. CRUK is still firmly committed to increasing the number of clinical academics doing cancer research, and we will find the best ways to work with the NHS to achieve this.

**WHAT IS IT SO IMPORTANT FOR CLINICIANS TO HAVE RESEARCH EXPERIENCE?**

The two tribes of clinical researchers and basic discovery researchers think quite differently. Discovery researchers like order and certainty and will work their way through a problem until they come up with an answer they can put their trust in, whereas doctors spend their whole professional lives managing uncertainty, and working out how you come up with a solution as pragmatically and quickly as possible. It’s really important to have clinicians, especially those who are going to follow an academic career, who understand at a fundamental day-to-day level how scientists work, and what they do. I would really like to see the converse as well – if we could give more of our discovery scientists meaningful experiences in healthcare settings, they could see what it is that their clinical colleagues have to contend with.

**WHAT ARE THE MOST IMPORTANT THINGS ON THE HORIZON?**

On a positive note, we’ve just funded another round of Centres of Network Accelerator Awards. My impression very clearly is that CRUK is in a pretty good place in terms of scientific strategy – lots of new initiatives, new ways of bringing researchers into the fold and new developments. To some degree it’s good to have a period of consolidation and now all the new things that have been rolled out to let people get used to them and fully bed them in.

**WHAT CAN WE EXPECT IN YOUR FIRST FEW MONTHS?**

Most of what I’ll be doing first is fact finding and listening. My impression very clearly is that CRUK is in a pretty good place in terms of scientific strategy – lots of new initiatives, new ways of bringing researchers into the fold and new developments. To some degree it’s good to have a period of consolidation and now all the new things that have been rolled out to let people get used to them and fully bed them in.

**WHAT WILL YOU MISS ABOUT SCOTLAND?**

I'm really going to miss Nic Jones of course, but I’m also looking forward to having Karen Vousden as a colleague. Like her two predecessors, she’s got world-class expertise in discovery science. We’ve received applications for lots of early phase clinical trials and translational research, so there are plenty of new ideas coming through.

Karen Vousden was appointed as Chief Scientist in February 2016, taking over from Nic Jones in July 2016. Here Karen tells us what she’s looking forward to in her new role.

**CONGRATULATIONS ON BEING APPOINTED AS CRUK’S CHIEF SCIENTIST – WHAT MADE YOU DECIDE TO TAKE THE JOB?**

I’d been at the Beatson for 14 years and it was time for a new challenge, and time for the Beatson to get a new Director. Of course I really wanted a new fan of CRUK, and that’s the opportunity to be Chief Scientist is exciting – it allows me to work more broadly with CRUK to build on the new strategy. One of the things I really like is that despite being big, CRUK maintains a family feel. That’s difficult to do and I know staff in London work really hard to retain this familiarity, something I believe is beneficial for the whole organisation.

**YOU’VE GOT A HARD ACT TO FOLLOW…**

Nic Jones has been fantastic as Chief Scientist – in my eyes, I’ll be doing well if I can approach being as good as he was. He’s built the science strategy into something that’s got a lot of people reinvigorated. Nic and I see pretty much eye to eye on most issues, so I won’t be doing anything that differently, although I suspect I’m not quite as even-tempered as he is!

**WHAT WILL YOU MISS ABOUT SCOTLAND?**

Nic Jones has been fantastic as Chief Scientist – in my eyes, I’ll be doing well if I can approach being as good as he was. He’s built the science strategy into something that’s got a lot of people reinvigorated. Nic and I see pretty much eye to eye on most issues, so I won’t be doing anything that differently, although I suspect I’m not quite as even-tempered as he is!

**WHAT CAN WE EXPECT IN YOUR FIRST FEW MONTHS?**

Most of what I’ll be doing first is fact finding and listening. My impression very clearly is that CRUK is in a pretty good place in terms of scientific strategy – lots of new initiatives, new ways of bringing researchers into the fold and new developments. To some degree it’s good to have a period of consolidation and now all the new things that have been rolled out to let people get used to them and fully bed them in.

**WHAT WILL YOU MISS ABOUT SCOTLAND?**

Nic Jones has been fantastic as Chief Scientist – in my eyes, I’ll be doing well if I can approach being as good as he was. He’s built the science strategy into something that’s got a lot of people reinvigorated. Nic and I see pretty much eye to eye on most issues, so I won’t be doing anything that differently, although I suspect I’m not quite as even-tempered as he is!

**WHAT CAN WE EXPECT IN YOUR FIRST FEW MONTHS?**

Most of what I’ll be doing first is fact finding and listening. My impression very clearly is that CRUK is in a pretty good place in terms of scientific strategy – lots of new initiatives, new ways of bringing researchers into the fold and new developments. To some degree it’s good to have a period of consolidation and now all the new things that have been rolled out to let people get used to them and fully bed them in.

**WHAT WILL YOU MISS ABOUT SCOTLAND?**

Nic Jones has been fantastic as Chief Scientist – in my eyes, I’ll be doing well if I can approach being as good as he was. He’s built the science strategy into something that’s got a lot of people reinvigorated. Nic and I see pretty much eye to eye on most issues, so I won’t be doing anything that differently, although I suspect I’m not quite as even-tempered as he is!

**WHAT CAN WE EXPECT IN YOUR FIRST FEW MONTHS?**

Most of what I’ll be doing first is fact finding and listening. My impression very clearly is that CRUK is in a pretty good place in terms of scientific strategy – lots of new initiatives, new ways of bringing researchers into the fold and new developments. To some degree it’s good to have a period of consolidation and now all the new things that have been rolled out to let people get used to them and fully bed them in.

**WHAT WILL YOU MISS ABOUT SCOTLAND?**

Nic Jones has been fantastic as Chief Scientist – in my eyes, I’ll be doing well if I can approach being as good as he was. He’s built the science strategy into something that’s got a lot of people reinvigorated. Nic and I see pretty much eye to eye on most issues, so I won’t be doing anything that differently, although I suspect I’m not quite as even-tempered as he is!

**WHAT CAN WE EXPECT IN YOUR FIRST FEW MONTHS?**

Most of what I’ll be doing first is fact finding and listening. My impression very clearly is that CRUK is in a pretty good place in terms of scientific strategy – lots of new initiatives, new ways of bringing researchers into the fold and new developments. To some degree it’s good to have a period of consolidation and now all the new things that have been rolled out to let people get used to them and fully bed them in.

**WHAT WILL YOU MISS ABOUT SCOTLAND?**

Nic Jones has been fantastic as Chief Scientist – in my eyes, I’ll be doing well if I can approach being as good as he was. He’s built the science strategy into something that’s got a lot of people reinvigorated. Nic and I see pretty much eye to eye on most issues, so I won’t be doing anything that differently, although I suspect I’m not quite as even-tempered as he is!

**WHAT CAN WE EXPECT IN YOUR FIRST FEW MONTHS?**

Most of what I’ll be doing first is fact finding and listening. My impression very clearly is that CRUK is in a pretty good place in terms of scientific strategy – lots of new initiatives, new ways of bringing researchers into the fold and new developments. To some degree it’s good to have a period of consolidation and now all the new things that have been rolled out to let people get used to them and fully bed them in.

**WHAT WILL YOU MISS ABOUT SCOTLAND?**

Nic Jones has been fantastic as Chief Scientist – in my eyes, I’ll be doing well if I can approach being as good as he was. He’s built the science strategy into something that’s got a lot of people reinvigorated. Nic and I see pretty much eye to eye on most issues, so I won’t be doing anything that differently, although I suspect I’m not quite as even-tempered as he is!

**WHAT CAN WE EXPECT IN YOUR FIRST FEW MONTHS?**

Most of what I’ll be doing first is fact finding and listening. My impression very clearly is that CRUK is in a pretty good place in terms of scientific strategy – lots of new initiatives, new ways of bringing researchers into the fold and new developments. To some degree it’s good to have a period of consolidation and now all the new things that have been rolled out to let people get used to them and fully bed them in.

**WHAT WILL YOU MISS ABOUT SCOTLAND?**

Nic Jones has been fantastic as Chief Scientist – in my eyes, I’ll be doing well if I can approach being as good as he was. He’s built the science strategy into something that’s got a lot of people reinvigorated. Nic and I see pretty much eye to eye on most issues, so I won’t be doing anything that differently, although I suspect I’m not quite as even-tempered as he is!

**WHAT CAN WE EXPECT IN YOUR FIRST FEW MONTHS?**

Most of what I’ll be doing first is fact finding and listening. My impression very clearly is that CRUK is in a pretty good place in terms of scientific strategy – lots of new initiatives, new ways of bringing researchers into the fold and new developments. To some degree it’s good to have a period of consolidation and now all the new things that have been rolled out to let people get used to them and fully bed them in.